

empty

Holistic

empty

The Benefits of Healthy Whole Foods

The Benefits of Healthy Whole Foods

<http://www.webmd.com/diet/features/the-benefits-of-healthy-whole-foods>

What's the difference between whole foods and processed foods? By R. Morgan Griffin

WebMD Feature Reviewed by Brunilda Nazario, MD

Healthy whole foods: you might know that you're supposed to eat them. But do you really know what they are?

"We live in a society that eats so much processed and manufactured food, that I think there's some genuine confusion about RD, a spokesperson for the American Dietetic Association. Even for the health conscious, the phrase gets tangled up with locally grown, or pesticide-free. But they aren't necessarily. The definition of healthy whole foods is much simpler.

"When you eat whole foods, you're getting the food in its natural state," Gidus tells WebMD. "You're getting it intact, with that are in the food." Basically, it's the healthy whole food, rather than the bits that remain after refinement and processing. juice , or a baked potato and mashed potatoes.

While whole foods might be associated with the upscale grocery store of the same name, they are available to all of us anywhere. eating healthy whole foods has all sorts of benefits. Their nutrients may help to keep your immune system strong and protei

"If you're trying to eat a healthier diet, relying on more whole foods is a great place to start," says Lucia L. Kaiser, PhD, con nutrition at the University of California, Davis.

Protein

Protein

<http://en.wikipedia.org/wiki/Protein>

This article is about a class of molecules. For protein as a nutrient, see Protein (nutrient). For other uses, see Protein (disambiguation).

A representation of the 3D structure of the protein myoglobin showing turquoise alpha helices. This protein was the first to be shown to have a heme prosthetic group attached to a protein. Towards the right-center among the coils, a prosthetic group called a heme group (shown in grey) with a bound oxygen molecule is visible.

Proteins (pron.: / ˈproʊˈtiːn/ or / ˈproʊˈtiːn/) are large biological molecules consisting of one or more chains of amino acids that are folded into specific three-dimensional structures. In living organisms, proteins include catalysing metabolic reactions, replicating DNA, responding to stimuli, and transporting molecules from one another primarily in their sequence of amino acids, which is dictated by the nucleotide sequence of their genes, and then into a specific three-dimensional structure that determines its activity.

A polypeptide is a single linear polymer chain of amino acids bonded together by peptide bonds between the carboxyl and amino groups of adjacent amino acid residues. The sequence of amino acids in a protein is defined by the sequence of a gene, which is encoded in the genetic code. In general, the genetic code specifies 20 different amino acids; however, in certain organisms the genetic code can include selenocysteine and—in certain archaea—pyrrolysine. Short polypeptides can fold into a specific three-dimensional structure that is called the native structure of the protein. In a cell, proteins are often chemically modified by posttranslational modification, which alters the physical and chemical properties, stability, and function of the proteins. Sometimes proteins have non-peptide groups attached, which can be called prosthetic groups or cofactors. Proteins can also form stable protein complexes.

Like other biological macromolecules such as polysaccharides and nucleic acids, proteins are essential parts of organisms and participate in virtually every process within cells. Many proteins are enzymes that catalyse biochemical reactions and are vital to metabolism. Structural proteins such as actin and myosin in muscle and the proteins in the cytoskeleton, which form a system of scaffolding that maintains a cell's shape, are also important. Other proteins are involved in cell signalling, immune responses, cell adhesion, and the cell cycle. Proteins are also necessary in animals' diets, since animals cannot synthesize all the amino acids they need and must obtain essential amino acids from food. Through the process of digestion, animals break down ingested protein into amino acids for use in metabolism.

Proteins may be purified from other cellular components using a variety of techniques such as ultra centrifugation, precipitation, and ion exchange chromatography. The advent of genetic engineering has made possible a number of methods to facilitate purification. Methods commonly used to purify proteins include immunoprecipitation, immuno histochemistry, site-directed mutagenesis, nuclear magnetic resonance and mass spectrometry.

Biochemistry

Main articles: Biochemistry, Amino acid, and peptide bond

Chemical structure of the peptide bond and the three-dimensional structure of a peptide bond between an alanine and an adjacent amino acid.

Resonance structures of the peptide bond that links individual amino acids to form a protein polymer

Most proteins consist of linear polymers built from series of up to 20 different L- α -amino acids. . . features, including an α -carbon to which an amino group, a carboxyl group, and a variable side chain as it contains an unusual ring to the N-end amine group, which forces the CO-NH amide moiety into a fixed conformation. The amino acids, detailed in the list of standard amino acids, have a great variety of chemical structures and properties; it is the combination of amino acids in a polypeptide chain that ultimately determines its three-dimensional structure and its chemical reactivity. The amino acids in a polypeptide chain, an individual amino acid is called a residue, and the linked series of carbon, nitrogen, and oxygen atoms form the backbone.

The peptide bond has two resonance forms that contribute some double-bond character and inhibit rotation around its axis, so that the other two dihedral angles in the peptide bond determine the local shape assumed by the protein backbone. The end of the polypeptide chain with a free amino group is known as the N-terminus or amino terminus. The end with a free carboxyl group is known as the C-terminus or carboxy terminus. The terms N-terminus and C-terminus are ambiguous and can overlap in meaning. Protein is generally used to refer to the complete biological molecule in a stable conformation, whereas a short amino acid

oligomer often lacking a stable three-dimensional structure. However, the boundary between the two is not well defined and often refers to any single linear chain of amino acids, usually regardless of length, but often implies an absence of a defined conformation.

Synthesis

Main article: Protein biosynthesis

A ribosome produces a protein using mRNA as template.

The DNA sequence of a gene encodes the amino acid sequence of a protein.

Proteins are assembled from amino acids using information encoded in genes. Each protein has its own unique amino acid sequence of the gene encoding this protein. The genetic code is a set of three-nucleotide sets called codons and each three-nucleotide codon, for example AUG (adenine-uracil-guanine) is the code for methionine. Because DNA contains four nucleotides, the total number of possible codons is 64, resulting in some redundancy in the genetic code, with some amino acids specified by more than one codon. Genes encoded in DNA are transcribed into messenger RNA (mRNA) by proteins such as RNA polymerase. Most organisms then process the pre-mRNA (also known as a primary transcript) through RNA modification to form the mature mRNA, which is then used as a template for protein synthesis by the ribosome. In prokaryotes, the mRNA is produced, or be bound by a ribosome after having moved away from the nucleoid. In contrast, eukaryotes make mRNA in the nucleus, which then moves through the nuclear membrane into the cytoplasm, where protein synthesis then takes place. The rate of protein synthesis is higher in prokaryotes, at about 20 amino acids per second.

The process of synthesizing a protein from an mRNA template is known as translation. The mRNA is loaded onto the ribosome, and the ribosome matches each codon to its base pairing anticodon located on a transfer RNA molecule, which carries the amino acid corresponding to that codon. Aminoacyl tRNA synthetase "charges" the tRNA molecules with the correct amino acids.

The growing polypeptide is often termed the nascent chain. Proteins are always biosynthesized from N-terminus to C-terminus.

The size of a synthesized protein can be measured by the number of amino acids it contains and by its total molecular mass, (synonymous with atomic mass units), or the derivative unit kilodalton (kDa). Yeast proteins are on average 466 amino acid proteins are the titins, a component of the muscle sarcomere, with a molecular mass of almost 3,000 kDa and a total length of

Chemical synthesis

Short proteins can also be synthesized chemically by a family of methods known as peptide synthesis, which rely on organic chemistry to produce peptides in high yield. Chemical synthesis allows for the introduction of non-natural amino acids into polypeptide chains and into amino acid side chains. These methods are useful in laboratory biochemistry and cell biology, though generally not for commercial synthesis of polypeptides longer than about 300 amino acids, and the synthesized proteins may not readily assume their native structure. These methods proceed from C-terminus to N-terminus, opposite the biological reaction.

Structure

Main article: Protein structure

Further information: Protein structure prediction

The crystal structure of the chaperonin. Chaperonins assist protein folding.

Three possible representations of the three-dimensional structure of the protein triose phosphate isomerase.

Most proteins fold into unique 3-dimensional structures. The shape into which a protein naturally folds is known as its native structure, unassisted, simply through the chemical properties of their amino acids, others require the aid of molecular chaperones to fold. There are four distinct aspects of a protein's structure:

Primary structure: the amino acid sequence.

Secondary structure: regularly repeating local structures stabilized by hydrogen bonds. The most common examples are the alpha helix and beta sheet. Secondary structures are local, many regions of different secondary structure can be present in the same protein molecule.

Tertiary structure: the overall shape of a single protein molecule; the spatial relationship of the secondary structures to one another, including nonlocal interactions, most commonly the formation of a hydrophobic core, but also through salt bridges, hydrogen bonds, disulfide bonds, and post-translational modifications. The term "tertiary structure" is often used as synonymous with the term fold. The tertiary structure is what confers the protein's function.

Quaternary structure: the structure formed by several protein molecules (polypeptide chains), usually called protein subunits, interacting to form a functional complex.

Proteins are not entirely rigid molecules. In addition to these levels of structure, proteins may shift between several related structures. In the context of these functional rearrangements, these tertiary or quaternary structures are usually referred to as "conformations". Conformational changes. Such changes are often induced by the binding of a substrate molecule to an enzyme's active site, and the enzyme then participates in chemical catalysis. In solution proteins also undergo variation in structure through thermal vibration and the effects of other molecules.

Molecular surface of several proteins showing their comparative sizes. From left to right are: immunoglobulin G (IgG, an antibody), adenylate kinase (an enzyme), and glutamine synthetase (an enzyme).

Proteins can be informally divided into three main classes, which correlate with typical tertiary structures: globular proteins, all globular proteins are soluble and many are enzymes. Fibrous proteins are often structural, such as collagen, the major collagen protein component of hair and nails. Membrane proteins often serve as receptors or provide channels for polar or charged molecules.

A special case of intramolecular hydrogen bonds within proteins, poorly shielded from water attack and hence promoting their stability.

Structure determination

Discovering the tertiary structure of a protein, or the quaternary structure of its complexes, can provide important clues about its function. Experimental methods of structure determination include X-ray crystallography and NMR spectroscopy, both of which can provide high-resolution structural information. However, NMR experiments are able to provide information from which a subset of distances between pairs of atoms can be determined by solving a distance geometry problem. Dual polarisation interferometry is a quantitative analytical technique for measuring conformation and conformational changes due to interactions or other stimulus. Circular dichroism is another laboratory technique for measuring the secondary structure composition of proteins. Cryoelectron microscopy is used to produce lower-resolution structural information about very large macromolecules. A variant known as electron crystallography can also produce high-resolution information in some cases, especially for two-dimensional crystals. Protein structures are usually deposited in the Protein Data Bank (PDB), a freely available resource from which structural data about a protein can be accessed in the form of Cartesian coordinates for each atom in the protein.

Many more gene sequences are known than protein structures. Further, the set of solved structures is biased toward proteins required in X-ray crystallography, one of the major structure determination methods. In particular, globular proteins are commonly solved by X-ray crystallography. Membrane proteins, by contrast, are difficult to crystallize and are under-represented in the PDB. Structural genomics programs aim to remedy these deficiencies by systematically solving representative structures of major fold classes. Protein structure prediction is a rapidly growing field, generating a plausible structure for proteins whose structures have not been experimentally determined.

Cellular functions

Proteins are the chief actors within the cell, said to be carrying out the duties specified by the information encoded in genes. Other biological molecules are relatively inert elements upon which proteins act. Proteins make up half the dry weight of a cell, while nucleic acids such as DNA and RNA make up only 3% and 20%, respectively. The set of proteins expressed in a particular cell is called its proteome.

The enzyme hexokinase is shown as a conventional ball-and-stick molecular model. To scale in the top right-hand corner are the atoms of a water molecule.

The chief characteristic of proteins that also allows their diverse set of functions is their ability to bind other molecules specifically. The site responsible for binding another molecule is known as the binding site and is often a depression or "pocket" on the molecular tertiary structure of the protein, which defines the binding site pocket, and by the chemical properties of the surrounding amino acids. Binding is extraordinarily tight and specific; for example, the ribonuclease inhibitor protein binds to human angiogenin with a sub-femtomolar dissociation constant and does not bind at all to its amphibian homolog onconase (>1 M). Extremely minor chemical changes such as the addition of a single amino acid sometimes suffice to nearly eliminate binding; for example, the aminoacyl tRNA synthetase specific to the amino acid valine does not bind to the amino acid isoleucine.

Proteins can bind to other proteins as well as to small-molecule substrates. When proteins bind specifically to other copies of themselves, they form fibrils; this process occurs often in structural proteins that consist of globular monomers that self-associate to form rigid fibers. Proteins also play a role in enzymatic activity, control progression through the cell cycle, and allow the assembly of large protein complexes that carry out various biological functions. Proteins can also bind to, or even be integrated into, cell membranes. The ability of binding partners to interact is essential to the construction of enormously complex signaling networks. Importantly, as interactions between proteins are reversible, they allow groups of partner proteins to form aggregates that are capable of carrying out discrete sets of functions. Study of these interactions is an important aspect of cellular function, and ultimately the properties that distinguish particular cell types.

Enzymes

Main article: Enzyme

The best-known role of proteins in the cell is as enzymes, which catalyze chemical reactions. Enzymes are usually highly specific for their substrates and reactions. Enzymes carry out most of the reactions involved in metabolism, as well as manipulating DNA in processes such as transcription and replication. Some enzymes act on other proteins to add or remove chemical groups in a process known as posttranslational modification. The rate acceleration conferred by enzymatic catalysis is often enormous—as much as 10^{17} -fold in the case of orotate decarboxylase (78 million years without the enzyme, 18 milliseconds with the enzyme).

The molecules bound and acted upon by enzymes are called substrates. Although enzymes can consist of hundreds of amino acid residues that come in contact with the substrate, and an even smaller fraction—three to four residues on average—that are directly involved in catalysis, the enzyme that binds the substrate and contains the catalytic residues is known as the active site.

Dirigent proteins are members of a class of proteins which dictate the stereochemistry of a compound synthesized by other enzymes.

Cell signaling and ligand binding

Ribbon diagram of a mouse antibody against cholera that binds a carbohydrate antigen

Many proteins are involved in the process of cell signaling and signal transduction. Some proteins, such as insulin, are extra cell in which they were synthesized to other cells in distant tissues. Others are membrane proteins that act as receptors who induce a biochemical response in the cell. Many receptors have a binding site exposed on the cell surface and an effector do activity or may undergo a conformational change detected by other proteins within the cell.

Antibodies are protein components of an adaptive immune system whose main function is to bind antigens, or foreign substances. Antibodies can be secreted into the extracellular environment or anchored in the membranes of specialized B cells known as their binding affinity for their substrates by the necessity of conducting their reaction, antibodies have no such constraints. A extraordinarily high.

Many ligand transport proteins bind particular small biomolecules and transport them to other locations in the body of a multi high binding affinity when their ligand is present in high concentrations, but must also release the ligand when it is present a canonical example of a ligand-binding protein is haemoglobin, which transports oxygen from the lungs to other organs and every biological kingdom. Lectins are sugar-binding proteins which are highly specific for their sugar moieties. Lectins typical phenomena involving cells and proteins. Receptors and hormones are highly specific binding proteins.

Transmembrane proteins can also serve as ligand transport proteins that alter the permeability of the cell membrane to small hydrophobic core through which polar or charged molecules cannot diffuse. Membrane proteins contain internal channels through Many ion channel proteins are specialized to select for only a particular ion; for example, potassium and sodium channels of

Structural proteins

Structural proteins confer stiffness and rigidity to otherwise-fluid biological components. Most structural proteins are fibrous critical components of connective tissue such as cartilage, and keratin is found in hard or filamentous structures such as hair. Some globular proteins can also play structural functions, for example, actin and tubulin are globular and soluble as monomers make up the cytoskeleton, which allows the cell to maintain its shape and size.

Other proteins that serve structural functions are motor proteins such as myosin, kinesin, and dynein, which are capable of generating crucial for cellular motility of single celled organisms and the sperm of many multicellular organisms which reproduce sexually contracting muscles and play essential roles in intracellular transport.

Methods of study

Main article: Protein methods

As some of the most commonly studied biological molecules, the activities and structures of proteins are examined both in vivo and in vitro. Proteins in controlled environments are useful for learning how a protein carries out its function: for example, enzyme kinetics, enzyme's catalytic activity and its relative affinity for various possible substrate molecules. By contrast, in vivo experiments on whole organisms can provide complementary information about where a protein functions and how it is regulated.

Protein purification

Main article: Protein purification

To perform in vitro analysis, a protein must be purified away from other cellular components. This process usually begins with cell disruption and its internal contents released into a solution known as a crude lysate. The resulting mixture can be purified using various cellular components into fractions containing soluble proteins; membrane lipids and proteins; cellular organelles, and so on. As salting out can concentrate the proteins from this lysate. Various types of chromatography are then used to isolate the protein, such as molecular weight, net charge and binding affinity. The level of purification can be monitored using various types of assays. Molecular weight and isoelectric point are known, by spectroscopy if the protein has distinguishable spectroscopic features, or by activity. Additionally, proteins can be isolated according to their charge using electro-focusing.

For natural proteins, a series of purification steps may be necessary to obtain protein sufficiently pure for laboratory applications. A common method is often used to add chemical features to proteins that make them easier to purify without affecting their structure or activity. A series of histidine residues (a "His-tag"), is attached to one terminus of the protein. As a result, when the protein is in a solution containing nickel, the histidine residues ligate the nickel and attach to the column while the untagged components of the lysate pass through. This method has been developed to help researchers purify specific proteins from complex mixtures.

Cellular localization

Proteins in different cellular compartments and structures tagged with green fluorescent protein ([here](#), [white](#))

The study of proteins in vivo is often concerned with the synthesis and localization of the protein within the cell. Although it is clear that cytoplasm and membrane-bound or secreted proteins in the endoplasmic reticulum, the specifics of how proteins are targeted to these locations are often unclear. A useful technique for assessing cellular localization uses genetic engineering to express in a cell a fusion protein of interest linked to a "reporter" such as green fluorescent protein (GFP). The fused protein's position within the cell can be clearly shown in the figure opposite.

Other methods for elucidating the cellular location of proteins requires the use of known compartmental markers for regions such as mitochondria, chloroplasts, plasma membrane, etc. With the use of fluorescently tagged versions of these markers or of anti-bodies, it is simpler to identify the localization of a protein of interest. For example, indirect immunofluorescence will allow for fluorescently labeled antibodies to be used to label cellular compartments for a similar purpose.

Other possibilities exist, as well. For example, immunohistochemistry usually utilizes an antibody to one or more proteins or either luminescent or chromogenic signals that can be compared between samples, allowing for localization information. A sucrose (or other material) gradient using isopycnic centrifugation. While this technique does not prove colocalization of interest, it does increase the likelihood, and is more amenable to large-scale studies.

Finally, the gold-standard method of cellular localization is immunoelectron microscopy. This technique also uses an antibody and electron microscopy techniques. The sample is prepared for normal electron microscopic examination, and then treated with gold conjugated to an extremely electron-dense material, usually gold. This allows for the localization of both ultrastructural details.

Through another genetic engineering application known as site-directed mutagenesis, researchers can alter the protein sequence and susceptibility to regulation. This technique even allows the incorporation of unnatural amino acids into proteins, using ribosomes of new proteins with novel properties.

Proteomics and bioinformatics

Main articles: Proteomics and Bioinformatics

The total complement of proteins present at a time in a cell or cell type is known as its proteome, and the study of such large-scale proteomes is named by analogy to the related field of genomics. Key experimental techniques in proteomics include 2D electrophoresis, mass spectrometry, which allows rapid high-throughput identification of proteins and sequencing of peptides (mass spectrometry), which allow the detection of the relative levels of a large number of proteins present in a cell, and two-hybrid screening, which allow the detection of protein–protein interactions. The total complement of biologically possible such interactions is known as the interactome. A database of proteins representing every possible fold is known as structural genomics.

The large amount of genomic and proteomic data available for a variety of organisms, including the human genome, allows for the identification of proteins in distantly related organisms by sequence alignment. Sequence profiling tools can perform more specific sequence analysis, open reading frame analyses for nucleotide sequences, and secondary structure prediction. From this data phylogenetic trees have been developed using special software like ClustalW regarding the ancestry of modern organisms and the genes they express. These tools can also annotate, and analyze genomic and proteomic data, applying computational techniques to biological problems such as gene

Structure prediction and simulation

Main articles: protein structure prediction and List of protein structure prediction software

Complementary to the field of structural genomics, protein structure prediction seeks to develop efficient ways to provide protein structure information for proteins whose structure has not yet been determined experimentally. The most successful type of structure prediction, known as homology modeling, relies on sequence similarity to the protein being modeled; structural genomics' goal is to provide sufficient representation in solved structures. Although producing accurate models remains a challenge when only distantly related template structures are available, it has become a bottleneck in this process, as quite accurate models can be produced if a "perfect" sequence alignment is known. Many structural models have been used in the emerging field of protein engineering, in which novel protein folds have already been designed. A more complex computational challenge is the prediction of protein-protein interactions, such as in molecular docking and protein-protein interaction prediction.

The processes of protein folding and binding can be simulated using such techniques as molecular mechanics, in particular, and increasingly take advantage of parallel and distributed computing (Folding@home project; molecular modeling on GPU). Techniques such as the villin headpiece and the HIV accessory protein have been successfully simulated in silico, and hybrid methods that combine quantum mechanics calculations have allowed exploration of the electronic states of rhodopsins.

Nutrition

Further information: Protein (nutrient)

Most micro-organisms and plants can biosynthesize all 20 standard amino acids, while animals (including humans) must obtain some amino acids that an organism cannot synthesize on its own are referred to as essential amino acids. Key enzymes that synthesize these — such as aspartokinase, which catalyzes the first step in the synthesis of lysine, methionine, and threonine from aspartate. Some micro-organisms can conserve energy by taking up the amino acids from their surroundings and down-regulating their biosynthesis.

In animals, amino acids are obtained through the consumption of foods containing protein. Ingested proteins are then broken down, typically involves denaturation of the protein through exposure to acid and hydrolysis by enzymes called proteases. Some amino acids are used for biosynthesis, while others are converted to glucose through gluconeogenesis, or fed into the citric acid cycle. This use of protein during starvation conditions as it allows the body's own proteins to be used to support life, particularly those found in muscle. Amino acid metabolism also provides nitrogen.[*citation needed*]

History and etymology

Further information: History of molecular biology

Proteins were recognized as a distinct class of biological molecules in the eighteenth century by Antoine Fourcroy and others. They were noted to coagulate or flocculate under treatments with heat or acid[*citation needed*]. Noted examples at the time included albumin from egg white and wheat gluten.

Proteins were first described by the Dutch chemist Gerardus Johannes Mulder and named by the Swedish chemist Jöns Jacob Berzelius. He analyzed common proteins and found that nearly all proteins had the same empirical formula, C₄₀₀H₆₂₀N₁₀₀O₁₂₀P₁S₁. They might be composed of a single type of (very large) molecule. The term "protein" to describe these molecules was derived from the Greek word *πρωτεϊος* (*protēios*), meaning "primary", "in the lead", to identify the products of protein degradation such as the amino acid leucine for which he found a (nearly correct

Early nutritional scientists such as the German Carl von Voit believed that protein was the most important nutrient for mainly generally believed that "flesh makes flesh." The central role of proteins as enzymes in living organisms was not fully appreciated until the enzyme urease was found to be a protein.

The difficulty in purifying proteins in large quantities made them very difficult for early protein biochemists to study. Hence purified in large quantities, e.g., those of blood, egg white, various toxins, and digestive/metabolic enzymes obtained from sources. Co. purified 1 kg of pure bovine pancreatic ribonuclease A and made it freely available to scientists; this gesture helped ribonuclease study for the following decades.

John Kendrew with model of myoglobin in progress.

Linus Pauling is credited with the successful prediction of regular protein secondary structures based on hydrogen bonding. Later work by Walter Kauzmann on denaturation, based partly on previous studies by Kaj Linderstrøm-Lang, contributed and mediated by hydrophobic interactions.

The first protein to be sequenced was insulin, by Frederick Sanger, in 1949. Sanger correctly determined the amino acid sequence that proteins consisted of linear polymers of amino acids rather than branched chains, colloids, or cyclols. He won the Nobel Prize in 1958.

The first protein structures to be solved were hemoglobin and myoglobin, by Max Perutz and Sir John Cowdery Kendrew, respectively. Protein structures were solved by X-ray diffraction analysis in the 1960s [citation needed] (Perutz and Kendrew shared the Nobel Prize for these discoveries) and by NMR in the 1980s. [citation needed] As of 2009, the Protein Data Bank has over 55,000 atomic-resolution structures. Cryo-electron microscopy of large macromolecular assemblies and computational protein structure prediction of small protein resolution.

<http://www.cdc.gov/nutrition/everyone/basics/protein.html>

Protein

What do you think about when you hear the word protein? Maybe it's an ad for some protein shake that promises massive results you read about? With all this talk about protein, you might think Americans were at risk for not eating enough. In fact, most of the calories in our diet come from many foods that we eat on a regular basis.

This section will help you learn more about protein. You'll find information about what foods have protein and what happens when you eat them.

To continue, check out the following topics:

What is protein?

What are the types of protein?

How much protein do I need?

What is Protein?

Proteins are part of every cell, tissue, and organ in our bodies. These body proteins are constantly being broken down and re into amino acids that are later used to replace these proteins in our bodies.

Protein is found in the following foods:

meats, poultry, and fish

legumes (dry beans and peas)

tofu

eggs

nuts and seeds

milk and milk products

grains, some vegetables, and some fruits (provide only small amounts of protein relative to other sources)

As we mentioned, most adults in the United States get more than enough protein to meet their needs. It's rare for someone w enough protein.

What are the types of protein?

Proteins are made up of amino acids. Think of amino acids as the building blocks. There are 20 different amino acids that jo these amino acids can't be made by our bodies, so these are known as essential amino acids. It's essential that our diet provic

In the diet, protein sources are labeled according to how many of the essential amino acids they provide:

A complete protein source is one that provides all of the essential amino acids. You may also hear these sources called high example, meat, poultry, fish, milk, eggs, and cheese are considered complete protein sources.

An incomplete protein source is one that is low in one or more of the essential amino acids. Complementary proteins are two provide adequate amounts of all the essential amino acids.

For example, rice contains low amounts of certain essential amino acids; however, these same essential amino acids are four beans contain lower amounts of other essential amino acids that can be found in larger amounts in rice. Together, these two essential amino acids the body needs.

Quick Q&A

Is it true that complementary proteins must be eaten together to count as a complete protein source?

In the past, it was thought that these complementary proteins needed to be eaten at the same meal for your body to use them combine complementary proteins that are eaten within the same day.¹

How much protein do I need?

Maybe you've wondered how much protein you need each day. In general, it's recommended that 10–35% of your daily calc Recommended Dietary Allowances (RDA) for different age groups.²

Recommended Dietary Allowance for Protein

Grams of protein
needed each day

Children ages 1 – 3 13

Children ages 4 – 8 19

Children ages 9 – 13 34

Girls ages 14 – 18 46

Boys ages 14 – 18 52

Women ages 19 – 70+ 46

Men ages 19 – 70+ 56

Here are examples of amounts of protein in food:

1 cup of milk has 8 grams of protein

A 3-ounce piece of meat has about 21 grams of protein

1 cup of dry beans has about 16 grams of protein

An 8-ounce container of yogurt has about 11 grams of protein

Added together, just these four sources would meet the protein needs of an adult male (56 grams). This doesn't count all the his diet.

Rather than just focusing on your protein needs, choose an overall healthy eating plan that provides the protein you need as

ChooseMyPlate.gov Daily Food Plan lets you enter your age, sex, weight, height and physical activity level to get a personal

Is there any harm in getting more protein than I need?

Most people eat more protein than they need without harmful effects. However, protein contributes to calorie intake, so if your calorie intake could be greater than your calorie needs and contribute to weight gain.

Besides that, animal sources of protein can be sources of saturated fat which has been linked to elevated low-density lipoprotein disease.

In addition, for people with certain kidney diseases, a lower-protein diet may be recommended to help prevent an impairment

Source: NIH Medical Encyclopedia

To help you get the amounts of protein you need:

Compare the amount of meat, poultry, fish, eggs, legumes, nuts, and seeds you are eating per day to what is recommended. . . Plan, a 48-year-old female who is active less than 30 minutes a day only needs about 5 ounces each day from the protein group. A pork chop or chicken breast, can be four to five ounces each. You can see how it would be easy to eat too much.

Save your money and don't buy the protein supplements. If you're healthy, you probably get all the protein you need from your

To help you make lower-fat protein choices —

Choose meats that are leaner cuts and trim away any fat you can see. For chicken and turkey, remove the skin to reduce fat.

Substitute pinto or black beans for meat in chili and tacos.

Choose low-fat or fat-free milk and yoghurt.

Choose low-fat or fat-free cheese.

Choose egg whites or pasteurized egg white products.

What if I am a vegetarian?

Because some vegetarians avoid eating all (or most) animal foods, they must rely on plant-based sources of protein to meet their needs. A well-planned vegetarian diet can easily meet the recommended protein needs of adults and children.

Choosemyplate.gov provides meal planning tips for vegetarians.

Sources

1Position of the American Dietetic Association and Dietitians of Canada: Vegetarian diets. JADA, 2003; 103(6) 748 – 765.

2Source for Acceptable Macro nutrient Distribution Range (AMDR) reference and RDAs: Institute of Medicine (IOM) Diet and Health: Making the Difference. Report on the Dietary Guidelines Advisory Committee's Consultation with the National Academies of Sciences, Engineering, and Medicine. This report may be accessed via www.nap.edu*

<http://www.cdc.gov/nutrition/everyone/basics/foodgroups.html>

Food Groups

Are you interested in healthy eating and having a balanced diet? If so, you'll want to learn more about food groups.

This section helps explain the food groups based on the Dietary Guidelines for Americans, 2010 and provides information a of vegetables, fruits, grains, dairy and a protein group which includes meat, poultry, fish and nuts.

MyPlateHYPERLINK "<http://www.cdc.gov/Other/disclaimer.html>" \t "_blank" illustrates the five food groups that are the image—a place setting for a meal —and display how much of each food group you need to eat for a healthy diet.

What are the basic food groups?

Food Groups

Vegetables

Fruits

Grains

Dairy

Protein Foods

*Oils are NOT a food group, but they provide essential nutrients such as vitamin E.

How much of each food group should I eat?

The amount of food you need to eat from each group depends on your age, sex, and level of physical activity.

Food Plans

A healthy eating plan will show you how much you need from each food group to stay within your calorie needs and promote you learn—

- How many calories you need each day and how to balance your calorie needs.
- How much of each food group you should consume.
- How to make healthy choices in each food group.

Vegetarian Plans can meet all the recommendations for nutrients. The key is to consume a variety of foods and the right amount.

274 Proteins, Peptides & Amino Acids

Proteins, Peptides & Amino Acids

<http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/proteins.htm>

1. Introduction

Proteins, from the Greek *proteios*, meaning first, are a class of organic compounds which are present in and vital to every living organism. In muscles, tendons and ligaments, proteins hold together, protect, and provide structure to the body of a multi-celled organism. Globulins, they catalyze, regulate, and protect the body chemistry. In the form of haemoglobin, myoglobin and various enzymes and other substances within an organism.

Proteins are generally regarded as beneficial, and are a necessary part of the diet of all animals. Humans can become seriously ill with kwashiorkor being an extreme form of protein deficiency. Protein based antibiotics and vaccines help to fight diseases. Clothing and shoes that are often protein in nature (e.g. wool, silk and leather).

The deadly properties of protein toxins and venoms is less widely appreciated. Botulinum toxin A, from *Clostridium botulinum* is well known. Based on toxicology studies, a teaspoon of this toxin would be sufficient to kill a fifth of the world's population. The organisms are nearly as poisonous. A list of highly toxic proteins or peptides would also include the venoms of many snakes.

Despite the variety of their physiological function and differences in physical properties--silk is a flexible fibre, horn a tough crystalline material--proteins are sufficiently similar in molecular structure to warrant treating them as a single chemical family. When compared to lipids, proteins are obviously different in fundamental composition. The lipids are largely hydrocarbon in nature, generally being 75% carbon, 12% hydrogen, and 13% oxygen, and like the lipids, usually have less than 5% nitrogen (often none at all). Proteins and peptides, on the other hand, have an equal amount of oxygen. The distinction between proteins and peptides is their size. Peptides are in a sense small proteins, but

2. Natural α -Amino Acids

Hydrolysis of proteins by boiling aqueous acid or base yields an assortment of small molecules. Amino acids and other components have been isolated, and the most common of these are listed in the following table. These are essential diet components, since they are not synthesized by human metabolic processes. The best food source of these nutrients varies. Not all proteins have equal nutritional value. For example, peanuts have a higher weight content of protein than fish or eggs, but peanut protein is only a third of that from the two other sources. For reasons that will become evident when discussing the structure of amino acids, each is assigned a one or three letter abbreviation.

Natural α -Amino Acids

Some common features of these amino acids should be noted. With the exception of proline, they are all 1°-amines; and with the exception of proline, the configurations of the chiral amino acids are the same when written as a Fischer projection formula, as in the drawing on the right. The R-substituent in this structure is the remaining structural component that varies from one amino acid to another. In proline, the nitrogen is joined to the alpha-carbon in a five-membered ring. Applying the Cahn-Ingold-Prelog notation, all these natural amino acids have an S-configuration.

For the first seven compounds in the left column the R-substituent is a hydrocarbon. The last three entries in the left column amino acids in the right column incorporate thiol and sulfide groups respectively. Lysine and arginine have basic amine functions. Tyrosine and histidine have less basic nitrogen heterocyclic rings as substituents. Finally, carboxylic acid side-chains are substituents on aspartic acid and glutamic acid. The last three entries in the right column are their corresponding amides.

The formulas for the amino acids written above are simple covalent bond representations based upon previous understanding, but are in fact incorrect. This is evident from a comparison of the physical properties listed in the following table. All four compounds have moderate to excellent water solubility. The first two are simple carboxylic acids, and the third is an amino alcohol. All three have relatively low melting points. The carboxylic acids have pKa's near 4.5, and the conjugate acid of the alanine is the last entry. By contrast, it is very high melting (with decomposition), insoluble in organic solvents, and a millic acid.

Physical Properties of Selected Acids and Amines

Compound

Formula

Mol.Wt.

Solubility

in Water

Solubility

in Ether

Melting

Point

pKa

isobutyric acid $(\text{CH}_3)_2\text{CHCO}_2\text{H}$ 88 20g/100mL complete -47 °C 5.0

lactic acid $\text{CH}_3\text{CH}(\text{OH})\text{CO}_2\text{H}$ 90 complete complete 53 °C 3.9

3-amino-2-butanol $\text{CH}_3\text{CH}(\text{NH}_2)\text{CH}(\text{OH})\text{CH}_3$ 89 complete complete 9 °C 10.0

alanine $\text{CH}_3\text{CH}(\text{NH}_2)\text{CO}_2\text{H}$ 89 18g/100mL insoluble ca. 300 °C 9.8

Show Zwitterionic Form

Show Spacefill Model

Show Stick Model

Show Tyrosine

Show Cysteine

Show Lysine

Show Aspartic Acid

These differences all point to internal salt formation by a proton transfer from the acidic carboxyl function to the basic amine structure, commonly referred to as a zwitterion, is also supported by the spectroscopic characteristics of alanine.



As expected from its ionic character, the alanine zwitterion is high melting, insoluble in nonpolar solvents and has the acid is a Jmol display of an L-amino acid. The model will change to its zwitterionic form by clicking the appropriate button beneath the model. Other amino acids may also be viewed in their favored neutral zwitterionic form. Note that in lysine the amine function farthest from the alpha amine. Consequently, the positively charged ammonium moiety formed at the chain terminus is attracted to the negative carboxylate.

Since amino acids, as well as peptides and proteins, incorporate both acidic and basic functional groups, the predominant molecular species will depend on the pH of the solution. In order to determine the nature of the molecular and ionic species that are present in a solution, the Henderson - Hasselbalch Equation, written below. Here, the pKa represents the acidity of a specific conjugate acid function. At the pKa, the concentrations of HA and A(-) must be equal (log 1 = 0).

The titration curve for alanine, shown below, demonstrates this relationship. At a pH lower than 2, both the carboxylate and the amino group of the molecule has a net positive charge. At a pH greater than 10, the amine exists as a neutral base and the carboxyl as its conjugate base with a net negative charge. At intermediate pH's the zwitterion concentration increases, and at a characteristic pH, called the isoelectric point, the neutral molecular species are present in equal concentration. This behavior is general for simple (difunctional) amino acids. Starting from a low pH, the titration curve shows the change in pH during the titration of the amino acid by added base, and the change in pH during the titration.

Titration curves for many other amino acids may be examined at a useful site provided by The University of Virginia in Charlottesville.

The distribution of charged species in a sample can be shown experimentally by observing the movement of solute molecules during electrophoresis. For such experiments an ionic buffer solution is incorporated in a solid matrix layer, composed of paper or agarose. A small amount of the amino acid, peptide or protein sample is placed near the centre of the matrix strip and an electric potential is applied across the strip as shown in the following diagram. The solid structure of the matrix retards the diffusion of the solute molecules, which will remain where they are held by the electrostatic potential. In the example shown here, four different amino acids are examined simultaneously in a pH 6.00 buffer. Click on the illustration. Note that the colors in the display are only a convenient reference, since these amino acids are colorless.

At pH 6.00 alanine and isoleucine exist on average as neutral zwitterionic molecules, and are not influenced by the electric field. The amino group of arginine functions exist as "onium" conjugate acids in the pH 6.00 matrix. The solute molecules of arginine therefore carry an excess positive charge and migrate toward the cathode. The two carboxyl functions in aspartic acid are both ionized at pH 6.00, and the negatively charged solute molecules migrate toward the anode. Structures for all these species are shown to the right of the display.

pKa Values of Polyfunctional Amino Acids

Amino Acid α -CO₂H

pKa1 α -NH₃⁺

pKa2 Side Chain

pKa3 pI

Arginine 2.1 9.0 12.5 10.8
 Aspartic Acid 2.1 9.8 3.9 3.0
 Cysteine 1.7 10.4 8.3 5.0
 Glutamic Acid 2.2 9.7 4.3 3.2
 Histidine 1.8 9.2 6.0 7.6
 Lysine 2.2 9.0 10.5 9.8
 Tyrosine 2.2 9.1 10.1 5.7

It should be clear that the result of this experiment is critically dependent on the pH of the matrix buffer. If we were to repeat it at a pH of 3.80, the aspartic acid would remain at its point of origin, and the other amino acids would move toward the cathode. Ignoring arginine would move twice as fast as the alanine and isoleucine because its solute molecules on average would carry a double

As noted earlier, the titration curves of simple amino acids display two inflection points, one due to the strongly acidic carboxyl group and the less acidic ammonium function ($pK_{a2} = 8.8$ to 9.7). For the 2°-amino acid proline, pK_{a2} is 10.6, reflecting the greater basicity of the nitrogen atom.

Some amino acids have additional acidic or basic functions in their side chains. These compounds are listed in the table on the next page. The basicity of the extra function, is listed in the fourth column of the table. The pI's of these amino acids (last column) are often different from those of the simpler members. As expected, such compounds display three inflection points in their titration curves, illustrated by the titration curves shown in Figure 1. For each of these compounds four possible charged species are possible, one of which has no overall charge. Formulas for the four species, together with the pH at which each is expected to predominate. The very high pH required to remove the last acidic proton is a reflection of the high basicity of the guanidine moiety at the end of the side chain.

3. The Isoelectric Point

As defined above, the isoelectric point, pI, is the pH of an aqueous solution of an amino acid (or peptide) at which the molecule has no net charge. In other words, the positively charged groups are exactly balanced by the negatively charged groups. For simple amino acids such as alanine, the pI is the average of the pKa's of the carboxyl (2.34) and ammonium (9.69) groups. Thus, the pI for alanine is calculated to be: $(2.34 + 9.69)/2 = 6.02$, the experimental value. For amino acids that have basic groups as side-chain functions, the pI is the average of the pKa's of the two most similar acids. To assist in the calculation, amino acids are divided into two classes. The first consists of acids that are neutral in their protonated form (e.g. CO₂H & SH). The second includes acids that have basic side chains (e.g. -NH₃⁺). In the case of aspartic acid, the similar acids are the alpha-carboxyl function ($pK_a = 2.1$) and the side-chain carboxyl function ($pK_a = 3.0$). For arginine, the similar acids are the guanidinium species on the side-chain ($pK_a = 12.5$) and the alpha-ammonium function ($pK_a = 9.0$)/2 = 10.75.

4. Other Natural Amino Acids

The twenty alpha-amino acids listed above are the primary components of proteins, their incorporation being governed by the way in which amino acids exist, and the structures of a few of these are displayed below. Some, such as hydroxylysine and hydroxyproline, are previously described compounds. These two amino acids are found only in collagen, a common structural protein. Homoserine is a namesake. The amino group in beta-alanine has moved to the end of the three-carbon chain. It is a component of pantothenic acid, $\text{HOCH}_2\text{C}(\text{CH}_3)\text{CH}_2\text{CH}(\text{OH})\text{CONHCH}_2\text{CH}_2\text{CO}_2\text{H}$, a member of the vitamin B complex and an essential nutrient. Acetyl coenzyme A is the pantothenic acid amide. The gamma-amino homolog GABA is a neurotransmitter inhibitor and antihypertensive agent.

Many unusual amino acids, including D-enantiomers of some common acids, are produced by micro-organisms. These include the antibiotic bacitracin A, and statin, found as part of a pentapeptide that inhibits the action of the digestive enzyme pepsin.

Reactions of α -Amino Acids

1. Carboxylic Acid Esterification

Amino acids undergo most of the chemical reactions characteristic of each function, assuming the pH is adjusted to an appropriate value. Esterification is usually conducted under acidic conditions, as shown in the two equations written below. Under such conditions, amine functions and carboxylic acids are not dissociated. The first equation is a typical Fischer esterification involving methanol. The initial product formed by neutralization of this salt is unstable, due to acylation of the amine by the ester function.

The second reaction illustrates benzylation of the two carboxylic acid functions of aspartic acid, using p-toluenesulfonic acid. In this esterified, zwitterionic species are no longer possible and the product behaves like any 1°-amine.

2. Amine Acylation

In order to convert the amine function of an amino acid into an amide, the pH of the solution must be raised to 10 or higher. In this reaction system, carboxylic acids are all converted to carboxylate anions at such a high pH, and do not interfere with amine acylation. In the first, an acid chloride serves as the acylating reagent. This is a good example of the superior nucleophilicity of amines. Water and hydroxide anion are also present as competing nucleophiles. A similar selectivity favoring amines was observed in the use of an anhydride-like reagent for the acylation. This is a particularly useful procedure in peptide synthesis, thanks to the ease with which the reagent is removed at a later stage. Since amides are only weakly basic ($\text{pK}_a \sim -1$), the resulting amino acid derivatives do not display the variety of carboxylic acid derivatives.

3. The Ninhydrin Reaction

In addition to these common reactions of amines and carboxylic acids, common alpha-amino acids, except proline, undergo a reaction with ninhydrin to form a purple colored imine known as a ninhydrin derivative. Among the products of this unusual reaction (shown on the left below) is a purple colored imine for these amino acids, most of which are colorless. A common application of the ninhydrin test is the visualization of amino acids on a chromatogram. As shown in the graphic on the right, samples of amino acids or mixtures thereof are applied along a line near the bottom of a rectangular sheet of paper. The paper is immersed in an aqueous buffer, and this liquid climbs slowly toward the top edge. As the solvent front passes the spots, they are carried along at a rate which is characteristic of their functionality, size and interaction with the cellulose matrix of the paper. Some spots move quickly while others may scarcely move at all. The ratio of the distance a compound moves from the baseline to the distance of the solvent front is called the retardation (or retention) factor R_f . Different amino acids usually have different R_f 's under suitable conditions. **Three samples have R_f values of 0.36 & 0.78.**

Paper Chromatography

4. Oxidative Coupling

The mild oxidant iodine reacts selectively with certain amino acid side groups. These include the phenolic ring in tyrosine, and the imidazole ring in histidine, which all yield products of electrophilic iodination. In addition, the sulfur groups in cysteine and methionine are also oxidized. The amount of iodine consumption has been used to determine the number of such residues in peptides. The basic functions in lysine and arginine are unreactive in that state.

Cysteine is a thiol, and like most thiols it is oxidatively dimerized to a disulfide, which is sometimes listed as a distinct amino acid. Disulfide bonds of this kind are found in many peptides and proteins. For example, the two peptide chains that constitute insulin are held together by disulfide bonds. Another fibrous protein called keratin, which contains an unusually large proportion of cysteine. In the manipulation called "permanent waving" of hair, the hair is then created after the hair has been reshaped. Treatment with dilute aqueous iodine oxidizes the methionine sulfur atom to a disulfide.

Cysteine-Cystine Interconversion

Synthesis of α -Amino Acids

1) Amination of alpha-bromocarboxylic acids, illustrated by the following equation, provides a straightforward method for the synthesis of amino acids. Primary amines, in turn, are conveniently prepared from carboxylic acids by reaction with $\text{Br}_2 + \text{PCl}_3$. Although this direct approach is simple, it is more effective for making amino acids, thanks to the reduced nucleophilicity of the nitrogen in the complex procedures that give good yields of pure compounds are often chosen for amino acid synthesis.

2) By modifying the nitrogen as a phthalimide salt, the propensity of amines to undergo multiple substitutions is removed, and only one 2°-alkylhalide takes place. This procedure, known as the Gabriel synthesis, can be used to advantage in the synthesis of primary amines. The following scheme illustrates the synthesis of an amino acid. Since the phthalimide substituted malonic ester has an acidic hydrogen (colored orange), it is activated and converted to an ambident anion and alkylated. Finally, base catalyzed hydrolysis of the phthalimide moiety and the esters, followed by decarboxylation, produces an amino acid and phthalic acid (not shown).

3) An elegant procedure, known as the Strecker synthesis, assembles an alpha-amino acid from ammonia (the amine precursor) and an aldehyde. This reaction (shown below) is essentially an imino analog of cyanohydrin formation. The alpha-amino nitrile is then hydrolyzed to the amino acid by either acid or base catalysis.

4) Resolution The three synthetic procedures described above, and many others that can be conceived, give racemic amino acids. If a single enantiomer is desired, it is necessary to resolve these racemic mixtures. A common method of resolving racemates is by diastereomeric salt formation. This is illustrated for a generic amino acid in the following diagram. Be careful to distinguish charge symbols, shown in colored circles in the diagram.

In the initial display, the carboxylic acid function contributes to diastereomeric salt formation. The racemic amino acid is first converted to its ammonium salt. Next, an ammonium salt is formed by combining the carboxylic acid with an optical active amine (strychnine). The structure of this amine is not shown, because it is not a critical factor in the logical progression of steps. Since strychnine is a single enantiomer (levorotatory in this example), an equimolar mixture of diastereomeric salts is formed (drawn in the diagram). By crystallization, chromatography or other physical manipulation, and in this way one of the isomers may be isolated for further use. Finally the salt is broken by acid treatment, giving the resolved (+)-amino acid derivative together with the reagent amine. Of course, the same procedure could be used to obtain the (-)-enantiomer of the amino acid.

Resolution of amino acid derivatives may also be achieved by enzymatic discrimination in the hydrolysis of amides. For example, an enzyme that cleaves an amide derivative of a natural L-amino acid much faster than it does the D-enantiomer. If the racemic mixture of an amide is treated with this enzyme, the L-enantiomer (whatever its rotation) will be rapidly converted to its free zwitterionic form, while the D-enantiomer remains unchanged. Here, the diastereomeric species are transition states rather than isolable intermediates. This separation of enantiomers is called kinetic resolution.

278 Amino acids

Amino acid

Amino acids are biologically important organic compounds made from amine and carboxylic acid functional groups, along with other elements. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen.

Chemical Families

- Acidic & Amides
- Aliphatic
- Aromatic
- Basic
- Cyclic
- Hydroxyl
- Sulfur-Containing

http://www.biology.arizona.edu/biochemistry/problem_sets/aa/acidic.html

Acidic Amino Acids and their Amides

Acidic amino acids are polar and negatively charged at physiological pH. Both acidic amino acids have a second carboxyl group.

Amides are polar and uncharged, and not ionizable. All are very hydrophilic.

http://www.biology.arizona.edu/biochemistry/problem_sets/aa/aa.html

The Chemistry of Amino Acids

Introduction

Essential amino acids

Why learn this?

Amino acids play central roles both as building blocks of proteins and as intermediates in metabolism. The 20 amino acids that differ in their side chains are of chemical versatility. The precise amino acid content, and the sequence of those amino acids, of a specific protein, is determined by the DNA sequence that encodes that protein. The chemical properties of the amino acids of proteins determine the biological activity of the protein. In living cells, they control virtually all cellular processes. In addition, proteins contain within their amino acid sequence information that determines that protein will fold into a three dimensional structure, and the stability of the resulting structure. The field of protein folding is an area of research for years, and remains today one of the great unsolved mysteries. It is, however, being actively investigated, and

As we learn about amino acids, it is important to keep in mind that one of the more important reasons to understand amino acids is to understand protein structure and properties. We will see that the vastly complex characteristics of even a small, relatively simple protein are determined by the amino acids which comprise the protein.

Essential amino acids

Humans can produce 10 of the 20 amino acids. The others must be supplied in the food. Failure to obtain enough of even 1 of these essential amino acids cannot make, results in degradation of the body's proteins—muscle and so forth—to obtain the one amino acid that is needed. The body cannot store excess amino acids for later use—the amino acids must be in the food every day.

The 10 amino acids that we can produce are alanine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, proline, and serine. The 10 essential amino acids (for adults), histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. These amino acids are essential because we are not able to make all the amino acids. Humans, on the other hand, do not have all the the enzymes required for the biosynthesis of all the amino acids.

Why learn these structures and properties?

It is critical that all students of the life sciences know well the structure and chemistry of the amino acids and other building blocks of life. It is impossible to think or talk sensibly about proteins and enzymes, or the nucleic acids, without a good understanding of the amino acids.

Amide

From Wikipedia, the free encyclopedia

Not to be confused with Imide.

Structures of three kinds of amides: an organic amide, a sulfonamide, and a phosphoramidate.

An amide is a compound with the functional group $R_nE(O)_xNR'_2$ (R and R' refer to H or organic groups). Most common are other important types of amides are known including phosphoramidates ($n = 2, E = P, x = 1$ and many related formulas) and both to classes of compounds and to the functional group ($R_nE(O)_xNR'_2$) within those compounds.

Amide can also refer to the conjugate base of ammonia (the anion H_2N^-) or of an organic amine (an anion R_2N^-). For discussion see Alkali metal amides.

The remainder of this article is about the carbonyl-nitrogen sense of amide.

Structure and bonding

The simplest amides are derivatives of ammonia wherein one hydrogen atom has been replaced by an acyl group. The ester is closely related and even more numerous are amides derived from primary amines ($R'NH_2$) with the formula $RC(O)NHR'$. Secondary amines ($R'RNH$) with the formula $RC(O)NR'R$. Amides are usually regarded as derivatives of carboxylic acids in which the hydrogen of ammonia.

The lone pair of electrons on the nitrogen is delocalized into the carbonyl, thus forming a partial double bond between N and C in amides is not pyramidal. It is estimated that acetamide is described by resonance structure A for 62% and by B for 28%

Amides possess a conjugated system spread over the O, C and N atoms, consisting of molecular orbitals in formamide is shown above.

Nomenclature

Main article: IUPAC nomenclature of organic chemistry#Amines and Amides

In the usual nomenclature, one adds the term "amide" to the stem of the parent acid's name. For instance, the amide derived from acetic acid (CH_3CONH_2). IUPAC recommends ethanamide, but this and related formal names are rarely encountered. When the amide substituents on nitrogen are indicated first in the name. Thus, the amide formed from dimethylamine and acetic acid is N,N-dimethylethanamide (CH_3). Usually even this name is simplified to dimethylacetamide. Cyclic amides are called lactams; they are necessarily secondary amides. Compounds consisting of $-P(O)NR_2$ and $-SO_2NR_2$ are phosphoramidates and sulfonamides, respectively.

Pronunciation

Some chemists make a pronunciation distinction between the two, saying / ˈmɪd/ for the carbonyl-nitrogen compound and / ˈæmɪd/ for the other, while still others pronounce both / ˈæmɪd/, making them homonyms.

Properties

Basicity

Compared to amines, amides are very weak bases. While the conjugate acid of an amine has a pKa of about 9.5, the conjugate acid of an amide has a pKa of about -6 to -10. Therefore amides don't have as clearly noticeable acid-base properties in water. This relative lack of basicity is explained by the amide group where the lone pair of electrons on the nitrogen is delocalized by resonance. On the other hand, amides are much stronger acids than ketones (conjugate acid pKa between -6 and -10). It is estimated in silico that acetamide is represented by resonance structures that are largely prevented in the very strained quinuclidone.

Because of the greater electronegativity of oxygen, the carbonyl (C=O) is a stronger dipole than the N-C dipole. The presence of the C=O dipole, allows amides to act as H-bond acceptors. In primary and secondary amides, the presence of N-H dipoles allows amides to act as H-bond donors. Amides can participate in hydrogen bonding with water and other protic solvents; the oxygen atom can accept hydrogen bonds and the nitrogen atom can donate H-bonds. As a result of interactions such as these, the water solubility of amides is greater than that of corresponding ketones.

The proton of a primary or secondary amide does not dissociate readily under normal conditions; its pKa is usually well above 10. Under acidic conditions, the carbonyl oxygen can become protonated with a pKa of roughly -1.

Solubility

The solubilities of amides and esters are roughly comparable. Typically amides are less soluble than comparable amines and alcohols. Amides can donate and accept hydrogen bonds. Tertiary amides, with the important exception of N,N-dimethylformamide, exhibit low solubility in water.

Characterization

The presence of the functional group is generally easily established, at least in small molecules. They are the most common functional groups in organic chemistry and can be distinguished from nitro and cyano groups by their IR spectra. Amides exhibit a moderately intense carbonyl absorption in the IR spectrum. In spectroscopy, CONHR signals occur at low fields. In X-ray crystallography, the C(O)N centre together with the three immediate neighbours are in a plane.

Applications and occurrence

Amides are pervasive in nature and technology as structural materials. The amide linkage is easily formed, confers structural strength, and is resistant to hydrolysis. Polyamides as are the very resilient materials Aramid, Twaron, and Kevlar. Amide linkages in a biochemical context are called peptide bonds. The defining molecular feature of proteins, the secondary structure of which is due in part to the hydrogen bonding abilities of amide groups. Dimethylformamide (HC(O)N(CH₃)₂), are common solvents. Many drugs are amides, including penicillin and LSD. Moreo- ver, amides are common biological functionalities.

Amide synthesis

Amides are commonly formed via reactions of a carboxylic acid with an amine. Many methods are known for driving the reaction to completion.



For the most part, these reactions involve "activating" the carboxylic acid and the best known method, the Schotten-Baumann method, involves the use of acid chlorides:

Reaction name Substrate Details

Beckmann rearrangement cyclic ketone reagent: hydroxylamine and acid

Schmidt reaction ketones reagent: hydrazoic acid

nitrile hydrolysis nitrile reagent: water; acid catalyst

Willgerdt-Kindler reaction aryl alkyl ketones sulphur and morpholine

Passerini reaction carboxylic acid, ketone or aldehyde

Ugi reaction isocyanide, carboxylic acid, ketone, primary amine

Bodroux reaction

carboxylic acid, Grignard reagent with an aniline derivative ArNHR'

Chapman rearrangement

aryl imino ether for N,N-diaryl amides. The reaction mechanism is based on a nucleophilic aromatic substitution.

Leuckart amide synthesis isocyanate Reaction of arene with isocyanate catalysed by aluminium trichloride, formation of a

Other methods

The seemingly simple direct reaction between an alcohol and an amine to an amide was not tried until 2007 when a special method was found to be effective in a so-called dehydrogenative acylation:

The generation of hydrogen gas compensates for unfavorable thermodynamics. The reaction is believed to proceed by one dehydrogenation followed by formation of a hemiaminal and the after a second dehydrogenation to the amide. Elimination of water in the hemiaminal

Amide reactions

Amides undergo many chemical reactions, usually through an attack on the carbonyl breaking the carbonyl double bond and hydroxyls and amines are all known to serve as nucleophiles. Owing to their resonance stabilization, amides are less reactive than esters. Enzymes, e.g. peptidases or artificial catalysts, are known to accelerate the hydrolysis reactions. They can be hydrolysed in acidic or basic conditions. Acidic conditions yield the carboxylic acid and the ammonium ion while basic hydrolysis yield the carboxylate ion and amine. Amides can also be converted to many other functional groups.

Reaction name Product Comment

dehydration nitrile reagent: phosphorus pentoxide

Hofmann rearrangement amine with one fewer carbon atoms reagents: bromine and sodium hydroxide

amide reduction amine reagent: lithium aluminium hydride

Vilsmeier-Haack reaction imine POCl₃, aromatic substrate, formamide

See also

Metal amides

Vitamins and Minerals

Vitamins and Minerals

<http://www.cdc.gov/nutrition/everyone/basics/vitamins/index.html>

Vitamins are organic substances (made by plants or animals), minerals are inorganic elements that come from the earth; soil and humans absorb minerals from the plants they eat. Vitamins and minerals are nutrients that your body needs to grow and

Vitamins and minerals, have a unique role to play in maintaining your health. For example Vitamin D helps your body absorb strong bones. A deficiency in vitamin D can result in a disease called rickets (softening of the bones caused by the body cannot produce calcium; therefore, it must be absorbed through our food. Other minerals like chromium, copper, iodine minerals because you only need very small amounts of them each day. The best way to get enough vitamins is to eat a balanced diet. Get all your vitamins from the foods you eat.

Vitamin and Mineral Supplements

Information about the role of vitamins and minerals in health and disease:

Calcium and Bone Health

Chromium

Folate

Iron and Iron Deficiency

Magnesium

Salt

Sodium and Potassium

Selenium

Vitamin A

Vitamin B6

Vitamin B12

Vitamin D

Vitamin E

Vitamin K: Interactions with Coumadin

Zinc

Many products are marketed as dietary supplements. It is important to remember that supplements include vitamins and minerals. Be cautious of substances.

Fruits and Vegetables

Fruits and Vegetables

<http://www.cdc.gov/nutrition/everyone/fruitsvegetables/index.html>

"Eat your fruits and vegetables." You've likely heard this statement since childhood. Research shows why it is good advice:

Healthy diets rich in fruits and vegetables may reduce the risk of cancer and other chronic diseases.

Fruits and vegetables also provide essential vitamins and minerals, fibre, and other substances that are important for good health.

Most fruits and vegetables are naturally low in fat and calories and are filling.

Did you know that 1/2 of your plate each meal should be fruits and vegetables?

Nutrient information for fruits and vegetables

Fruits and vegetables are sources of many vitamins, minerals and other natural substances that may help protect you from different colors gives your body a wide range of valuable nutrients, like fibre, folate, potassium, and vitamins A and C. This Vegetables provides examples of fruits and vegetables that are sources of specific nutrients.

Not sure how many fruits and vegetables you should be eating each day?

Visit the Fruit and Vegetable Calculator. Here you can calculate your fruit and vegetable recommendations based on your c: This site also has helpful tips and photographs of 1/2 cup and 1 cup fruit and vegetable examples.

Curious as to whether fruits and vegetables can help you manage your weight?

Take a look at this How to Use Fruits and Vegetables to Help Manage your Weight brochure and learn about fruits and vegetable plan. Tips to cut calories by substituting fruits and vegetables are included with meal-by-meal examples. You will also find these helpful tips, you will soon be on your way to adding more fruits and vegetables into your healthy eating plan.

Food safety basics for fruits and vegetables

To prevent food borne illness, review Food Safety Basics for Fruit and Vegetables. As you strive to meet your individual fruit remember that proper handling and preparation can reduce the risk of food contamination and food borne illness.

Related Resources

The State Indicator Report on Fruits & Vegetables, 2009 provides national and state-specific information on fruit and vegetable environmental supports. The behavioral indicators are derived from objectives for F&V outlined in Healthy People 2010. The state's ability to support the consumption of F&V through increased access, availability, and reduced price in schools and community decision makers and track progress.

The National Action Guide summarizes the national data on F&V consumption, policy, and environmental supports and provides business leaders, coalitions, community-based organizations, and professionals can take to improve Americans' nutrition allocation.

Dietary Fat

Dietary Fat

<http://www.cdc.gov/nutrition/everyone/basics/fat/index.html>

What counts as fat? Are some fats better than other fats? While fats are essential for normal body function, some fats are bad and cholesterol are less healthy than polyunsaturated and monounsaturated fats.

How much total dietary fat do I need?

The Dietary Guidelines for Americans 2010 recommend that Americans:

Consume less than 10% of calories from saturated fats.

Replace solid fats with oils when possible.

Limit foods that contain synthetic sources of trans fatty acids (such as hydrogenated oils), and keep total trans fatty acid con

Eat fewer than 300 mg of dietary cholesterol per day.

Reduce intake of calories from solid fats.

Age Group Total Fat Limits

Children ages 2 to 3 30% to 40% of total calories

Children and adolescents ages 4 to 18 25% to 35% of total calories

Adults, ages 19 and older 20% to 35% of total calories

Quick Q&A

If some fats are healthier than others, can I eat as much of these fats as I want?

No, it's best to keep your total fat intake between 20 and 35% of your total calories each day.

Know your limits on fats. You can meet this recommendation by following a healthy eating plan that meets your needs. Cho provide your daily allowance of oils and solid fats, based on your age, gender, height, weight, and physical activity level.

Carbohydrates

Carbohydrates

<http://www.cdc.gov/nutrition/everyone/basics/carbs.html>

Not sure what to think about carbohydrates?

What are carbohydrates?

What are the types of carbohydrates?

Complex Carbohydrates

Dietary fibre

Simple carbohydrates (sugars)

What are carbohydrates?

Your body uses carbohydrates (carbs) to make glucose which is the fuel that gives you energy and helps keep everything go

Your body can use glucose immediately or store it in your liver and muscles for when it is needed.

You can find carbohydrates in the following:

Fruits

Vegetables

Breads, cereals, and other grains

Milk and milk products

Foods containing added sugars (e.g., cakes, cookies, and sugar-sweetened beverages).

Healthier foods higher in carbohydrates include ones that provide dietary fibre and whole grains as well as those without ad.

What about foods higher in carbohydrates such as sodas and candies that also contain added sugars? Those are the ones that diet.

Quick Q&A

I've heard there are "good" carbs and "bad" carbs? Can you provide me more information?

Some diet books use "bad" carbs to talk about foods with refined carbohydrates (i.e., meaning they're made from white flour).

Examples include white bread, cakes, and cookies.

"Good" carbs is used to describe foods that have more fibre and complex carbohydrates. Complex carbohydrates are carbohydrates; such as vegetables, fruits, whole grains and beans.

These terms aren't used in the Dietary Guidelines for Americans 2010. Instead, the guidelines recommend choosing fibre-rich and grain groups and avoid added sugars.

It is also recommended that at least half of your daily grain choices are whole grains.

Soluble fibre is found in the following:

Oatmeal

Oat bran

Nuts and seeds

Most fruits (e.g., strawberries, blueberries, pears, and apples)

Dry beans and peas

Insoluble fibre found in the following:

Whole wheat bread

Barley

Brown rice

Couscous

Bulgur or whole grain cereals

Wheat bran

Seeds

Most vegetables

Fruits

Which type is best? Both! Each has important health benefits so eat a variety of these foods to get enough of both. You're all miss if you just chose 1 or 2 high-fibre foods.

How much dietary fibre do I need each day?

Most Americans greatly under consume dietary fibre. Breads, rolls, buns and pizza crust made with refined flour are not and contribute to a large portion our diets. To meet the recommendations for fibre, most people need to increase the consumption of grains, and other foods with naturally occurring fibre.

At first, you may find it challenging to eat all of your daily fibre grams. Just take it slowly and try to choose higher-fibre foods eating more fibre!

Try these tips to jump start your intake of dietary fibre:

Choose whole fruits more often than fruit juice. Fresh, frozen, or canned—it doesn't matter—they all count!

Try to eat two vegetables with your evening meal.

Keep a bowl of veggies already washed and prepared your refrigerator—try carrots, cucumbers, or celery for a quick snack.

Make a meal around dried beans or peas (also called legumes) instead of meat.

Choose whole grain foods more often. Take a look at the "whole grains buzz words list" below to help you decide. A good example of whole grains.

Start your day with a whole grain breakfast cereal low in added sugar. Top your cereal with fruit for even more fibre. While even more variety by also trying sliced peaches or berries. You can often find these fruits year-round in the frozen foods section.

Whole Grains

Whole grains are a good source of fibre and nutrients. Whole grains refer to grains that have all of the parts of the grain seed. The bran, germ, and endosperm are called the bran, the germ, and the endosperm.

If the whole grain has been cracked, crushed, or flaked (as in cracked whole grain bread or flake cereal), then the whole grain bran, germ, and endosperm to be called a whole grain.

When whole grains are processed, some of the dietary fibre and other important nutrients are removed. A processed grain is

Some refined grain products have key nutrients, such as folic acid and iron, which were removed during the initial processing of grains. White rice and white bread are enriched grain products.

Some enriched grain foods have extra nutrients added. These are called fortified grains.

Whole grains are a good source of fibre and nutrients. Whole grains refer to grains that have all of the parts of the grain seed. The bran, germ, and endosperm are called the bran, the germ, and the endosperm.

If the whole grain has been cracked, crushed, or flaked (as in cracked whole grain bread or flake cereal), then the whole grain bran, germ, and endosperm to be called a whole grain.¹

When whole grains are processed, some of the dietary fibre and other important nutrients are removed. A processed grain is

Some refined grain products have key nutrients, such as folic acid and iron, which were removed during the initial processing of grains. White rice and white bread are enriched grain products.

Some enriched grain foods have extra nutrients added. These are called fortified grains.

Whole grains are a good source of fibre and nutrients. Whole grains refer to grains that have all of the parts of the grain seed kernel are called the bran, the germ, and the endosperm.

If the whole grain has been cracked, crushed, or flaked (as in cracked whole grain bread or flake cereal), then the whole grain bran, germ, and endosperm to be called a whole grain.¹

When whole grains are processed, some of the dietary fibre and other important nutrients are removed. A processed grain is

Some refined grain products have key nutrients, such as folic acid and iron, which were removed during the initial processing of grains. White rice and white bread are enriched grain products.

Some enriched grain foods have extra nutrients added.

These are called fortified grains.

brown rice

buckwheat

bulgur (cracked wheat)

millet

wild rice

popcorn*

quinoa

triticale

whole-grain barley

whole-grain corn

whole oats/oatmeal

whole rye

whole wheat

*Popcorn is a whole grain that can have added fat and salt. Try air-popping your popcorn to avoid these extras. If you're buying a variety pack, you may also want to try the snack size bag to help with portion control.

Grains Galore!

Here are some explanations of less-familiar grains:

Bulgur. A staple of Middle Eastern dishes. Bulgur wheat consists of kernels that have been steamed, dried, and crushed. It is

Millet. A staple grain in parts of Africa and Asia. Millet comes in several varieties and has a bland flavor that is a background

Quinoa. A grain that has been traditionally used in South American cuisine. Its texture has been compared to that of couscous

Triticale. A grain that is a hybrid of wheat and rye. It comes in several varieties including whole berry, flakes, and flour.

Simple Carbohydrates

Simple carbohydrates include sugars found naturally in foods such as fruits, vegetables, milk, and milk products. Simple carbohydrates are processed and refined. What's the difference? In general, foods with added sugars have fewer nutrients than foods with natural

How can I avoid added sugars?

One way to avoid these sugars is to read the ingredient lists on food labels.

Look for these ingredients as added sugars:

Brown sugar
Corn sweetener
Corn syrup
Dextrose
Fructose
Fruit juice concentrates
Glucose
High-fructose corn syrup
Honey
Invert sugar
Lactose
Maltose
Malt Syrup
Molasses
Raw sugar
Sucrose
Sugar
Syrup

If you see any of these in the ingredient list, you know the food has added sugars. The closer to the top of the list, the more c

You can learn more about sugars on the food label by visiting [How to Understand and Use the Nutrition Facts Label](#).

Other tips for avoiding added sugars include—

Choose water instead of sugar-sweetened sodas.

Choose 4 fluid ounces (1/2 cup) of 100% fruit juice rather than a fruit drink.

Have a piece of fruit for dessert and skip desserts with added sugar.

Choose breakfast cereals that contain no or less added sugars.

If you want to learn more about avoiding added sugar in what you drink, check out [Re-think your Drink](#).

You probably already know sugars and starches can play a role in causing cavities. But it's worth mentioning again, particul
brush, floss, and drink fluoridated water to help prevent cavities.

It's important to choose carbohydrates wisely. Foods containing carbohydrates are part of a healthful diet.

empty

Natural Healing Methods

Natural Healing Methods By Pearlyn Goodman-Herrick

http://www.zimbio.com/Alternative+Medicines/articles/Tlnr6tKoH_M/Natural+Healing+Methods

http://www.zimbio.com/Alternative+Medicines/articles/Tlnr6tKoH_M/Natural+Healing+Methods

A lot of people are convinced the only approach to receive good body healing treatment solutions are through mainstream medicine isn't the situation. Several varieties of healing processes can now give the body healing results you're in search of. Healing solutions and healing exercises.

Concentration of Healing

Healing solutions focus initially on prevention and lifestyle. When you pay attention to living and lifestyle, quite a few illnesses diabetes may often be prevented by sustaining a proper weight and working out frequently.

Yet, for individuals who already developed the problem, healing strategies may often turn back effects and raise the probability of illness.

These healing techniques could also be used for a lot of remedies for a trivial cut or scrape to something significant, like a chronic condition. These approaches have several advantages over traditional body healing processes.

Benefits of Natural Healing

Remember the fact that if you use healing strategies it's not necessary to wait to see a physician or waste your money on applying a lot of body healing without the need to take high-priced prescription medications that include really intimidating uncomfortable side effects.

All natural healing works by using things like vitamins and minerals to deal with common colds or the flu. Natural healing takes less time than the time that it requires to establish a doctor's visit and fill a prescription you could have had time to use a natural body healing solution. Several healing remedies are free of charge and could be used very quickly.

The Different All Natural Healing Approaches

You'll find also a lot of healing tactics like yoga, Reiki, and acupuncture that could provide total healing. But healing doesn't always work. Most people consider all natural healing a lifestyle decision that begins within the diet and consists of the daily utilization of natural healing. If there is an accident or a physical injury, Reiki could be used efficiently to funnel body healing energy.

Many individuals use other body healing items like magnets, copper bracelets, or particular herbal products to keep the right balance.

The majority of naturalists believe that your body can achieve healing itself the natural way without the assistance of drugs :

Long before there were medical doctors, prescription medications, and foods stuffed with chemical preservatives and additives, your body was healthy and your body figured out how to heal itself with endurance and naturally healthful defence mechanisms to fight disease.

About the Author:

Holistic treatment focuses on bringing you back into balance. Pearlyn Goodman-Herrick is one of the foremost holistic medical practitioners.

A lot of people are convinced the only approach to receive good body healing treatment solutions are through mainstream medicine. But it isn't the situation. Several varieties of healing processes can now give the body healing results you're in search of. Healing solutions include natural healing exercises.

Concentration of Healing

Healing solutions focus initially on prevention and lifestyle. When you pay attention to living and lifestyle, quite a few illnesses like diabetes may often be prevented by sustaining a proper weight and working out frequently.

Yet, for individuals who already developed the problem, healing strategies may often turn back effects and raise the probability of recurrence.

These healing techniques could also be used for a lot of remedies for a trivial cut or scrape to something significant, like a chronic condition. These approaches have several advantages over traditional body healing processes.

All natural healing works by using things like vitamins and minerals to deal with common colds or the flu. Natural healing takes less time than the time that it requires to establish a doctor's visit and fill a prescription you could have had time to use a natural body healing solution. Several healing remedies are free of charge and could be used very quickly.

The Different All Natural Healing Approaches

You'll find also a lot of healing tactics like yoga, Reiki, and acupuncture that could provide total healing. But healing doesn't always require a medical system. Most people consider all natural healing a lifestyle decision that begins within the diet and consists of the daily utilization of natural healing. If there is an accident or a physical injury, Reiki could be used efficiently to funnel body healing energy.

Many individuals use other body healing items like magnets, copper bracelets, or particular herbal products to keep the right balance.

The majority of naturalists believe that your body can achieve healing itself the natural way without the assistance of drugs :

Long before there were medical doctors, prescription medications, and foods stuffed with chemical preservatives and additives, healthy and your body figured out how to heal itself with endurance and naturally healthful defence mechanisms to fight disease.

Handbook

Where To Buy Homoeopathic Remedies: A Quick and Easy Guide to Common Disorders and Their Homoeopathic Treatments

Discount Homoeopathic Remedies: A Quick and Easy Guide to Common Disorders and Their Homoeopathic Treatments

Natural

empty

What is Glucosamine 1

What is Glucosamine

Glucosamine for joint health

Glucosamine, an amino monosaccharide produced in the body by the combination of glucose with glutamine, through the enzyme glucosyltransferase, plays a key role in the formation of articular surfaces, tendons, ligaments, synovial fluid, skin, bone, nails, heart valves, blood vessels and the respiratory, and urinary tracts. MSM is important in building healthy new cells, relieves pain and inflammation. Chondroitin sulfate binds to glucosamine and gives joints their strength and resilience.

Research indicates that damaged cartilage can be replaced by healthy new cartilage. Therefore, treatment of osteoarthritis aims at inhibiting cartilage breakdown and promoting cartilage repair.

1 What is Glucosamine?

Glucosamine is beneficial to sufferers of osteoarthritis pain -- both humans and pets. It has been proven effective in easing pain, renewing synovial fluid, and repairing joints that have been damaged from osteoarthritis.

Each person and animal produces a certain amount of glucosamine within their bodies. As you grow older, your body loses cartilage in your weight-bearing joints, such as the hips, knees, and hands is destroyed, then hardens and forms bone spurs, causing pain, movement and limping.

There have been many double blind placebo controlled trials and studies done on glucosamine. In many trials and studies, glucosamine has been shown to:

- Easing osteoarthritis pain
- Easing articular joint pain
- Rehabilitating damaged cartilage
- Slowing deterioration of cartilage from osteoarthritis
- Improving mobility
- Stimulating the production of proteoglycans, glycosaminoglycans, and synovial fluid

With such great news spreading very quickly, the glucosamine industry became very large. Almost every major nutraceutical product, and today it can be bought in just about every food store, health food store, vitamin store, wellness clinic, and chiro

All glucosamine products are not the same. There are six main factors that you need to analyze when selecting a glucosamin

- Amount of glucosamine per daily dose
- Type of glucosamine
- Quality of Ingredients
- Delivery System
- Synergistic Ingredients
- Price Per Day

One of the most important of these factors is the system of delivery. In a rush to market these products in 1999, 2000, and 2001 put their glucosamine in pill or capsule form. However, with glucosamine and all other vitamins and supplements, it is well effectively than solids. Absorption is a very important to look at, simply because if you are not absorbing the glucosamine, how much you take.

3 Q. Why is better, stronger, healthier cartilage important?

A. When your cartilage is damaged, either as a result of primary osteoarthritis or flowing from an injury (secondary osteoarthritis), you will suffer the consequences. Since cartilage protects the bones from coming into contact with one another, the opposite result is extremely painful. In a great many cases, it can result in surgery.

As your cartilage begins to lose its "fluid-like" capabilities, the process of osteoarthritis begins. Whether the result of aging, genetics, overuse or injury, some 70 million Americans suffer from this debilitating condition. Whether you suffer from this condition or are trying to prevent it, every step that you can take to avoid the consequences is well worth it.

Q. What exactly IS glucosamine?

A. Glucosamine is a charged sugar molecule that is a key component of the extra cellular matrix of cartilage (ground between the cartilage cells). It absorbs and releases water with each step, thereby acting as a shock absorber for the joints. Glucosamine is a natural sugar produced by your body. It is the essential and principal ingredient that determines the quantity of proteoglycans (water-holding) molecules that also form in the body. The greater the amount of glucosamine in the body, the greater the amount of proteoglycans. The proteoglycans are large, water-binding molecules made up of (both) proteins and sugars. It is important to understand that they are a major building block of healthy, vital cartilage. Glucosamine also stimulates the production of glycosaminoglycans (GAG's), which are important proteins found in

empty

Glucosamine for joint health 2

empty

220

Why is healthy cartilage important 3

221

What Are the Different Types of Non-Pharmacological Pain Management

What Are the Different Types of Non-Pharmacological Pain Management

<http://www.wisegeek.com/what-are-the-different-types-of-non-pharmacological-pain->

Non-pharmacological pain management refers to different methods utilized to either decrease a patient's pain or increase his functional abilities despite subjective complaints of pain. These techniques can be employed for pain control, either on their own or as adjunct measures in combination with drugs. Methods of non-pharmacological pain management do not include the "just grin and bear it" method or stoicism. Patients are taught to control, distract or distance themselves from their pain, not simply ignore it. Non-pharmacological pain management methods include exercise, stress reduction,

Methods of non-pharmacological pain management that do not require medical intervention include relaxation techniques, stress reduction and exercise. Relaxation exercises are frequently taught to the patient experiencing pain using a biofeedback system to provide positive reinforcement as the skills are mastered. Patients then often utilize a recording of a progressive relaxation exercise to reach their maximum attainable level of comfort. Reducing or eliminating areas of emotional stress is suggested. Patients are also strongly encouraged to perform whatever kinds of exercise are available to

There are some non-pharmacological pain management techniques that are medically based or require special training to perform. Acupuncture, for instance, requires training on the part of the therapy provider but provides relief or reduction of pain symptoms for some patients. Transcutaneous nerve stimulation (TENS) therapy seeks to “lose” nerve signals for pain under the distraction of competing electrical signals. In some cases, the nerve or nerves that transmit the pain impulse are blocked with anaesthesia. A permanent treatment of this type involves surgical interruption of the pain sensation by cutting. Most methods of non-pharmacological pain management are not introduced to patients with time-limited acute pain conditions, such as a post-operative recovery periods. They play, however, a much larger role in the lives of cancer patients and patients in chronic pain who often report years of increasing pain and disability in performing activities of daily living (ADLs). Non-pharmacological pain management techniques are more important to the rehabilitation of patients in chronic pain, as opposed to acute pain, because of the negative consequences of long-term pain medication use. Furthermore, these techniques are under the control of the patient and are a part of the overall philosophy of the patient controlling his pain, as opposed to pain controlling the patient’s life. Regaining some degree of control is associated with

222

empty

223

What Are the Different Types of Natural Pain Management

What Are the Different Types of Natural Pain Management

<http://www.wisegeek.com/what-are-the-different-types-of-natural-pain-management.htm>

Among the many different types of natural pain management are hypnotherapy, meditation, acupuncture, deep breathing exercises and natural dietary supplements. Music therapy and guided imagery are also deemed to be useful for pain treatment. Chiropractic adjustments and restful sleep are also sometimes recommended for use as natural pain management. Among the many different types of natural pain management are hypnotherapy, meditation, acupuncture, deep breathing exercises and natural dietary supplements. Music therapy and guided imagery are also deemed to be useful for pain treatment. Chiropractic adjustments and restful sleep are also sometimes recommended for use as natural pain management. Researchers specializing in pain management, also known as algiatry, have found that the mind/body connection, and the perception of pain between the two, greatly contributes to the actual experience of pain. While pain medicine is often prescribed for pain, patients experiencing chronic pain often benefit from disciplining the mind in such a way as to minimize pain. This type of natural pain management is often accomplished through hypnotherapy and guided imagery. Natural pain management is often useful in treating acute pain, such as that which is associated with childbirth and minor injuries. Along with medical treatment, individuals may also rely on guided imagery, deep breathing exercises and music therapy to reduce the perception of pain. Lamaze coaches even assist with breathing exercises and guided imagery during

Medical practitioners will often recommend natural pain management for patients with adverse side effects to other pain medications, such as nausea, vomiting and loss of appetite. Learning certain energy therapies, such as Reiki, and engaging in natural pain management techniques like acupuncture are often helpful ways of reducing pain for those who do not tolerate medications well. Additionally, techniques like meditation, hypnosis and guided imagery help relieve stress and Pain often interrupts normal sleeping patterns. A lack of sound rest, however, may also exacerbate the perception of pain. In an effort to help patients manage pain, doctors sometimes recommend treatments to increase restful sleep. Dietary changes and supplements may also be an effective source of natural pain management for some people. For instance, foods high in antioxidants are believed to help relieve menstrual pain. Foods with anti-inflammatory ingredients, such as the Omega-3 fatty acids found in certain types of fish, are also believed to be helpful as natural sources for pain management for conditions such as arthritis and other inflammatory conditions. Nutritionists and natural health practitioners often recommend a diet rich in these foods for natural pain management or may advise patients to try taking

empty

empty

Are There Many Advantages And Disadvantages Of Holistic Therapy

Are There Many Advantages And Disadvantages Of Holistic Therapy

<http://www.readobot.com/are-there-many-advantages-and-disadvantages-of-holistic-therapy>

Knowing the advantages and disadvantages of holistic treatments may help you make an educated decision about which remedies are right for you and your loved ones. Some homoeopathic treatments are actually passed down for years and have turned into a trusted element of natural self care for lots of people.

Nonetheless, there are several homoeopathic treatments that ought to be approached with care. Not every home remedy is safe and sound for those of all ages, and some are utilized only as a final option when old fashioned medicine has failed or there are no other options. Natural options will often be extremely effective, but like any other treatment, there is also

The Pros of Homoeopathic Treatments

Homoeopathic remedies are often easily accessible, low-priced, and easy on your body. The majority of people who utilize homoeopathic treatment options enjoy not having to visit a doctor and take unpleasant fabricated medications for common. Actually, many advocates of homoeopathic treatments say these natural treatments are more advantageous than conventional medicines solutions. Homoeopathic therapies are most often gathered from all natural ingredients which can be more in balance with the body's all natural functioning, and work by solving problems at the source instead of simply. A large number of homoeopathic treatments are fairly harmless, even if they aren't fully effective, since they are composed of natural elements. For instance, if you treat an earache with a beeswax candlestick, but later discover the earache was a consequence of seasonal allergies, the holistic treatment may cause no harm to your body's typical functioning.

The Drawbacks of Holistic Treatments

However, in spite of the many advantages of holistic treatments, there are many drawbacks. Homoeopathic remedies are not regulated by any sort of governing agency, and so are not consistent. If you buy a homoeopathic remedy, there isn't any guarantee that the formula and ingredients are precise, nor is there any sort of proof that the treatment method will work as described. Lots of scammers take advantage of consumers' desires to heal the body with all-natural medicine by developing. Although holistic treatments are made from nature, it is essential to note that some concentrated traditional medicines (and poisons) are made from nature as well. A lot of plants are toxic to humans, and life-changing drugs such as digitalis are created from plant extracts. St. Johns Wart is a very common homoeopathic treatment for depression that, when taken incorrectly, can lead to overdose or adverse reactions that could require emergency medical care.

Using holistic treatments is a superb way to take a natural approach to treating the body and treating problems without harsh medications. Nonetheless, holistic treatments must be used with great care and respect for the energy of natural

Why Should People Select Holistic Medicine

Why Should People Select Holistic Medicine Posted by Pearlyn Goodman-Herrick

<http://homeopathyamerica.wordpress.com/2012/12/18/why-should-people-select-holistic-medicine/>

A lot of people who find that they are not feeling well decide to visit a doctor for assistance. They might search for over the counter medicine at a pharmacy that might help them. Nevertheless, there is another choice that they can consider.

There are several reasons people should think about using homoeopathic treatments in order to address health issues they

Homoeopathy operates by stimulating the body's healing reply to disease. Homoeopathic remedies are specially prepared and extremely diluted. These treatments do not have side effects. Lots of prescribed drugs and some over the counter medications have side effects that are worse than the health conditions that cause people to take them.

Homoeopathy manages the entire person, not only the disease. This is something that many conventional medical providers don't support. It can be used to treat allergies, eczema, hay fever, severe headaches, stress, cuts, irritable bowel, and plenty of other conditions. Remedies have been regulated since 1938 in America and are safe. They're composed of plant extracts, animals, minerals, and other substances. They can also include water and alcohol.

Individuals who use homoeopathic remedies can have a sense of self mastery and independence because they can treat their selves instead of having to rely on medical researchers for everything. This can permit them to have more time to do other things since they will not have to spend time waiting in a doctor's office. It is typically very liberating for people to understand that they have the ability to help themselves or the ones they care about recuperate.

Natural options are simple to disburse. Much of the times kids love the tastes and usually do not fuss about taking them. Some over the counter and medications taste awful and are hard to dispense. Loads of kids try to escape when it is time for them to take their medicine. Parents can feel stressed and uncomfortable about having to disburse non-prescription

228

empty

229

Holistic and Naturopathic Treatments

Holistic and Naturopathic Treatments by Pearlyn Goodman-Herrick

Information: Holistic treatment focuses on bringing you back into balance

<http://homeopathyamerica.wordpress.com/2012/03/25/pros-and-cons-of-homeopathic-remedies/>

Pros and Cons of Homoeopathic Remedies

Knowing the pluses and minuses of homoeopathic treatments will help you make an informed decision about which treatments are right for you and your family. Some homoeopathic treatments are actually passed down for years and have turned into a trusted component of natural self care for lots of people.

Even so, there are numerous holistic treatments that ought to be approached with extreme caution. Not every home therapy is harmless for those in various age groups, and some are utilized only as a final option when old fashioned medicine has failed or there are no other options. Natural options are sometimes quite effective. but like every other treatment. there is

The Pros of Homoeopathic Treatments

Homoeopathic treatment in San Francisco are often easily accessible, inexpensive, and easy on your body. Lots of people who make use of homoeopathic cures enjoy not needing to visit the doctor and take harsh fabricated medications for The truth is, many advocates of homoeopathic treatments say these natural treatments are better than conventional medicine's solutions. Homoeopathic treatments are often gathered from all-natural ingredients that are far more in balance with the body's natural functioning. and get the job done by repairing problems at the source instead of just treating A lot of homoeopathic therapies are fairly safe, even if they aren't fully effective, because they are comprised of natural elements. For example, if you treat an earache with a beeswax candlestick, but later find the earache was a consequence of seasonal allergies, the homoeopathic treatment will cause no injury to your body's normal functioning.

The Cons of Holistic Treatments

However, regardless of the many benefits of holistic treatments, there are several drawbacks. Homoeopathic remedies usually are not regulated by any sort of governing agency, and therefore are not consistent. If you do buy a homoeopathic therapy, there is absolutely no guarantee that the formulation and substances are accurate, nor is there any proof that the treatment method will work as described. A lot of scammers benefit from consumers' hopes to heal the body with pure medicine by developing false statements and malfunctioning products defined as homoeopathic treatments. Although homoeopathic treatments are created from nature, it is very important note that some powerful standard medicines (and poisons) are made from nature at the same time. A large number of plants are toxic to humans, and life-altering medicines such as digitalis are made from plant extracts. St. John's Wart is a really common holistic treatment for depression that. when taken erroneously. can lead to overdose or complications that could require unexpected emergency Making use of holistic treatments is a fantastic way to take an all-natural approach to curing the body and treating problems without harsh drugs. Still, homoeopathic treatments should be used with great care and reverence for the power

230

empty

231

Medicinal

232

Empty page

233

MEDICINAL PLANTS

MEDICINAL PLANTS

Traditions of yesterday - drugs of tomorrow

Medicinal plants: Traditions of yesterday and drugs of tomorrow Ameenah Gurib-Fakim

Faculty of Science, University of Mauritius, Reduit, Mauritius

Review

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of->

Abstract

Conclusion

1. Introduction

Throughout the ages, humans have relied on Nature for their basic needs for the production of food stuffs, shelters, clothing, means of transportation, fertilizers, flavors and fragrances, and, not the least, medicines.

Plants have formed the basis of sophisticated traditional medicine systems that have been in existence for thousands of years and continue to provide mankind with new remedies.

Although some of the therapeutic properties attributed to plants have proven to be erroneous, medicinal plant therapy is based on the empirical findings of hundreds and thousands of years.

The first records, written on clay tablets in cuneiform, are from Mesopotamia and date from about 2600 BC; among the substances that were used were oils of

Cedrus species (Cedar) and *Cupressus sempervirens* (Cypress), *Glycyrrhiza glabra* (Licorice), *Commiphora* species (Myrrh) and *Papaver somniferum* (Poppy juice), all of which are still in use today for the treatment of ailments ranging from coughs and colds to parasitic infections and inflammation. Egyptian medicines report on the use of bishops weeds (*Ammi majus*) to treat vitiligo, a skin condition characterized by a loss of pigments. More recently, a drug (b-methoxypsoralen) has been produced from this plant to treat psoriasis and other skin disorders, as well as T-cell

lymphoma. The interest in Nature as a source of potential chemotherapeutic agents continues. Natural products and their derivatives contribute no less than 25% of the total. During the last 40 years, at least a dozen potent drugs have been derived from flowering plants including *Dioscorea* spp.—derived diosgenin from which all oral contraceptive agents have been derived; reserpine and other anti-hypertensive and tranquilizing alkaloids from *Rauwolfia* species; pilocarpine to treat glaucoma and dry mouth, derived from a group of South American trees (*Pilocarpus* spp.) in the *Citrus* family; two powerful anti-cancer agents from the Rosy Periwinkle (*Catharanthus roseus*); laxative agents from *Cassia* sp. and as a cardiotonic agent to treat heart failure from *Digitalis* species. Approximately half (125,000) of the world's flowering plant species live in the tropical forests. Tropical rain forests continue to support a vast reservoir of potential drug species. They continue to provide natural product chemists with invaluable compounds of starting points for the

Use of herb since antiquity to date ...

Use of herb since antiquity to date ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of->

2. Use of herb since antiquity to date

The vast majority of people on this planet still rely on their traditional materia medica (medicinal plants and other materials) for their everyday health care needs. It is also a fact that one quarter of all medical prescriptions are formulations based on substances derived from plants or plant-derived synthetic analogs, and according to the WHO, 80% of the world's population—primarily those of developing countries—rely on plant-derived medicines for their healthcare. It is likely that the profound knowledge of herbal remedies in traditional cultures developed through trial and error over many centuries, and that the most important cures were carefully passed on verbally from one generation to another. The history of pharmacy was for centuries identical with the history of pharmacognosy, or the study of materia medica, which were obtained from natural sources—mostly plants but minerals, animals, and fungi. Pharmacognosy was for the first time *Sometimes this concept worked:*

Chelidonium majus

, contains yellow flowers and a yellow alkaloid containing latex, and has been used successfully to treat jaundice. People who use traditional remedies may not understand the scientific rationale behind their medicines, but they know from personal experience that some medicinal plants can be highly effective if used at therapeutic doses.

Since we have a better understanding today of how the body functions, we are thus in a better position to understand the healing powers of plants and their potential for their potential as multi-functional chemical entities for treating complicated. Medicinal plants typically contain mixtures of different chemical compounds that may act individually, additively or in

A single plant may, for example, contain bitter substances that stimulate digestion, anti-inflammatory compounds that reduce swellings and pain, phenolic compounds that can act as an antioxidant and venotonics, anti-bacterial and anti-fungal tannins that act as natural antibiotics, diuretic substances that enhance the elimination of waste products and toxins and Modern allopathic usually aims to develop a patentable single compound or a magic bullet to treat specific conditions.

Traditional medicine often aims to restore balance by using chemically complex plants, or by mixing together several different plants in order to maximize a synergistic effect or to improve the likelihood of an interaction with a relevant In most societies today, allopathic and traditional systems of medicine occur side by side in a complimentary way.

The former treats serious acute conditions while the latter is used for chronic illnesses, to reduce symptoms and improve the quality of life in a cost-effective way.

2.1. African traditional medicine

African traditional medicine is the oldest and perhaps the most diverse of all medicine systems.

Africa is considered to be the cradle of Mankind with a rich biological and cultural diversity marked regional difference in healing practices. Unfortunately, the systems of medicines are poorly recorded and remain so to date.

Yet the documentation of medicinal uses of African plants is becoming increasingly urgent because of the rapid loss of the natural habitats of some of these plants because of anthropogenic activities.

The African continent is reported to have one of the highest rates of deforestation in the world. The paradox is that it is also a continent with a high rate of endemism with the Republic of Madagascar topping the list at 82%. African traditional medicines in its varied forms, is a holistic involving both the body and the mind.

The healer typically diagnoses and treats the psychological basis of an illness before prescribing medicines to treat the

Famous African medicinal plants include *Acacia senegal* (Gum Arabic), *Agathosma betulina* (Buchu), *Aloe ferox* (Cape Aloes), *Aloe vera* (North African Origin), *Artemisia afra* (African wormwood), *Aspalanthus linearis* (Rooibos tea), *Boswellia sacra* (Frankincense), *Catha edulis* (Khat), *Commiphora myrrha* (Myrrh), *Harpagophytum procumbens* (Devils Claw), *Hibiscus sabdariffa* (Hibiscus, Roselle), *Hymenocallis hemerocallidea* (African potato), *Prunus africana* (African Madagascar by herself has contributed with the *Catharanthus roseus* (Rosy Periwinkle) and has the potential of contributing more in view of the diversity of her flora and fauna.

2.2. American traditional medicine (North, Central and South)

2.2.1. North America

In the US, just like in any other cultures, the indigenous healer or Shaman approaches illnesses by addressing both the physical and spiritual dimension of diseases.

These Shamanistic ceremonies involve chanting, dancing and other rituals aimed at expelling evil forces so that the patient or the community as a whole can be healed.

Early settlers learnt from native practices and they eventually adopted many of the herbal remedies, which later formed the basis of the Pharmacopeia of the United States.

Among the famous medicinal plants of the United States are the Echinacea (*Echinacea purpurea*) and Goldenseal

During most of the 20th century, herbs or botanicals have been regarded with scepticism and the practice of herbal

Plants were viewed mainly as a potential source of pure chemical compounds for the development of medicine.

In recent years, herbs and botanicals have become very popular in the US and Canada but they are still considered as nutritional supplements rather than medicines in their own rights.

2.2.2. Central and South America

Just like Africa, Central and South American countries have a rich and diverse healing cultures and which are poorly known and have not been properly recorded.

They will no doubt be a source of new herbal remedies in the years to come.

South and Central America have made enormous contributions to agriculture and a large number of food crops (maize, potatoes, tomatoes, pumpkins, cassava, peanuts, sweet potato) originate from there.

Traditional Indian medicinal herbs are also used extensively but the influence of Spanish, European, Indian and African is

Famous examples of medicinal plants are:

Cinchona pubescens (Peruvian bark), *Erythroxylum coca* (Coca), *Ilex paraguariensis* (Mate), *Myroxylon balsamum* (Tolubalsam), *Paullinia cupana* (Guarana), *Peumus boldus* (Boldo), *Psidium guajava* (Guava), *Spilanthes acmella* (Brazilian cress), *Tabebuia impetiginosa* (Lapacho) and *Uncarina tomentosa* (Cat's claw).

2.3. Australian and South east Asian medicine

This region has witnessed a resurgence of interest in traditional medicine and many countries now promote research into medicinal plants as a potential source of new remedies.

The Aborigines had a complex healing system but much of the traditional knowledge in Australia was lost before it could. In contrast, many healing places like Malaysia, Thailand, Vietnam, New Zealand, Borneo, and the Polynesian Islands remain intact and are being recorded and developed.

A strong Chinese influence is being observed in most countries.

Among the well-known medicinal products originating from this region are *Croton tiglium* (Purging croton), *Duboisia hopwoodii* (Pituri), *Eucalyptus globulus* (Bluegum), *Mela-leuca alternifolia* (Tea tree), *Myristica fragrans* (Nutmeg and Mace), *Piper methv-sticum* (Kava kava), *Strvchnos nux-vomica* (Strvchnine), *Stvrax benzoin* (Benzoin) and *Svzveium*

2.4. Ayurvedic medicine (Indian Traditional Medicine)

Ayurveda is perhaps, the most ancient of all medicinal traditions is probably older than the traditional Chinese medicine. It is considered to be the origin of systemized medicine.

It is actually a practical and holistic set of guidelines to maintain balance and harmony in the system.

Dioscorides (who influenced Hippocrates) is thought to have taken many of his ideas from India.

Ancient Hindu writings on medicine contain no references to foreign medicines whereas Greek and Middle Eastern texts do refer to ideas and drugs of Indian origin.

Ayurveda is derived from the Indian words *Ayar* (Life) and *veda* (Knowledge or Science) and hence means the Science of Following the system would help ensure a long life, which is considered to be the instrument for achieving righteousness (dharma), wealth (artha) and happiness (sukha). In India, knowledge and wisdom have been passed on from one generation to the next through songs and poems, which scholars and physicians had to learn by heart and recite.

The Veda is an ancient text in four parts (Rig Veda, Sama Veda, Yajur Veda and Atharva Veda), the earliest of which date The principles of Ayurvedic medicine and the medicinal plants uses of herbs are contained in thousands of poetic hymns in The first school to teach Ayurvedic medicine was at the University of Banaras in 500 BC and the great Samhita (or encyclopaedia of medicine) was written.

700 Years later, another great encyclopaedic was written and these two together form the basis of the Ayurveda.

Ayurveda is similar to Galenical Medicine in that it is based on bodily humours (dosas) and the inner life force (prana) that is believed to maintain digestion and mental activity.

The living and the non-living environment, including humans, is composed of the elements earth (prithvi), water (jada), fire (tejac), air (vaju) and space (akasa).

For an understanding of these traditions, the concept of impurity and cleansing is also essential.

Illness is the consequence of imbalance between the various elements and it is the goal of the treatment to restore his

Famous Ayurvedic medicinal plants include *Azadirachta indica* (Neem), *Centella asiatica* (Gotu Kola), *Cinnamomum camphora* (Camphor), *Elettaria cardamomum* (ela or cardamomum), *Rauwolfiaserpentina* (Indiansnakeroot), *Santalum album* (Sandalwood), *Terminalia species* (Mvrobolan) and *Withania somnifera* (Aswargandha).

2.5. Chinese traditional medicine

The civilizations of China and India were flourishing when only modestly sophisticated cultures were developing in Expectedly writings on medicinal plants and the aesthetics of vegetation were numerous.

This ancient system of medicine, believed to be more than 5000 years old, is based on two separate theories about the natural laws that govern good health and longevity, namely yin and yang, and the five elements (wu xing).

The legendary emperor Shen Nung discussed medicinal herbs in his works—which were probably written 2500 years B.P. instead of their traditional date of 3500 B.P.

By the Traditional Chinese medicine was systematized and written between 100 and 200 BC.

The most complete reference to Chinese herbal prescriptions the Modern Day Encyclopaedia of Chinese materia medica It lists nearly 6000 drugs out of which 4800 are of plant origin.

Yin and Yang denotes opposites that complement each other.

The five-element theory is similar to the four humours and elements of the Greeks or the three humours of Ayurveda.

The five elements are earth, metal, water, wood and fire each of which is linked to the main organ systems of the body (respectively the spleen, lungs, kidney, liver and heart), the emotions (reflection, grief, fear, anger, joy), the climates (damp, drv. cold, windv. cold), the seasons (late summer, autumn, spring, summer) and tastes (sweet, pungent, salty, sour). Medicine is used to restore or maintain balance between these elements and to grant vital energy (qi) which has both yin

Treatment is therefore based not only on symptoms but also on pattern of imbalances, often detected by taking the pulse or observing the patient's tongue.

Warming or hot herbs such as ginger, and cinnamon, are used to treat ailments associated with cold symptoms such as cold hands, abdominal pains and indigestion.

In common with Western and African traditional medicines, Chinese herbs are usually given in fixed mixtures or formulas of up to 20 herbs, carefully prepared according to traditional recipes contained in ancient compendia.

There are hundreds such recipes being used alongside with Western Medicines.

As in other healing cultures, traditional recipes are used preferentially against chronic illnesses while acute or serious illnesses are cured by Western Medicines.

The spread of traditional Chinese medicine to most continents has undoubtedly contributed to the current popularity of herbal medicines throughout the world.

Examples of famous Chinese medicinal herbs are *Angelica polymorpha* var. *sinensis* (dang gui), *Artemisia annua* (qing hao), *Ephedra sinica* (ma huang), *Paeonia lactiflora* (bai shao yao), *Panax ginseng* (ren shen) and *Rheum palmatum* (da

2.6. European medicine

In the ancient Western world, the Greeks contributed significantly to the rational development of the use of herbal drugs.

However, the European healing system is said to have originated with Hippocrates (460–377 BC) and Aristotle (384–322BC), whose own ideas were rooted in ancient beliefs from India and Egypt.

The philosopher and natural scientist, Theophrastus (c. 300 BC), in his *History of Plants*, dealt with the medicinal qualities of herbs, and noted the ability to change their characteristics through cultivation. Dioscorides, a Greek physician (100 AD) during his travels with Roman armies, recorded the collection, storage and the use of medicinal herbs and Galen (130–200 AD) who practised and taught pharmacy and medicine in Rome, published no less than 30 books on these subjects, and is well known for his complex prescriptions and formulas used in compounding drugs, sometimes containing dozens of Greek and Roman medicine was based on the belief that the world is composed of four elements—earth, wind, fire and water. Each of these has its corresponding humours, linked to the four vital fluids in the body.

The four humours—blood, phlegm, black bile and yellow bile, influence both health and temperament (respectively sanguine, phlegmatic, melancholic and choleric).

In order to restore balance, drastic measures such as blood letting (reduce excess blood) and purging (to remove excess black bile) was used. The four humours were also associated with cold, heat, dampness and dryness and each of these had a corresponding range of cold, hot, damp or dry herbs that were supposedly able to restore imbalances.

European tradition also had many regional influences on local folk practices and traditions.

One of the most powerful influences was the famous book *De Materia Medica*, written by the Greek physician Dioscorides. It is generally accepted to be the first European herbal and was the standard reference in Europe for more than 1000 years, providing the base for most of the later herbals.

As early as AD 800, medicinal plants were cultivated according to a standardized layout in monasteries in Central Europe.

One of the famous healers of this era was Hildegard of Bingen (1098–1179).

In later years a Swiss alchemist known as Paracelsus (1493–1541) emphasized the importance of the correct dose for

Herbal medicine is part of everyday life in many countries in Europe and to this day has remained popular as a sophisticated and rational method of treating ailments, often considered to be supportive than curative.

In several European countries to date, the use of herbal tea is still very popular.

In addition to these, natural products taken in their crude form (unprocessed) as teas or decoction, sophisticated phytomedicines (standardized and formulated extracts of plants, often subject to rigorous testing in humans) remain a popular alternative to medicinal products derived from pure synthetic chemicals.

A large number of traditional herbal remedies in Europe have become widely known as a result of commercialization and a number of active compounds have been isolated from medicinal plants and are used today as single chemical entities.

2.7. Classical Arabic and North African traditional medicine

The oldest written information in the Arabic traditions comes from the Sumerians and Akkadians of Mesopotamia, thus originating from the same areas as the archaeological records of Shanidar IV (Heinrich et al., 2004).

The Middle East is known as the cradle of civilisation and many plants grown nowadays have been domesticated in this region. The Babylonians, Assyrians and Sumerians recorded herbal remedies in cuneiform writing on numerous clay tablets.

Of special interest is the Code of Hammurabi (ca. 1700 BC), a comprehensive set of civil laws carved in stone and commissioned by the King of Babylon.

It lists several medicinal herbs.

Similar documents have survived several millennia in Egypt.

The Egyptians documented their knowledge (including medical and pharmaceutical) in wall-paintings of tombs dating from the Old Kingdom and on papyrus, the latter being made from *Cyperus aquaticus*.

The most important of these writings is the Ebers Papyrus, which originates from around 1500 BC is reported to contain ancient medicinal knowledge from before 3000 BC.

This famous 20 m Papyrus scroll reputedly found in a tomb is inscribed in Egyptian hieroglyphics and named after Prof. Ebers Georges at Thebes in 1872.

It was brought in 1873 and deposited at the University of Leipzig and two years later G. Ebers published a facsimile

The Ebers Papyrus is a medical handbook covering all sorts of illnesses and includes empirical as well as symbolic forms

The diagnostic precision documented in this text is impressive.

If during the Dark and Middle Ages (5–12th Centuries, AD), the monasteries in countries such as England, Ireland, and Germany have preserved the remains or this Western Knowledge, it was the Arabs who were responsible for the preservation or much or the Greco-Roman expertise. and for expanding it to include the use of their own resources.

The Arabs were the first to establish privately owned drug stores in the 8th century, and the Persian pharmacists, physician, philosopher and poet, Avicenna, contributed much to the sciences or pharmacy and medicine throughout the works such as Canon medicinae, regarded as the “final codification of all Greco-Roman medicine”. Canon medicinae include elements of other healing cultures and forms the basis for a distinct Islamic healing system known today as Unani-Tibb.

Among the famous medicinal plants of the Middle East and Egypt are:

Alliumcepa (Onion), Astracantha gummifera (Tragacanth), Carthamus tinctorius (Safflower), Carum carvi (Caraway), Ferula assafoetida (Asofoetida), Lawsonia inermis (Henna), Papaver somniferum (Opium poppy), Peganum harmala (Syrian rue), Pru-nus dulcis (Almond), Punica granatum (Pomegranate), Rosa x damascena (DamaskRose), Ricinus communis (Castor Oil Plant). Salvadora persica (Toothbrush tree). Senna alexandrina (Senna). Sesamum indicum

236

Book - Medicinal plants Traditions of yesterday and drugs of tomorrow

Medicinal plants: Traditions of yesterday and drugs of tomorrow Ameenah Gurib-Fakim

[http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-Faculty of Science, University of Mauritius, Reduit, Mauritius](http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-Faculty-of-Science, University of Mauritius, Reduit, Mauritius)

2005 Elsevier Ltd. All rights reserved.

Review

Contents

1. Introduction	32.	Use of herb since antiquity to date
.	42.1.	African traditional medicine
American traditional medicine (North, Central and South)	62.2.1.	North America.
.	62.2.2.	Central and South America
72.3.		Australian and South east Asian medicine
72.4.		Ayurvedic medicine (Indian Traditional Medicine)
.	72.5.	Chinese traditional medicine.
82.6.		European medicine
22. Cancer drugs from plants	6223.	Plants used against infectious diseases
.	6923.1.	Anti-malarial properties
.	6923.2.	Plants and AIDS
.	7324.	Medicinal plants, functional foods and nutraceuticals
7624.1.		The functional food concept
7724.2.		Categories of botanical functional food ingredients
.	7724.3.	Traditional functional foods
	7824 3 1	Vitamins
	8025	The need

237

Medicinal plants: Traditions of yesterday and drugs of tomorrow - Author Ameenah Gurib-Fakim

Medicinal plants: Traditions of yesterday and drugs of tomorrow - Author Ameenah Gurib-Fakim

Review

Medicinal plants: Traditions of yesterday and drugs of tomorrow

Ameenah Gurib-Fakim

Faculty of Science, University of Mauritius, Reduit, Mauritius

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-Abstract>

Plants have provided man with all his needs in terms of shelter, clothing, food, flavors and fragrances as not the least, Plants have formed the basis of sophisticated traditional medicine systems among which are Ayurvedic, Unani, Chinese

These systems of medicine have given rise to some important drugs still in use today.

Among the lesser-known systems of medicines are the African and Australian, Central and South American amongst

The search for new molecules, nowadays, has taken a slightly different route where the science of ethnobotany and ethnopharmacognosy are being used as guide to lead the chemist towards different sources and classes of compounds.

It is in this context that the flora of the tropics by virtue of its diversity has a significant role to play in being able to

Nonetheless the issue of sovereignty and property rights should also be addressed in line with the Convention for

This paper highlights the above, provides an overview of the classes of molecules present in plants and gives some

examples of the types of molecules and secondary metabolites that have led to the development of these pharmacologically

The paper also presents some data on the use of plant products in the development of functional foods, addresses the needs for validation of plant extracts and always stressing on safety, efficacy and quality of phyto-medications.

2005 Elsevier Ltd. All rights reserved.

Keywords:

Medicinal plants; Pharmacognosy; Ethnobotany; Traditional medicine; Validation; Drugdiscovery0098-2997/\$ - see front

2005 Elsevier Ltd. All rights reserved. doi:10.1016/j.mam.2005.07.008

E-mail address:

Contents

Introduction

Use of herb since antiquity to date

African traditional medicine

American traditional medicine (North, Central and South)

North America

Central and South America

Australian and South east Asian medicine

Ayurvedic medicine (Indian Traditional Medicine)

Chinese traditional medicine

European medicine

Classical Arabic and North African traditional medicine

Ethnobotany and medicine

Ethnobotany

The search of new drugs through ethnomedicine

Value of ethnobotany and ethnopharmacology to the search for new `biodynamic compounds or new leads

Secondary plant metabolites in drug discovery

Methods used in natural product chemistry

Isolation methods

Assays used in evaluating the activity of extracts

Bioassay

Requirements for screening medicinal plant material

Common pharmacological screening methods

Characterization and structure elucidation of bioactive compounds

Important plant families having given molecules/drugs of importance

Plant parts used

Dosage forms

Modes of administration.

Phytochemistry and the modes of action of plant metabolites.

Biological and pharmacological activity and therapeutic applications

Factors affecting biological activity

Physicochemical properties

Chemical parameters

Current status of drug discovery

Plants used for the endocrine system—diabetes
Hypoglycaemic and anti-diabetic herbs.
Plants used in cardiovascular ailments.
Arrhythmias and heart failures
Heart failure, dropsy or oedema
Venous insufficiency
Anti-platelet and anti-sclerotic drugs
Plants used against problems of the CNS
Hypnotics and sedatives
Plants used against the respiratory systems
Broncho-dilators and decongestants
Immuno-stimulants
Cancer drugs from plants
Plants used against infectious diseases
Anti-malarial properties
Plants and AIDS
Medicinal plants, functional foods and nutraceuticals
The functional food concept
Categories of botanical functional food ingredients
Traditional functional foods
Vitamins
The need for validation
Quality and safety: Production, standardization and quality control
Standardisation for plant-derived ingredients in medicinal products
Why is standardization important?
Some of the existing Legal Framework for plant-derived ingredients with medicinal properties.
The World Health Organisation (WHO)
European Union (EU)
The United States (US)
Standardised extracts
Quantified extracts
Quality control
Side-effects (toxicity) of plant extracts
Adulteration
Microbial contaminations
The convention for biological diversity
Mutually agreed terms (MAT) and prior informed consent (PIC).

238

Empty page

239

Ethnobotany and medicine ...

Ethnobotany and medicine ...

[http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-](http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-3)
3. Ethnobotany and medicine

3.1. Ethnobotany

The term Ethnobotany was first used by Harshberger in 1896.

He defined it as a study of plants used by primitive and aboriginal people.

The term was broadened by Robbins, Harrington and Freire-Marreco, in 1916 and they suggested that the science of ethnobotany should include the investigation and evaluation of the knowledge of all phases of life amongst primitive societies and of the effects of the vegetal environment upon the life customs, beliefs and history of these tribal peoples. *Twenty-five years later, Jones (1941) advanced a more concise definition: "The study of the interrelationships of primitive men and plants"*. Schultes in 1967, expanded this to include the relationships between man and his ambient vegetation.

3.2. The search of new drugs through ethnomedicine

As mentioned above, plants have formed the basis for traditional medicine systems, which have been used for thousand or years in countries such as China (Chang and But, 1986) and India (Kapoor, 1990).

The use of plants in traditional medicine systems of many cultures has been extensively documented.

These plant-based systems continue to play an essential role in health care and the World Health Organisation estimates that 80% of the world's inhabitants continue to rely mainly on traditional medicines systems for their health care.

Plant products also play an important role in health care systems of the remaining 20% of the population, mainly residing in rural areas. Analysis of the data on prescriptions dispensed from community pharmacies in the US from 1959 to 1980, indicates that 25% contained plant extracts or active principles derived from higher plants and at least 119 chemical substances, derived from 90 plant species, can be considered as important drugs currently in use in one or more countries (Farnsworth et al.). Of these 119 drugs, 74% were discovered as a result of chemical studies directed at the isolation of the active substances from plants used in traditional medicine.

In addition, the use of so-called complementary or alternative herbal products has expanded in recent decades.

The isolation of the anti-malarial drug, quinine from the bark of *Cinchona* species (e.g. *C. officinalis*) was reported in 1820 by the French pharmacists, Caventou and Pelletier.

The bark had long been used by indigenous groups in the Amazon region for the treatment of fevers, and was first introduced into Europe in the early 1600s for the treatment of malaria.

There are four basic ways in which plants that are used by tribal peoples are valuable for modern medicine:

1. Plants from the tropics are sometimes used as sources of direct therapeutic agents (e.g. the alkaloid D-tubocurarine is extracted from the South American jungle plant *Chondrodendron tomentosum* is widely used as a muscle relaxant in surgery. Chemists are still unable to produce this drug synthetically in a form that has all the attributes of the natural product and therefore collection from the wild is still relied upon.

Surprisingly harvesting of medicinal plants is often less costly than artificial drug synthesis.

Another good example to illustrate this feature is Reserpine, an important hypotensive agent extracted from *Rauwolfia*. The synthesis of this molecule would cost three times as much as opposed to collection).

2. Tropical plants are also used as sources of starting points for the elaboration of semi-synthetic compounds.

An example of this would be saponin extracts that are chemically altered to produce sapogenins necessary for the manufacture of steroids. Until relatively recently, 95% of all steroids were obtained from extracts of neo-tropical yams of the genus *Dioscorea*.

3. Flora from the tropics can serve as sources of substances that can be used as models for new synthetic compounds.

Cocaine from *Coca* plants, *Erythroxylum coca*, has served as model for the synthesis of a number of local anaesthetics. New and unusual chemical substances found in plants will continue to serve as blueprints for novel synthetic substances and will prove to be increasingly important in the future.

4. Plants can also be used as taxonomic markers for the discovery of new compounds.

From a phytochemical standpoint, the Plant Kingdom has been investigated in a haphazard manner; some families have been relatively well-studied while others have been almost completely overlooked.

For example, many uses have been documented for the *Liliaceae* and the family is known to be rich in alkaloids.

Little, on the other hand is known on the *Orchidaceae*.

Some plants from the family have been investigated because of their close relationship to the *Liliaceae*.

Research has shown that they are not only rich in alkaloids but that some of the alkaloids are unique and could prove

4. Value of ethnobotany and ethnopharmacology to the search for new biodynamic compounds or new leads?

Ethnobotany and Ethnopharmacology are interdisciplinary fields of research that look specifically at the empirical knowledge of indigenous peoples concerning medicinal substances, their potential health benefits and their health risks. As can be seen, many of the plant-derived pharmaceuticals and phytomedicines currently in use, were used by native

Some of this knowledge has been documented and codified or studied scientifically.

Also of the hundreds of thousands of species of living plants, only a fraction has been investigated in the laboratory.

This poor understanding of plants is particularly acute in the tropics.

Brazil, which has some 55,000 species of plants, has reports on only 0.4% of the flora!

The importance of ethnobotanical inquiry as a cost-effective means of locating new and useful tropical plant compounds cannot be over emphasized. Most of the secondary plant compounds employed in modern medicine were first discovered. Of the 119 pure chemical compounds extracted from higher plants used in medicine throughout the world and 74% of these compounds have the same or related use as the plants from which they were derived.

The Rosy Periwinkle (*Catharanthus roseus*, Apocynaceae) represents a classical example of the importance of plants used. This herbaceous plant, native to south eastern Madagascar, is the source of over 75 alkaloids, two of which are used to treat childhood leukaemia and Hodgkins disease with a very high rate of success.

This species was first investigated in the laboratory, mainly because of its use by local people as an oral hypoglycaemic

Like the *Catharanthus*, many drugs that are commonly used today (e.g. aspirin, ephedrine, ergometrine, tubocurarine, digoxin, reserpine, atropine etc.) came through the use of indigenous medicine that is through the bioscientific

Table 1 lists just a few of the many examples of drugs derived from plants.

Thus it can be seen that the investigation of plants used for medicinal purposes by unsophisticated peoples can provide us with new biodynamic compounds that may have important applications in our society.

When one considers the importance of medicinal plants in the developing countries, it is not surprising that most of the worlds populations depends on traditional medicine for their primary health care needs. In many cases, developing countries simply cannot afford to spend millions of dollars on imported medicines.

Several African and Asian nations are now encouraging traditional medicines as an integral component of their public. Indigenous medicines are relatively inexpensive and locally available and are readily accepted by the local population.

240

Empty page

241

Secondary plant metabolites in drug discovery ...

Secondary plant metabolites in drug discovery ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-5>. *Secondary plant metabolites in drug discovery*

Although natural products, particularly secondary metabolites, have formed the basis of medicines and the presence of these compounds in the biochemistry of the plant is very often difficult to justify.

It has been suggested that these compounds may have been synthesized by the plant as part of the defence system of the plant. e.g. plants are known to produce phytoalexins as a response to attack by bacteria and fungi.

The presence of highly toxic natural products has also been highlighted in some animals namely the Amazonian frogs so as to deter predation by other animals.

Whatever the reasons for the presence of these compounds in Nature, they provide an invaluable resource that have been used to find new drug molecules.

6. Methods used in natural product chemistry

Spectroscopic methods coupled with good extraction techniques like chromatography, have contributed to the phenomenal success of natural product chemistry over the past 50 years.

A sound isolation strategy has helped in the isolation and characterisation of many bioactive molecules.

Nowadays, bioassay-guided fractionation of medicinal plants is a feature of routine in the attempt to isolate bioactive

These techniques are not only being restricted to plant sources but they are also being applied to microbial and even fungal. In practice as soon as the material is collected, in the case of plants, it needs to be identified by a taxonomist so as to ascertain the correct identity of the material.

Voucher specimens for herbarium specimens are kept.

Various parts of the plant are collected separately (leaves, flowers, stem, wood, bark, root, root bark etc.) and are dried

Quick drying avoids degradation of the components by air or by microbes.

Sometimes the plant samples are lyophilised at high vacuum, but again care must be exercised so as to avoid the excessive loss of volatile components as the latter may also exhibit interesting biological activities.

Once the material has been dried to constant weight, it is ground up to smaller particles and extracted usually using a

Nonetheless, in the process or validation or the ethnobotanical information, the utilisation by the lay people must be mimicked as far as possible so that the same natural bioactive products are extracted. This is a very critical stage in the work as if the extraction technique is not adapted, it may result in the loss of access to the. Additionally, improper extraction methods may result in the degradation of the natural product.

Numerous extraction techniques are available namely:

Cold extraction: whereby the plant material is extracted in solvent of differing polarity at room temperature.

It allows for maximum extraction of most components.

Hot percolation: the plant is heated in the solvent usually under reflux.

This extraction method allows for the extraction of a large number of metabolites, from the most insoluble material like the waxes to the lipophilic natural products.

Supercritical fluid extraction:

In this extraction technique, some gases behave as though they are liquids with solvating properties, under pressure.

In this instance, the gas commonly used is carbon dioxide, which has the advantage of being able to be blown away from the extractant after the extraction is over.

The polarity of carbon dioxide can be enhanced by adding a modifying agent such as carbon tetrachloride.

Soxhlet extraction:

Perhaps the most widely and commonly used extraction technique for the extraction of natural product.

The polarity gradient of the solvent is applied.

Although some components may be destroyed in the process, it is still the best method of extraction used in natural product

Once the extraction is complete, the extractant is usually concentrated under vacuum, for large volumes or solvents and blown down under nitrogen for small volumes, ensuring at the same time that volatiles are not lost.

Aqueous extracts are generally freeze-dried and stored at 4°C as this low temperature reduces the degradation of the

Extraction protocols may sometimes be modified depending on the type of molecules being extracted, e.g. sometimes acids may be added to extract alkaloids as their salts.

6.1. Isolation methods

Once the extract has been obtained, the activity within can be demonstrated by bioassay methods using both the crude extract or by using the fractionated extracts.

Fractionation has the added advantage of getting to the biologically active material faster.

One of the simplest separation methods is partitioning which is a widely used method as an initial extract purification step

A combination of solvents—miscible and immiscible ones are used to separate the phytochemicals making up the extract.

This method relies on the ability of the components to be either soluble in water or in the organic phase.

Chromatography

Chromatographic techniques have been instrumental in the separation of natural products.

Some of the techniques are discussed here. One of the fastest and most widely used chromatographic techniques is Thin

TLC:

This method employs glass or aluminium plates pre-coated with the sorbent (e.g. Silica gel) to varying thickness depending on the compound mixture. The compound mixture is loaded both in the preparative or analytical plates at around 2 cm from the bottom and lowered in a tank containing the solvent.

The latter migrates up the plates and separates the compound mixture according to the polarity of the components.

Several reagents are available for visualization of the separated materials.

TLC has the advantage of being a highly cost-effective qualitative technique in as much as a large number of samples can be analysed or separated simultaneously.

The few drawbacks include poor detection and control of elution compared to High Performance Liquid Chromatography

HPLC:

This method is very popular and widely used for the analysis and isolation of bioactive natural products.

The analytical sensitivity is further enhanced depending on the detector that is being used.

The detectors can be UV detection such as photodiode array (PDA), which enables the acquisition of UV spectra of eluting peaks between 190 nm to 800 nm.

PDA UV detection has the advantage of detecting even compounds with poor UV characteristics and this is particularly useful in the analysis of natural products such as terpenoids or polyketides, which may not necessarily have chromophores. Coupled with electronic library searching of compounds along with the finger-printing of biologically active extracts, HPLC becomes a very powerful quality control technique of herbal medicines.

It has now become a tool of choice for the analysis of a majority of natural products in the pharmaceutical industry.

It suffers from one drawback in the sense that it is expensive both from the machine and consumable viewpoints.

Another clean up chromatographic technique that has become increasingly popular and useful is Gel Chromatography or sometimes referred to as Size Exclusion Chromatography (SEC).

This technique employs cross-linked dextran which upon contact with a suitable solvent swells up to form a gel matrix.

The latter contains pores of a finite size allowing smaller molecules to be retained and excluding large molecules.

This method is excellent for separating out fatty acids, chlorophyll etc prior to biological assays.

This is a non-destructive method for the recovery of a high quantity of extract.

It is a method of choice for large molecules such as proteins, polypeptides, carbohydrates etc.

7. Assays used in evaluating the activity of extracts

7.1. Bioassay 7.1.1. Requirements for screening medicinal plant material

Bioassay is a very crucial stage in assessing the pharmacological actions of plant extracts and their ethnomedical uses.

In the initial stages, *in vitro* testing has priority over *in vivo* studies involving laboratory animal models.

This decision is usually based on scientific, economic and ethical grounds.

In vivo studies may be preferable at later stages of the research project but still depends on the amount and the nature of evidence or bioactivity already collected by means of, *in vitro*, studies and the quest for additional information under life. Bioactive components that are candidates for therapeutic application will still have to undergo extensive clinical and toxicological screening programmes before they can be registered as medicines.

7.1.2. Common pharmacological screening methods

There are many types of pharmacological screens.

They are specific for bacteria, fungi, protozoa, intestinal worms, viruses etc.

The efficacy of compounds against health problems such as cancer and inflammation is often probed while the effect on physiological and anatomical systems such as reproduction, digestion etc can be judged.

Among the commonly used assays are the brine shrimp, antimicrobial (bacteria and fungi) screens *amongst others*:

- Brine shrimps are small aquatic animals that can be grown in solutions similar to seawater.

In order to test the potential toxicity of the plant—and thus its probability of containing anti-cancer agents—measured amounts of plant extracts are added to containers holding known numbers of brine shrimps.

The surviving brine shrimps are counted after 6 and 24 h, and the acute and chronic LD values are calculated, respectively; this corresponds to the concentration of the compound in solution that kills 50% of the brine shrimps

- Bacteria are grown on agar medium in Petri dishes.

When measured amounts of a plant extract are placed on paper disks or in wells set on the surface of the bacteria-inoculated agar under sterile conditions, after 18–24 h, bacteria-free circles can be seen around the disk or wells, indicating. Plant extracts can also be tested for phototoxic and fungicidal activity against yeasts and other strains of fungi.

It is worth pointing out that advances in plant drug research will provide information on bioactivity in terms of molecular interactions with other target groups.

Developments in the fields of genetics, molecular biology, bioinformatics and techniques used in determining the steric structure of plant metabolites and target macromolecules appear important now.

Fundamental understanding of molecular biodiversity seems important in the process of using plant resources for drug

Animal models are being replaced by testing on cell cultures and this implies that smaller amounts of test compounds will. Also they will provide information at cellular level.

This can only lead to more extensive studies on medicinal plants.

After the screening process, a series of active extracts will need to be dereplicated (i.e. ascertain that no compounds are present that are already known and are present in the extract assayed).

Dereplication ensures that novelty is brought into the isolation process and it thus ensures that new compounds are identified and will eventually get patented.

8. Characterization and structure elucidation of bioactive compounds

Once the biological evaluation has been performed and the separation of the natural product has been achieved, the chemist will try to attempt the elucidation of the compound.

Structure elucidation depends on classical spectroscopic techniques such as:

Nuclear Magnetic Resonance (NMR) 1-D and 2-D Proton NMR as well as C-13NMR, Infra Red (IR), Mass Spectrometry
For exploring nature's chemo diversity, the situation has changed dramatically in recent years by the introduction of high throughput screening (HTS) methods.

By using molecular targets, a large number of samples (up to 100,000 in 24 h) can be screened for a single activity.

Obviously synthetic chemists are not able to produce such numbers or new compounds.

Their answer was the development of combinatorial chemistry and testing mixtures of compounds obtained through this novel solid-phase chemical synthetic methods.

HTS offers new possibilities for natural products. It allows rapid screening of large number of extracts and it is very suitable for bioassay-guided fractionation. which in the past was the major bottleneck in studies of active compounds in
Powerful chromatographic methods in combination with HTS are now a very efficient way to new leads for drug

Searching data bases such as Chemical Abstracts, NAPRALERT as well as the Dictionary of Natural Products ensure that no time is wasted on re-investigating existing and known molecules.

These databases lead to primary literature information ranging from molecular weights to spectroscopy data, which help to recognize common metabolites at an early stage.

Structure-elucidation is crucial in assessing the biological activity of the molecule as it is a well-known fact that biological activity depends to a large extent on the 3-D arrangement of functional groups on the molecule.

9. Important plant families having given molecules/drugs of importance

Apiaceae

(previously known as the Umbelliferae):

Originating from the temperate regions of the world, this family, comprising of some 3000 mostly herbaceous species, has given rise to many of the common spices and herbs used to date.

The plants are aromatic and rich in essential oils.

Among the common herbs used medicinally are the following:

- Caraway (*Carum carvi*)—Used against bloats
- Coriander (*Coriander sativum*)—Carminative
- Fennel (*Foeniculum vulgare*)—Mildly Carminative
- Anis (*Pimpinella anisum*)—Expectorant, Spasmolytic, Carminative

Apocynaceae:

This family has wide distribution both in temperate and tropical regions of the world.

Among the world famous species is the Rosy Periwinkle (*Catharanthus roseus*).

Members of this family are well known for their alkaloidal contents with potent pharmacological activity.

Araliaceae:

This family is of over 700 species widely distributed in both the tropical and subtropical parts of the world.

The best-known European specimen is the Ivy (*Hedera helix*).

Another world famous species of this family is the Ginseng (*Panax ginseng*).

In the tropics there are several endemic species of the Araliaceae family, which are classified as being heterophyllous plants—plants having differing foliage shapes and sizes on the same plant.

The reasons for this phenomenon are still unknown.

Phyto-pharmacologically, these plants are characterized by the presence of saponins, triterpenoids and some acetylenic

Panax ginseng owes its pharmacological activity to the triterpenoids (ginsenosides) and the secretolytic activity effect of *H. helix* is partly responsible to the presence of saponins (hederasaponins).

Areaceae(Palmae):

The Palm family which comprises of some 2700 species almost exclusively woody is an important family as it includes many species widely used as food and over the past years at least one of its members has become medicinally important. The Saw palmetto (*Serenoa repens*) is now being used for difficulty in micturition in benign prostrate hyperplasia in the Phytopharmacologically, the plant is known to accumulate polyphenols, some relatively simple alkaloids (especially pyridine derivatives) and steroidal saponins as well as fatty acids.

The pharmaceutical use of the Saw palmetto seems to be due to the presence of a relatively large amount of the

Asphodelaceae:

(Members from this family have often been grouped under the Liliaceae family).

This family, with about 600 species, is widely distributed in South Africa and some species occur in the Mediterranean. The best-known members in this family are Aloe vera and *A. ferox*.

This family, with about 600 species, is widely distributed in South Africa and some species occur in the Mediterranean. The genus Aloe is characterized by the presence of polysaccharides accumulating in the leaves as well as anthranoids and anthraglycosides (aloe-emodin).

Contrary to other related families, the Asphodelaceae do not accumulate steroidal saponins.

Asteraceae:

(The Daisy family and previously known as the Compositae family).

This large family comprises of some 25,000 species and 1400 genera and is distributed and is well represented in most. Phytochemically, this family is characterized by the presence of polyfructanes (especially inulin) as storage carbohydrates as opposed to polysaccharides, in the perennial taxa.

In some taxa, some segments of the family accumulate sesquiterpene lactones (e.g. Parthenolides), which are important natural products responsible for the pharmacological activity of many botanical drugs e.g. Fever few (*Chrysanthemum*). Some taxa accumulate pyrrolizidine alkaloids e.g. in the *Senecio* species and these compounds are known for their

Other taxa accumulate unusual diterpenoids e.g. the diterpene glycoside—Stevioside, known for its intensely sweet taste.

GymnospermsGinkgoaceae: (The Ginkgo family)

This family is perhaps the most ancient of the seed bearing plants and had been widely distributed in the Mesozoic.

Only one species exists today.

Phytochemically, this plant is characterized by the presence of the ginkgolides which are unusual two-ringed diterpenoids. Biflavones and glycosylated flavonoids are other groups of typical natural products.

Ginkgolide C Hypericaceae:

This family of some 900 species, distributed both in the temperate and tropical regions, has gained importance by virtue of at least one of its members—St. Johns Wort (*Hypericum perforatum*).

This plant has become one of the most important medicinal plants in the 20th century.

Phytochemically, several members of this family contain resins, balsam and the flowers contain naphthodianthrones e.g. hypericin and pseudohypericin—characteristic of the *Hypericum* genus.

Hyperforin Hypericin Lamiaceae:

This family, with over 5000 species, has been one of the most important ones in the contribution of medicinally important. They are aromatic and have also yielded commercially important essential oils.

Several species accumulate Rosmarinic acid and other derivatives of Caffeic acid.

Rosmarinic acid is one some pharmaceutical importance because of its non-specific complement activation and inhibition of leukotrienes (leading to an anti-inflammatory effect).

Papaveraceae:

This rather small family has produced a multitude of pharmacologically important genera (e.g. *Chelidonium* *Glaucium*)

This family is particularly rich in the isoquinoline alkaloids including morphine, papaverine, codeine, thebaine and

Other alkaloids present include the benzyloquinoline (papaverine, noscapine).

Some of the isolated molecules from these plants have been particularly useful and are:

- Celidone (Chelidonium majus)—employed as a cholagogue.
- Morphine and other alkaloids (Papaver somniferum)—well known analgesic and potent narcotics.

Morphine Piperaceae:

The Pepper family consists of herbs and shrubs comprise some 2000 species is mostly restricted in the tropics. An important genus is the Piper.

This family is also characterized by pungent acidic amides such as piperine and also essential oils present in many

Some of the isolated molecules from these plants are:

- Kavain (Piper methysticum)—well known in Oceania for conditions of nervous anxiety.

Rhamnaceae:

This family consists of trees and comprises some 900 species.

An important genus of this family is the Rhamnus.

This family is known to accumulate anthraquinones.

Alkaloids of the benzyloquinoline type and the cyclo-peptide type are also known from many taxa.

- Rhamnus species (R. purshiana and R. frangula) are used as strong purgatives.

Rubiaceae:

This large family of over 10,000 species, has yielded one of the most important stimulants—Coffee (Coffea arabica and C. Another medicinally important species having been brought into the Old World is the Cinchona bark, extracted from The Rubiaceae is characterized by the presence of iridoids (a group of monoterpenoids), alkaloids (including indole alkaloids such as Quinine from Cinchona species), methylxanthines such as caffeine, theobromine, theophylline and

Rutaceae:

This family comprises of some 1700 species distributed throughout the world but the tropics are particularly rich in them. Perhaps the most well known examples from this family are the Citrus with orange, lime, grapefruit, mandarin etc. This family is characterized by essential oils found in the secretory cavities in the pericarp and parenchyma. Alkaloids are also found and among them are the benzyltetrahydroxyisoquinoline, acridone and imidazole types.

Furano- and pyrano-coumarins e.g. bergapten as well as other simple coumarins have been isolated from Citrus species.

- Pilocarpine (Pilocarpus jaborandi) has been used in ophthalmology.

Many species from this family have been used as aromatic plants in perfumery and also as foods.

Pilocarpine Solanaceae:

- Pilocarpine (Pilocarpus jaborandi) has been used in ophthalmology.

Important genera of this family include Atropa, Datura and Hyoscyamus.

Some of the pharmacologically active molecules isolated from these genera include the following:

Atropine (Atropa belladonna) Nicotine (Nicotiana tabacum)

Zingiberaceae:

This family, distributed throughout the tropics, is rich in essential oils with terpenes (borneol, camphene and cineole (all oxygen-containing monoterpenes), sesquiterpenes (zingiberene) and phenyl propanoid derivatives (cinnamic acid

Important medicinal plants from this family are the following:

Ginger (*Zingiber officinalis*)—used against a large variety of illnesses including travel sickness.

Elaiti (*Elettaria cardamomum*)—used as a spice but also as a medicine.

Turmeric (*Curcuma longa*)—used as a spice and useful against inflammatory and liver diseases in most Asian medical systems for a large variety of illnesses.

10. Plant parts used Root:

The fleshy or woody parts of many species are used medicinally. Roots maybe fibrous (Urtica dioica or U. radix of the Urticaceae family, Stinging nettle), solid (Glycyrrhiza glabra of the Leguminosae family, Liquorice) or fleshy (Harpagophytum procumbens of the Pedaliaceae family. Devils claw).

Medicinally important rhizomes include Kava kava (*Piper methysticum* of the Piperaceae family) and the Ginger (*Zingiber officinalis* of the Zingiberaceae family).

Bulb:

A bulb is the fleshy structure made up of numerous layers of bulb scales which are leaf bases.

Bulbs popular for medicinal use include the Onion and Garlic (*Allium cepa* and *A. sativum* respectively, both of the *Tuber:*

A tuber is a swollen, fleshy structure below the ground, usually of stem origin but often partly stem and partly roots.

The African Potato (*Hypoxis* sp. of the Hypoxidaceae family) is a well known example.

Bark:

The bark is the outer most protective layer of a tree trunk and is formed by layers of living cells just above the wood itself.

There are usually high concentrations of the active ingredients in the bark and several examples of the bark exists e.g. the Quinine bark (*Cinchona* sp., Rubiaceae) and Cinnamon and Camphor (*Cinnamomum camphora* and *C camphora* both of *Wood:*

The wood is the thick stem or the wood itself. Important examples of useful woods include Sandalwood (*Santalum album* *Leaf:*

The leaves can sometimes be used alone or mixed with the petiole.

Example of plants where only the leaves are used is the Ginkgo (*Ginkgo biloba* of the Ginkgoaceae family).

Aerial parts:

All parts of the plant found above the ground are referred to as the aerial parts.

Very often the plants, which have useful aerial parts, are harvested when flowering.

One such example is the St. Johns Wort (*Hypericum perforatum* of the Hypericaceae family).

Flowers:

Flowers are very commonly used and popular in traditional medicine.

Several flowers commonly used in medicine include the Clove (*Syzygium aromaticum*, Myrtaceae), Camomille flower (*Chamaemelum nobile*, Asteraceae), Roselle (*Hibiscus sabdariffa*, Malvaceae), and the Marigold (*Calendula officinalis*, *Fruit:*

Fruit:

Among the most commonly used seeds, one finds the following:

Aniseeds (*Pimpinella anisum*) and the Fennel fruit (*Foeniculum vulgare*) both of the Apiaceae family.

In some instances, the fruit peel is used specifically, e.g. Pomegranate (*Punica granatum*, Punicaceae) and the fruit peel of Citrus fruits (*Citrus* sp., Rutaceae).

Seeds:

Seeds are contained in the fruit and in some instances are used by themselves.

Examples exist for the use of the seeds e.g. Castor oil (*Ricinus communis*, Euphorbiaceae), and the seeds of the Fennel

Gum:

Gums are solids consisting of mixtures of polysaccharides.

Gums sometimes flow from a damaged stem as a defence mechanism or sometimes as a protective system against the invasion of bacteria and fungal rots.

Well known examples of gums are Gum Arabic (*Acacia Senegal*, Leguminosae), Benjoin (*Terminalia bentzoe*, Combretaceae) and Aloe gel (*Aloe vera* gum of the Liliaceae family mixed with water).

Resins:

Resins are excreted from specialized cells or ducts in plants.

They consist of a mixture of essential oils and polymerized terpenes, usually insoluble in water.

Well-known examples of resins since Biblical times include Frankincense (*Boswellia sacra*) and Myrrh (*Commiphora myrrha*) both of the Burseraceae family.

Fatty oils:

These are non-volatile, insoluble oils pressed either from the seeds or from the fruits of plants.

Oils are often referred to as acylglycerides because they are derived from glycerol molecules.

Olive oil is a useful example in as much as these oils over their own therapeutic potential are also used in carriers as liquid

Essential oil:

These are volatile oils usually extracted from plants through a process of either steam distillation or microwave extraction.

They consist of terpenes (mono- and sesquiterpenoids and coumarins).

They are of considerable importance as active ingredients of medicinal plants.

Well known examples include Peppermint oil (*Mentha x piperita*, Lamiaceae), Ylang ylang oil (*Cananga odorata*,

11. Dosage forms

Extracts

Extracts are made either in liquid, powdered or viscous forms from the crude mixtures plant parts.

The chemical compounds can then be extracted from plant material using water or organic solvents such as alcohol

Volatile oils

Volatile oils are extracted by steam distillation or less often by solvent extraction.

The herb to extract ratio (HER) is typically 5:1 for normal extracts, or say 100:1 for a herb with 1% essential oil.

The extract draws its origins from tradition but it is still commonly used today.

Mixtures

Mixtures are products with medicinal properties and which contain 2 or more plants or herbs that can act individually, additively or even synergistically to restore or maintain health.

In Chinese, Indian and African Traditional medicines, medicinal plants are typically used in mixtures.

Teas

Teas or Infusions prepared by steeping herbs in boiling water.

They are called Teas because of the similarity in preparations.

Decoction

Decoction refers to a preparation that is made by adding cold water to the required amount of the drug and then boiled and allowed to simmer for 5–10 min.

The mixture is strained afterwards.

Maceration

Maceration refers to a preparation made by adding cold water to the required amount of the drug, which is allowed to soak at room temperature for 6–8 h before it is strained.

Juice

Juice is prepared by crushing the freshly harvested plant parts and then expressing the juice.

The product can be pasteurized or treated at ultra-high temperatures to extend their shelf-life.

Syrup

Syrup is a preparation containing about 66% sucrose and generally has a viscous consistency.

Saturated sugar solutions

Saturated sugar solutions are free of micro-organisms because no free water for microbial growth is available.

Syrups are mainly used as flavoring agent to mask an unpleasant taste of other ingredients.

When used as a cough mixture, it is slowly sipped so as to allow maximum contact with the inflamed mucous membrane.

Tincture

Tincture refers to an alcoholic solution (usually 30–70% water) prepared from medicinal plant materials.

The herbal mixture is extracted for an indefinite period after which it is pressed and/or strained to separate the liquid and

A mother tincture is prepared by using 70% ethanol and the solution is then diluted with clean water to a predetermined

Glycerides may be prepared by using glycerol as opposed to the alcohol.

Medicinal essences

Medicinal essences are volatile compounds dissolved in alcohol or alcohol-water mixtures.

Medicinal spirits

Medicinal spirits are produced by mixing aromatic herbs with alcohols and then recovering the alcohol and volatile

Capsules

Capsules are usually small but soft or hard containers normally made from gelatin.

They contain medicinal products or extracts in a predetermined dose and also to protect them from air, light and moisture.

Tablets

There are two types of tablets—uncoated and coated tablets.

Uncoated ones are made by compression of powdered active material after addition of a suitable inert excipient or binder (to provide bulk) and sometimes also other additives to improve colour, flavor or disintegrators to ensure that the tablet

Pills

Pills are made by dividing semi-solid preparations into smaller portions of pre-determined size or weight, or rolling the portions before allowing them to harden.

The manufacture of pills is now fully mechanized.

Suppositories

Suppositories are tablet-like products usually oblong to oval in shape and that are intended for inserting into the rectum, vagina or urethra and left there to melt.

Herbal products are rarely used in this form.

Ointments

Ointments are usually semi-solid preparations aimed at external application.

They usually contain medicinal substances in a suitable carrier substance (watery or oily solvents).

Poultice

Poultice is a paste made from the crushed fresh plant.

It can either be mixed with oil, alcohol or simply made in water and applied on the parts of the body.

12. Modes of administration

Oral:

A decoction, infusions, tinctures, syrups and tablets are most often taken orally and sometimes sublingually.

Nasal

(Smoking, snuffing or steaming): Essential oils suspended in hot liquids or powdered materials may be snuffed so that the active compounds are absorbed through the mucosa.

Smoke

Smoke from burning materials is inhaled and the active compounds absorbed into the lungs (in the same way that nicotine

Topical:

Lotions, oils or creams containing extracts of medicinal plants are applied directly to the skin, where the active compound

Rectal:

The liquid preparations can be administered as enemas.

The active compounds are absorbed by the mucous membrane of the rectum.

In some instances, depending on the nature of the extracts, it may be desirable to bypass the stomach.

Bathing

Herbs or herbal extracts may be added to bath water.

Subcutaneous or intramuscular injections:

Some phytomedicines (often pure chemical entities derived from medicinal plants) are injected into the bloodstream.

Interestingly, sometimes some compounds are completely inactive when taken through the mouth and yet highly active

The meat killed from the killed animals is harmless to eat.

242

Empty page

243

Phytochemistry and the modes of action of plant metabolites ...

Phytochemistry and the modes of action of plant metabolites ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of->

13. Phytochemistry and the modes of action of plant metabolites

Phytochemistry deals with the chemistry of plant metabolites and their derivatives. The metabolic system of a plant may be regarded as being constituted of regulated processes within which biochemical conversions and mass transfer take place. Understanding in this field has advanced to a stage in which definite metabolic processes, biosynthetic pathways and their interconnections are distinguished and studied in the context of their function and genetic control.

The metabolic performance of living organisms can be distinguished into primary metabolism and secondary metabolism.

Primary metabolism is associated with fundamental life processes common to all plants. It comprises processes such as photo-synthesis, pentose cycle, glycolysis, the citric acid cycle, electron transport, phosphorylation and energy regulation

Primary metabolites are produced and converted molecular entities, needed in anabolic pathways to build, maintain and reproduce the living cell. In catabolic pathways, primary metabolites (and food products) provide the chemical energy and Primary and secondary metabolisms are interconnected in the sense that the biosynthesis of accumulating secondary metabolites can be traced back to ubiquitous primary metabolites.

However, in contrast to primary metabolites, secondary metabolites represent features that can be expressed in terms of ecological, taxonomic and biochemical differentiation and diversity.

The biosynthesis and accumulation of secondary metabolites provide a basis for biochemical systematics and chemosystematics. In addition, the wide molecular diversity of secondary metabolites throughout the plant kingdom represents an extremely rich biogenic resource for the discovery of novel drugs and for developing innovative drugs. Not only do plant species yield raw material for useful compounds; the molecular biology and biochemistry provide pointers for rational drug development.

Primary and secondary metabolites can be classified on the basis of their chemical structure into much the same

Carbohydrates, Lipids, Amino acids, Peptides, Proteins, Enzymes, Purine and pyrimidine derivatives.

Within such compounds classes, secondary metabolites generally show greater individuality and diversity in their molecular structure than primary metabolites. Certain compound classes also appear to be extraordinarily rich in secondary metabolites, e.g. the structurally diverse groups of alkaloids, phenolics, acetogenins and terpenoids.

Ubiquitous primary metabolites belonging to these compound classes seem to be restricted to only a limited number of key compounds functioning as biosynthetic precursors. Most of the plant compounds that have been found to be medicinally Also despite enormous structural diversity, Nature just uses a few building blocks, e.g. Shikimic acid and Shikimate, to

Shikimic acid accounts for the synthesis of many aromatic amino acids including phenylalanine, tyrosine, tryptophan as well as organic acids like benzoic and gallic acids and aldehydes like vanillin, benzaldehyde. The basic building blocks are the acetate (C2), isoprenoid (C5) and phenylpropanoid (C9) units.

The acetate unit is used in the polyketide biosynthesis and is particularly well developed in micro organisms. The isoprenoid pathways lead to allterpenoids by coupling two or more C5 units.

The terpenoids are found in all organisms. The phenylpropanoid pathway is most typical for plants and it is based on phenylalanine and tyrosine via cinnamic acid and this pathway leads to amongst others lignin and lignans.

In combination with three acetate units the C9 unit leads to the flavonoids and the anthocyanins, well known for their role

Quite a number of natural product groups can be constructed from the amino acid phenylalanine, in particular, flavonoids, coumarins, lignans etc. all of which possess a common substructure based on aromatic 6-C ring (C6 unit) with a 3-C chain. Many reactions can occur to this C9 unit including oxidation, reduction, methylation, cyclization, glycosylation (adding of sugar molecules) and dimerization all of which contribute to the value of natural products as a resource of biologically active molecules enhancing at the same time, to the structural complexity of the molecule with the presence of chirality and

The metabolites synthesized by the plants are of many different types and include the following:

Carbohydrates

These compounds are the first products plant produce by photosynthesis from water and carbon dioxide. They can be grouped into sugars, and polysaccharide.

The sugars are either monosaccharides such as glucose, fructose or oligosaccharides containing 5–6 monosaccharide units. Monosaccharide can be trioses, tetroses, pentoses and heptoses and are C compounds.

The polysaccharides are macromolecules containing a large number of monosaccharide residues.

Carbohydrates make up a large portion of plant biomass, e.g. cellulose is part of the cellular framework and starch as food reserves. Sugars can unite with a wide range of compounds such as Safrole, Chrysin (a flavonoid), Umbelliferone (a coumarin) unit

Examples of secondary plant metabolite variety of compounds to form glycosides, increasing the water solubility of the Glycosides vary in their chemical structure and pharmacological activity due to their aglycone component.

In addition to their use as bulking agents in pharmaceuticals, carbohydrates have recently been recognized to have useful. Several polysaccharides exhibit immuno-modulatory, anti-tumour, anticoagulant (e.g. heparin), hypoglycaemic or antiviral. The various carbohydrate products traded include fibre, cellulose and its derivatives, starch (glucose polymers) and its derivatives, dextrans, fructans (fructose polymers; e.g. Inulin), alginic acids, agar and gums.

Lipids

Vegetable oils are major sources of β -sitosterol, which is a steroid drug precursor. One vegetable oil, obtained from groundnut, yields lecithins, which are used to enhance food digestibility.

Lecithins are also used in pharmaceutical formulations. Recently, some vegetable oils have been found to be rich in α -linoleic acid, which is a precursor of prostaglandin, leukotrienes and thromboxanes.

All these compounds are involved in platelet aggregation and in inflammatory processes. Only members of Onagraceae, Saxifragaceae and Boraginaceae contain α -linoleic acid (Padua et al., 1999).

-Linoleic acid

Vegetable oils are significant in both the food and pharmaceutical industries. Some are used as solvents for lipid-soluble drugs such as vitamins and antibiotics.

Others e.g. almond and olive oils are used in cosmetics. Castor oil is also well known for its purgative activity, but has fallen out of favour because of its unpleasant taste.

Acetogenins

These molecules are long-chain aliphatic compounds with over 35 carbon atoms, ending with a γ -lactone, most often unsaturated and cyclized into one or two tetra-hydrofuran rings that may or may not be adjacent.

They have been isolated from members of the Annonaceae (e.g. *Annona*, *Goniothalamus*, *Rollinia* and *Uvaria*).

Their potential applications are linked to their anti-tumour (e.g. asimicin, bullatacine), anti-bacterial (e.g. cherimolin) and insecticidal (e.g. asimicin, annonin, annonacin) properties.

Annonacin Amino acids and their derivatives

The function of amino acids is not only the building blocks of proteins but they are also considered to be a form of nitrogen storage (e.g. Canavanine, Hemoarginine) and a germination inhibitor.

The few studies of the pharmacological activities of amino acids include reports of cucurbitine being used as a taenicide.

Many toxic amino acids have been identified; examples include α -glutamylamino propionitrile and α -oxalyl-diaminopropanoic acid which are responsible for the toxicity of grass pea (*Lathyrus sativus* L.) that brings about osteolathyrism and neurolathyrism in livestock and mimosine from *Leucaena* inhibiting proteins and nucleic acid synthesis which results in livestock losing appetite and weight and their growth being inhibited (Padua et al., 1999).

(i) Cyanogenic glycosides

Cyanogenic glycosides are compounds also derived from amino acids.

Enzymatic acid hydrolysis of these compounds yield hydrocyanic acid, which is the toxic principle.

Biosynthetically, the aglycones of cyanogenic glycosides are derived from L-amino acids.

Cyanogenic glycosides are prevalent in the families of the Rosaceae, Leguminosae, Graminae, Araceae, Euphorbiaceae

Examples include linamarin, amygdalin, prunasin.

(ii) Sulphur-containing compounds

The pharmacological significance of sulphur-containing compounds like allein, allicin, ajoene, and other related

Initially isolated from garlic, allicin and ajoene (the latter is a condensation product of allicin) exhibit many biological activities, including anti-hypercholesterolaemic, anti-platelet aggregation, anti-hypertensive, fibrinolytic and anti-fungal. Recently diallylcysteine, an odourless active ingredient of garlic was found to be biosynthesized.

(iii) Lectins

Lectins are proteins or glycoproteins that are able to bind with the carbohydrate moiety on cell membranes in a specific and reversible fashion, without displaying enzymatic activity.

Most lectins in higher plants are located in seeds. They are commonly found in legumes such as groundnut, soya bean and common bean. Some lectins have the ability to agglutinate red blood cells of a specific blood group.

These lectins are referred as phytohaemagglutinin. The haemagglutination activity is important in immunological studies.

Some lectins are toxic, e.g. Ricin from Castor (*Ricinus communis* L.) seeds and abrin from Jequirity bean (*Abrus precatorius* L.) seeds. (iv) Enzymes Plant-derived enzymes used as drugs include papain (*Carica papaya*) and bromelain. Both are proteolytic enzymes useful as an anti-inflammatory drug. Ficin, extracted from the Fig (*Ficus carica* L.) has

Alkaloids

The term alkaloid has been defined as a cyclic organic compound containing nitrogen in a negative oxidation state, which has limited distribution in living organisms.

Based on their structures, alkaloids are divided into several subgroups: non-heterocyclic alkaloids and heterocyclic alkaloids, which are again divided into 12 major groups according to their basic ring structure.

Mescaline is an example of non-heterocyclic or pseudo-alkaloid, Tetrandrine is another example of a bisbenzylisoquinoline alkaloid while Solasodine is a triterpene alkaloid. *Mescaline Tetrandrine Solasodine*

Free alkaloids are soluble in organic solvents and react with acids to form water-soluble salts.

There are exceptions like Berberine, which is a quaternary ammonium alkaloid.

Most alkaloids are solids except for Nicotine, which is a liquid.

Alkaloids, usually having a marked physiological action on humans or animals, are believed to be waste products and they are thought to play an important role in plant protection and germination and to be plant growth stimulants.

Alkaloids are more common in dicotyledons than in monocotyledons.

Families reported to be rich in alkaloids are :

Liliaceae, Amaryllidaceae, Apocynaceae, Berberidaceae, Leguminosae, Papaveraceae, Ranunculaceae, Rubiaceae and

Alkaloids are pharmaceutically significant, e.g. morphine as a narcotic analgesic, Codeine in the treatment of coughs, Colchicine in the treatment of gout, quinine as an anti-malarial, quinidine as an anti-arrhythmic and L-hyoscyamine (in the form of its racemic mixture known as atropine) as antispasmodic and for pupil dilation.

Recently, the extracts of *Erythroxylum pervillei* collected in Madagascar, have yielded nine tropane alkaloids out of which six of the new compounds (pervilleins A-F) were found to reverse multi drug resistance (MDR), using a KB-VI (vinblastine-resistant oral epidermoid carcinoma).

These compounds show promise as they are novel inhibitors of the MDR phenotype (Kinghorn et al., 2003).

A. Gurib-Fakim / *Molecular Aspects of Medicine* 27 (2006) 1–93

3.3 Phenols and phenolic glycosides

Phenols are among the largest group of secondary metabolites.

They range from simple structures with one aromatic ring to complex polymers such as tannins and lignins.

Example of phenolic classes of pharmaceutical interests are:

Simple phenolic compounds:

These compounds have a monocyclic aromatic ring with an alcoholic, aldehydic or carboxylic group.

They may have a short hydrocarbon chain. Capsaicin, isolated from *Capsicum* sp., is a vanillyl amide of isodecenoic acid and is marketed as an analgesic.

Eugenol is widely used in dentistry due to its anti-bacterial and anti-inflammatory and local anaesthetic activities.

(2) Tannins:

The chemistry of these compounds is very complex.

The distinction made in the literature between hydrolysable and condensed tannins is based on whether acids or enzymes can hydrolyse the components or whether they condense the components to polymers.

Although not altogether watertight, this distinction largely corresponds to group based on gallic acid and those based on

Several vegetable tannins have been discovered but only the tanning constituents of the most important groups will be reported here, i.e. the group of gallotannins and ellagitannins, the group of proanthocyanidins.

Gallotannins and ellagitannins are esters of gallic acid or its dimers digallic acid and ellagic acid with glucose or polyols.

Proanthocyanidins are oligomers of 3-flavanols (catechins) and 3,4-flavandiols (leucoanthocyanidins).

These phenolic compounds are biosynthesized via the Shikimic acid or acetate pathway.

Gallic acid Ellagic acid 3-Flavanol 3,4-Flavandiol

Tannins are able to react with proteins.

Upon being treated with a tannin, a hide absorbs the stain and is protected against putrefaction and thereby becomes

Although tannins are widespread in plants, their role is still unclear.

They may be an effective defence against herbivores.

Tannins are used against diarrhoea and as an antidote in poisoning by heavy metals.

Their use declined after the discovery of hepatotoxic effects of absorbed tannic acids.

Recent studies have re-reported that tannins have anti-cancer and anti-HIV activities.

(3) Coumarins and their glycosides:

Coumarins are, shikimate-derived, benzo-a-pyrone derivatives that are present in plants both in a free state and as

They have limited distribution in the plant kingdom and have been used in chemo-taxonomy in order to classify plants.

They give a characteristic odour of new-mown.

They are found in the following plant families:

Apiaceae, Rutaceae, Asteraceae and Leguminosae.

Common derivatives are:

Umbelliferone, Herniarin, Aesculetin, Scopoletin, Fraxin and Chicorin.

Some coumarins are phytoalexins and are manufactured by the plant in the event of an infection by bacteria and fungi. Scopoletin is among such compounds and are synthesized by the potato plant (*Solanum tuberosum*) when attacked by

Aesculin extracted from the Horse Chestnut (*Aesculus hippocastanum*) goes into the phytotherapeutic preparations for the treatment of capillary fragility. *Umbelliferone Herniarine*

(4) Quinones:

Quinones are oxygen-containing compounds that are oxidized homologues of aromatic derivatives and are characterized by a 1,4-diketo-cyclo-hexa-2,5-diene pattern (paraquinones) or by a 1,2-diketo-cyclohexa-3,5-diene pattern (ortho-quinones). In naturally-occurring quinones, the dione is conjugated to an aromatic nucleus (benzoquinones), or to a condensed polycyclic aromatic system: naphthalene (naphthoquinones), anthracene (antraquinones), 1,2-benzanthracene (anthracenquinones), naphthodianthrene (naphthodianthrone), pyrene, phenanthrene and abietane-quinone. Naphthoquinones and anthroquinones have some importance medicinally.

(i) Naphthoquinones:

These are yellow or orange pigments from plants.

Biosynthetically, the naphthoquinones are derived almost exclusively from the Shikimic acid pathway.

Naphthoquinones are found in families like:

Bignoniaceae, Ebenaceae, Droseraceae, Juglandaceae, Plumbaginaceae, Boraginaceae, Lythraceae, Proteaceae and

The pharmaceutical significance of this group is limited except for a few examples like Plumbagin isolated from *Plumbago* species, exhibit anti-bacterial and cytotoxic properties.

Lawsone from Henna (*Lawsonia inermis* L.) is a powerful fungicide and well-known hair dye. *Plumbagin*

(5) Flavonoids:

Flavonoids are compounds that are responsible for the colour of flowers, fruits and sometimes leaves.

The name refers to the Latin word flavus meaning yellow.

Some may contribute to the colour by acting as co-pigment.

Flavonoids protect the plant from UV-damaging effects and play a role in pollination by attracting animals by their

The basic structure of flavonoids is 2-phenyl chromane or an Ar-C₃-Ar skeleton.

Biosynthetically they are derived from a combination of the Shikimic acid and the acetate pathways.

Small differences in basic substitution patterns give rise to several sub-groups.

In the plant, flavonoids can either occur as aglycones or as O- or C-glycosides.

Chalcones

Flavanols Flavanones Flavones Flavonols Isoflavonoids Basic structures of some flavonoids.

Recently, flavonoids have attracted interest due to the discovery of their pharmacological activities as anti-inflammatory, analgesic, anti-tumour, anti-HIV, anti-infective (anti-diarrhoeal, anti-fungal), anti-hepatotoxic, anti-lipolytic, anti-Biologically active flavonoids comprise of hesperidin and rutin for decreasing capillary fragility and quercetin for its anti-

Anthocyanins:

Anthocyanins are the compounds responsible for bright colors of most flowers and fruits.

These water-soluble pigments occur as glycosides (anthocyanins *sensu stricto*) and their aglycones (anthocyanidins).

They are derived from the 2-phenyl benzopyrylium cation, more commonly referred to as the flavylum cation. Cyanidin is an example of an anthocyanin

The application of anthocyanins is as food additives, e.g. in beverages, jams and confectionary products. The pharmacological activities are similar to flavonoids; for instance for decreasing capillary permeability and fragility, and as Phloroglucinols are derivatives of 1,3,5-trihydroxybenzene which are found in e.g. *Cannabis sativa* L.

This compound is a well-known stimulant of the Central Nervous system.

Tetrahydrocannabinol and its derivatives influence behaviour inducing euphoria and relaxation at low doses.

Sometimes hallucination and tinnitus are observed. Other effects are bronchodilatation and a lowering of intra-ocular

(6) Lignans and related compounds:

Lignans and related compounds are derived from condensation of phenyl propane units.

Neolignans are also condensation products of phenylpropanoid units.

Norlignans are probably specific to gymnosperms and have a C17 skeleton.

Lignins are substances deposited at the end of the formation of the primary and secondary cell walls.

Chemically, they are polymers arising from the copolymerisation of alcohol with a p-hydroxycinnamic structure (p-hydroxycinnamyl, coniferyl or sinapyl alcohol).

Lignins are always combined with polysaccharides. The pharmacological activity of lignans is anti-tumour.

Kadsurenone, aneolignan, exhibits anti-allergic and anti-rheumatic activity.

The major application of Lignin is as a precursor of vanillin, which is widely used in the food industry.

(7) Terpenoids and steroids:

Terpenoids and steroids are derived from the isoprene (a 5-C unit), which is biosynthesized from acetate via mevalonic

Monoterpenes

Monoterpenes are the most simple of constituents in the terpene series and are C10 compounds.

They arise from the head to tail coupling of two isoprene units.

They are commonly found in essential oils.

Iridoids and pyrethrins are included in this group.

Examples of monoterpenes commonly found in essential oils are found below:

-Pinene

-Pinene Linalool Menthol Borneol 1,8-cineole

Iridoids are monoterpenes characterized by a cyclopenta [C] pyranoid skeleton, also known as the iridane skeleton.

Secoiridoids, which arise by cleavage of the 7,8-bond of the cyclopentane ring, are also included in the iridoids.

Iridoid

Secoiridoid

Examples of secoiridoids are the bitter constituents of gentian e.g

gentiopicric acid, amarogentin and esters of sweroside and swertiamarin.

Other examples of irregular monoterpenes arising from the non-classic coupling of isopentenyl pyrophosphate and dimethylallyl pyrophosphate are the class of compounds known as the Pyrethrins.

These compounds are toxic to cold blooded animals such as fish, amphibians and insects and are widely used as

The pharmacological properties of iridoids are quite limited except for the analgesic and anti-inflammatory activities of the Harpagosides (Harpagophytum Sesquiterpenes

Sesquiterpenes are also constituents of essential oils of many plants, e.g. bisabolol, humulene and caryophyllene.

Sesquiterpene lactones are well known as bitter principles.

They occur in families like the Asteraceae.

These compounds possess a broad range of activities due to the α -methylene- γ -lactone moiety and epoxides.

Their pharmacological activities are anti-bacterial, anti-fungal, anthelmintic, anti-malarial and molluscicidal.

Examples are Santonin, which is used as an anthelmintic and as an anti-malarial.

Santonin Diterpenes Diterpenes constitute a vast group of C compounds arising from the metabolism of 2E,6E,10E-

- They are present in animals and plants.

These compounds have some therapeutic applications.

For example, Taxol and its derivatives are anti-cancer drugs.

Other examples are Forskolin, which has anti-hypertensive activity. Zoapatanol is an abortifacient while Stevioside is a sweetening agent. Taxol is another very famous diterpene.

(iii) Triterpenes and steroids

Triterpenes are C compounds arising from the cyclization of squalene. The basic skeleton arises from the cyclization of 3S-2,3-epoxy,2,3-squalene.

Oleanane is an example of a pentacyclic triterpene and testosterone of a steroid.

Tetracyclic terpenes and steroids have similar structures but have different biosynthetic pathway. Steroids contain a ring system of three 6-membered and one 5-membered ring because of the profound biological activities encountered, many natural steroids together with a considerable number of synthetic and semi-synthetic steroidal compounds are employed in medicine (e.g. steroidal saponins, cardio-active glycosides, corticosteroid hormones and The pharmaceutical applications of triterpenes and steroids are considerable. Cardiac glycosides have been used in medicine without replacement by synthetic drugs. Saponins from ginseng and liquorice exhibit many therapeutic effects.

(iv) Saponins

Saponins constitute a vast group of glycosides, which occur in many plants. They are characterized by their surfactant properties; they dissolve in water and when shaken, form a foamy solution. Saponins are classified by their aglycone structure into triterpenoids and steroid saponins; most triterpenoid saponins are derivatives of one of the triterpene oleanane, ursane and lupane, while steroid saponins generally possess the typical steroid skeleton with 2 extra rings E. a furan structure and F. a pyran structure respectively. Many saponins have The steroidal saponins are important precursors for steroid drugs including anti-inflammatory agents, androgens,

Well-known steroid saponins are diosgenin from Dioscorea, hecogenin from Agave and smilagenin from Smilax.

Triterpene saponins exhibit various pharmacological activities: anti-inflammatory, molluscicidal, anti-tussive, expectorant, analgesic and cytotoxic.

Examples include ginsenosides, which are responsible for some of the pharmacological activity of ginseng and the active triterpenoid saponins from

Smilagin Cardiac glycosides

The aglycone part of cardiac glycosides is a tetracyclic steroid with an attached unsaturated lactone ring that may have 5 or

Cardiac glycosides are classified into two groups according to the lactone ring:

the C cardenolides with an α, β -unsaturated δ -lactone (= butenolide), and the C bufadienolides with α, β -unsaturated γ -lactone (= pentadienolide).

The *sugar* moiety is normally attached via the C-3 hydroxyl group or the aglycone. The majority of the saccharides found in cardiac glycosides are highly specific. They are 2,6-dideoxyhexoses, such as D-digoxose, L-oleandrose or D-diginose. These sugars give a positive reaction with the Keller-Killiani reagent. Cardiac glycosides have been used as drugs for the treatment of cardiac insufficiency.

An example is digitoxin from Digitalis, where the sugar moiety is attached to the aglycone digitoxigenin via the C-3 hydroxyl group (Padua et al., 1999).

Digitoxigenin Carotenoids

Carotenoids contain 8 isoprene (C) units that are responsible for the orange and yellow colours of some vegetables and Among these compounds, the hydro-carbons are collectively referred to as carotenes and the hydroxylated derivatives as Carotenoids are either acyclic (e.g. lycopene) or comprise of one or two pentacyclic or hexacyclic rings at one end or the other (e.g. b, w-carotene) or at both ends (e.g. b, b-carotene). Carotenoids became interesting agents after the discovery of a negative correlation between the plasma concentration of b-carotene and the prevalence of certain forms of cancer. Some doctors prescribe b-carotene for cancer patients. Further-more, in the intestine b-carotenes are converted to retinol (Vitamin A). They can be used for the treatment of photosensitization, retinal diseases and glaucoma. Carotenoids are also safe colouring agents for food substances and cosmetics (Padua et al., 1999).

14. Biological and pharmacological activity and therapeutic applications

Tastes (sweet, bitter, sour and astringent) are among the many classical examples of biological action of plant materials in Other sensations include irritations,itchiness, pungency, acidity as well as the types of euphoria and hallucinations. It is only recently that biological activity is understood in terms of molecular interactions. Plant and plant constituents have a key position in the advancement of modern studies and knowledge on biological

There are several reasons for this:

- Firstly, plant species whether traditionally used or not, continue to be important sources of food, medicine and
- Secondly, the bioactive plant compounds are themselves products (or derived products) of metabolism, and hence function in life processes in a similar way to compounds that operate in humans and animals. Researching hoping to develop drugs from plants need to understand the basics of such functions and mechanisms in relation to the bioactive
- Thirdly, plants also yield products, which are auxiliaries in medicine and pharmacy and sustain or condition pharmacological activity and therapeutic efficacy.

In addition, a series of these auxiliary substances are used in biomedical research and in clinical tests.

Testing the biological activity of medicinal or potentially medicinal plant materials demands a special approach.

Investigations may be focused on understanding the bioactivity of a compounded plant extract or simply directed at isolating a single bioactive chemical compound.

In the latter case, results often lead to over simplification or wrong explanations of the bioactivity of extract preparations.

On the other hand,thorough studies on single bioactive constituents provide important information for plant drug research.

However, the much more complex array of molecular interactions and bioactivity mechanisms that arises from plant extracts represents a much greater and more fascinating challenge to science.

244

Empty page

245

Factors affecting biological activity ...

Factors affecting biological activity ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of->

15. Factors affecting biological activity

Various aspects of bioactivity apply to any chemical whether of natural or synthetic origin.

These aspects will be dealt with briefly and are:

15.1. Physicochemical properties

These relate to the transport of the bioactive compound to its site of action, usually a receptor or other biomacromolecule at the cellular or subcellular level. Under experimental conditions, either in vivo or clinical, or real life conditions, the extent to which a drug passes through semi-permeable membranes before reaching its site of action depends on its

Under in vitro conditions, many of these barriers are absent. In vitro bioactivity therefore represents only a stage in this basic assessment of pharmacological effects. In plant drug research, the solubility of active constituents may be revealed

Extraction programmes separate lipophilic constituents from water-soluble compounds. Further extraction of an extract may lead to further refinement of physicochemical properties. After the bioactive molecular entity has been identified, detailed data on solubility, partition coefficients and the electrolytic behaviour can be determined. Solubility characters are closely related to drug absorption and the degree of absorption is an important determinant of drug action. Many bioactive plant constituents are weak acids and bases, and their degree of ionization when dissolved, is. As a rule, the ionic form is more water-soluble. These factors are important when bioactivity is regarded in the context of drug distribution between intestine and plasma, between kidney tubules and urine, and between plasma and other body fluids. Generally, but simplified, one may say that only the lipid-soluble and undissociated forms of a bioactive molecule will pass through membranes. However, at the site of action, bioactive compounds may generate their action by binding to a

15.2. Chemical parameters

The structural features of a compound can be related to its pharmacological properties, either qualitatively or

The principles, concepts and numerical rules governing qualitative and quantitative relationships between structure and activity help explain the pharmacological activity of a new compound, which is why it is important to evaluate the

The basic aspects of molecular structures involved in bioactivity include:

•Resonance and Inductive effect:

This is a phenomenon that a molecule can be represented by two or more structures that differ only in their electron, but

The electron density and electron distribution patterns help explain the molecule's activity and hence its molecular

While resonance is explained as at above, inductive effect is a measurable electro-static phenomenon caused by actual electron shift or displacements along chemical bonds.

Both negative and positive inductive effects can lead to a change in bioactivity.

•Oxidative and reductive potentials:

This phenomenon represents the tendency of a compound to lose or gain electrons.

Electron transfer is vital for living processes and without which living cells would not function.

Bioactive compounds derived from plant sources function in enzyme systems in plants in the same way to those in animals

•Types of bonding:

The phenomenon of biological activity is concerned with covalent and non-covalent interactions.

Covalent bonds are formed enzymatically and are common to all biomolecules.

Hydrogen bonds, ionic forces, hydrophobic (or lipophilic bonding), charge-transfer interactions, all representing non-covalent interactions are also common to functional life processes.

Some agents can affect physiological functions by forming irreversible covalent bonds with target biomacromolecules and these molecules would be considered to be toxic at cellular level and would be difficult to control clinically and medically.

In plant drug research, agents exerting their activity through much weaker and reversible bonding processes would be

•Spatial arrangement of the molecule:

In terms of activity, it is important to have a good steric and electronic complementarity between ligand and target

Bioactive compounds interact with enzymes by fitting sterically into a binding pocket—the space sterically provided by

Thus the molecular dimensions, inter atomic distances, arrangements of electrons and the stereochemical properties of both ligand and target are decisive in determining biological activity.

16. Current status of drug discovery

A recent analysis of natural products as a source of new drugs over the period 1981–2002 shows that 67% of the 877 small molecules, new chemical entities are formally synthetic but 16.4% correspond to synthetic molecules containing a natural product moiety. Furthermore, 12% are actually modeled on a natural product inhibitor of the molecule target of interest, or mimic the endogenous substrate or the active site, such as ATP.

Thus only 39% of the 877 molecules can be classified as truly synthetic in origin.

In the area of the anti-infectives (anti-bacterial, anti-fungal, parasitic, and viral), close to 70% are naturally derived or inspired, while in the cancer treatment area 67% are in this category. In recent years, there has been a steady decline in the output of the R&D programs of the pharmaceutical industry and the number of new active substances, also known as the new chemical entities hit a 20-year low or 37 in 2001. Further evidence of this drop in productivity is evident from the report of the FDA in 2001, down from 24 the previous year. This downturn has been attributed in part to disruption of laboratory activities by the surge in company merges and acquisitions, the mounting costs of drug development, and the FDA over-caution in the drug approval process. Recently, there has been rekindling of interest in rediscovering natural products. As stated by one authority ‘‘We would not have the top-selling drug class today, the statins; the whole field of angiotensin antagonists and angiotensin converting enzyme inhibitors; the whole area of immuno suppressives, nor most of the anti-cancer drugs. Imagine all of these drugs not being available to physicians or patients today’’. It is clear that Nature has played and will continue to play, a vital role in the drug discovery process (Cragg and Newmann,

246

Empty page

247

Medicinal plants by tradition
Medicinal plants by tradition

248

Empty page

249

Adulteration

Adulteration

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-Today>
27. *Adulteration*

Over and above the dosage factor, is adulteration either accidentally or intention-ally.

Foxglove (*Digitalis purpurea*) has shown up as an adulterant in herbal mixture where it is not among the listed ingredients. Sometimes herbal remedies have been found to be tainted with heavy metals.

In other instances, when one medicinal plant has been replaced by another similarly looking one, this led to disastrous results. Although *Aristolochia* species are used in Chinese medicine, the replacement by *Aristolochia fangchi* has caused the death of several patients who were attending a weight loss clinic in Belgium (Schaneberg and Khan, 2004).

28. *Microbial contaminations*

With requirements of Good Agricultural Practices (GAP) and Good Manufacturing Practices (GMP) being improved more and more on producers of medicinal plants, Microbial contamination can be controlled. It is a fact that natural materials harbour a large number of spores and other micro-organisms but nonetheless, the maximum number of micro-organisms is limited. The European Pharmacopoeia, for example, excludes the presence of *Escherichia coli* and *Salmonella* sp. And limits aerobic micro-organisms up to 10⁵ per g or ml and this includes up to 10³ yeast and fungi per g or ml and up to 10³ per ml.

29. *The convention for biological diversity*

It is a fact that the role of ethnobotanist is crucial in the search for new drugs and this role has become so much more significant in the second half of the 20th century. The study of ethnobotany has gained in importance and the Western use

National and indigenous rights on these resources have become acknowledged by both academic and industrial researchers. It is also recognized that the need for basic scientific investigations of plants used in indigenous medical systems. The relevance of such data coupled with the ever-increasing rights expected from communities on their data along with the battle for conservation, have re-shaped the entire approach towards bioprospecting. The major ideas concerning bioprospecting and conservation were first presented by the American scientist Thomas Eisner (1989, 1991). He entitled the activity chemical prospecting and described it as the exploratory process by which new

He proposes chemical prospecting to be substantially intensified. He also highlighted the loss of species and the concomitant loss of chemicals of great value for the progress of medicine.

The penning of the Convention on Biological Diversity (CBD) (UN Convention on Biodiversity) ushered a new era in natural products drug discovery and development. The CBD encompasses all of Eisner's ideas and takes into account the It was opened for signature at the UN Conference on Environment and Development in Rio de Janeiro in 1992. By January 1999, 175 states and the European Union had ratified the Convention.

Thus the CBD is one of the international conventions with the highest number of State Parties. It entered into force after being ratified by 30 States in December 1993. The US is one of the States not being Party to the Convention.

The objectives of the CBD as spelled out in Article 1

The objectives of the Convention, to be pursued in accordance with its relevant provisions, are the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising out of the utilization of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of appropriate technologies, taking into account all rights over those resources and to technologies, and by appropriate The CBD regulates a number of important issues related to the global conservation and sustainable use of biological resources and covers a much broader field than access to genetic resources.

In Article 15, the CBD also called for recognition of the sovereign rights of countries to control utilization of their natural resources and genetic materials while Article 8, addresses issues related to the global conservation and sustainable use of biological resources, and it covers a much broader field than access to genetic resources. Article 15 should—as the Broadly speaking, it gives citizens and companies of developed countries access to the genetic resources in developing countries—on certain conditions. One of them is the obligation for developed countries to provide and facilitate access for and transfer to developing countries, or technologies that make use of genetic resources.

This is spelt out in Article 16. Article 15 is in itself a compromise between these interests. In Paragraph 1, it makes a case for the legal starting point concerning sovereign rights of States over their natural resources.

“Recognising the sovereign rights of states over their natural resources, the authority to determine access to genetic resources rests with the national government and is subject to national legislation”.

Countries in the North achieved acceptance of their demands for access to genetic resources from the developing countries.

On the other hand, the developing countries achieved the recognition of national sovereignty over genetic resources, and the principle of prior informed consent and benefit sharing as a basic condition for access. Broadly speaking, the developed countries had two main interests in biological diversity.

The growing scientific recognition and political concern for the extinction of species and biotypes lead to a demand for

This concern is also addressed in Article 3 of the Convention:

Article 3 of the Convention expresses the principle of states sovereign right to exploit their own resources pursuant to their own environmental policies, combined with an obligation to ensure that activities within their jurisdiction or control do not cause damage to the environment or other states or areas beyond natural jurisdiction.

This principle is firmly established in international law.

Developed countries had, as well a commercial interest in the exploitation of the genetic material through bioprospecting; the use of genetic materials in scientific research, and as a basis for new products in pharmaceutical, medical, agricultural Such use in the short-term perspective pre-supposes access possibilities.

Access in a long-term perspective pre-supposes both effective conservation and access legislation.

This feature is also embodied in the Articles of the CBD namely:

While confirming the states sovereign right over its genetic resources, the CBD Article 15 nevertheless implies a certain limitation on the exercise of this right.

The State is not entirely free to decide on the use of its genetic resources but it has an . . .

obligation to create conditions to facilitate access to genetic resources for environmentally sound uses by other Contracting The developing countries, on the other hand, had sovereignty over the resources as their main objective.

This was seen as a pre-requisite for receiving benefits from the use of their biodiversity.

Furthermore, such benefits would increase these countries possibility to make conservation efforts.

Exploitation of genetic material for re-search and industrial purposes adds new economic value top the forest areas.

This is also taken on board in Article 15 of the CBD.

Article 15, Paragraphs 4 and 5, imply that access to genetic resources should be granted by the source state through a system of individual permit and/or mutual agreement between the interested parties.

29.1. Mutually agreed terms (MAT) and prior informed consent (PIC)

As mentioned above, CBD Article 15, Paragraphs 4 and 5, contain the basic legal conditions for access to genetic Access when granted shall be on mutually agreed terms

(MAT) and shall be subject to Prior Informed Consent (PIC) by the providing parties or unless otherwise determined by MAT and PIC are general principles of the CBD and is expressed in several articles as well. MAT and PIC have significantly changed the basic conditions for research involving traditional knowledge in particular ethnopharmacological Countries and Peoples providing the resources for natural products research and drug development now have well-defined This will have a direct impact on the sharing of bene fits accruing from collaborations. It goes without saying that these clauses of the CBD will and have had a definite impact on bioprospecting.

This exercise, which focuses on the development of new drugs with enormous financial returns for big international companies, requires high-throughput screening svstems and extracts.

For this to materialize correctly, cooperation, collaboration and trust are pre-requisites between donor countries and

It is therefore clear that the development of new drugs will benefit from the breadth of the contribution of ethnobotany and ethnopharmacology, from the indigenous and orally transmitted medical systems to drug development.

Modern science stands to benefit from the conservation of plant specimens and also on the preservation of oral traditions, which have stood the test of time in some primitive societies.

30. Conclusion

This paper has given an overview of the importance of medicinal plants from antiquity to date date.

It cannot be denied that pharmacognosy has had a chequered history but has evolved over the years to become one of the pillars of areas like pharmacy, medicine and natural product chemistry amongst others.

All these scientific disciplines now recognize the importance of plants as sources of medicines and have initiated active research programmes either to isolate new lead compounds or to produce standardized extracts.

With the estimated 10–100 million species or organisms living on earth and higher plants forming a group of some 250,000 species out of which only 6% has been investigated for biological activities and 15% for their chemical constituents, it looks increasingly like we have only scratched the surface of this worlds wonderful resource.

While the pharmaceutical industry in the developed world, will continue to investigate promising leads from natural products in their effort to produce new drugs entities, the production of new medicines in the developing world may have In these parts of the world, when a plant is readily available and has the potential to provide inexpensive therapy for the treatment of a disease, then a product may well be developed.

Close collaboration is expected between clinicals and scientists with a common endeavour—production of safe, quality Pharmacognosy, an area or science once considered moribund, has a very bright future ahead as it will continue to provide new lead molecules for major ailments facing us.

Several hard evidence has been given in the text to back this evidence and it can only be hoped that research will shed more light on these facts provided that the critical mass of researchers are involved and enough funds put to disposal. Nonetheless, issues like conservation of both ethnobotanical data and biodiversity must addressed as ignoring it will pose a serious challenge to the search of new leads.

With the interest that has been generated both the general public, university researchers and multinationals across the globe into natural products, there is now more than ever a golden opportunity to continue making worthwhile contribution to fakima@uom.ac.mu www.elsevier.com/locate/mam *Molecular Aspects of Medicine* 27 (2006) 1–93

250

Empty page

251

Empty page

252

Immuno-stimulants ...

Immuno-stimulants ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of->

21. *Immuno-stimulants*

Medicinal compounds are described as being immuno-stimulants when they stimulate an immune action, usually measured by an increase in the number of immune cells circulating in the blood or by enhanced phagocytosis after there has been. It is also understood that claims for an extract to be an immuno-stimulant are difficult to substantiate and that large number. Nonetheless some herbs such as Echinacea and Astragalus are being used extensively for the same purpose.

Radix and Herba Echinacea of several species of Echinaceae are widely distributed in North America and have been used traditionally both by Amerindians and settlers since the 19th century.

Both the aerial parts and the secondary roots are used against a variety of conditions such as pain, in inflammatory skin conditions. Radix Echinaceae (*E. angustifolia* and *E. pallida*) are known to contain an essential oil (0.2–2%) and other identified components are cynarin, chicoric acid, alkaloids, caffeic acid esters and chlorogenic acid derivatives. Trace amounts of pyrrolizidine alkaloids (tussilagine and isotussilagine) are also present.

Echinacoside A. Gurib-Fakim / Molecular Aspects of Medicine 27 (2006) 1–93

The claims for the effectiveness of Radix Echinaceae as a stimulator of the immune system are based on over 350 scientific studies, spanning a period of 50 years. Experimental pharmacology data based on in vitro and in vivo studies have documented the activation of an immune response after treatment with Radix Echinaceae extracts.

The immunostimulant effect is brought about three mechanisms:

Activation of phagocytosis, stimulation of the fibroblasts, increasing respiratory activities and causing increased mobility. Chemically standardized extracts, derived from roots and aerial parts from the various species have been assessed for their phagocytic potential. All ethanolic root extracts increased phagocytosis in vitro.

One placebo-controlled clinical study on patients with infections of the upper respiratory tract have shown significant improvement when they were treated with aqueous-ethanolic tincture (1:5) at 90 drops/day (900 mg roots).

The duration of the illness decreased from 13 to 9.8 days for bacterial infections and from 12.9 to 9.1 days for viral

22. Cancer drugs from plants

Cancer remains a major obstacle to overall public health and is responsible for one in every four deaths in the US alone.

In 2003, the American Cancer Society had estimated that there would be some over one million new cases of invasive cancer diagnosed with over half a million deaths from basal and squamous cell skin cancers.

Plants have a long history of use in the treatment of cancer (Hartwell, 1982), though many of the claims for the efficacy of such treatments should be viewed with some scepticism because cancer, as a specific disease entity, is likely to be poorly defined in terms of folklore and traditional medicine (Cragg et al., 1994).

A contribution towards the chemotherapy of cancer, natural product secondary metabolites from plants and microbes in particular play a very important role in the amelioration of this group of diseases.

In a recent review dealing with an analysis of anti-neoplastic drugs available in western countries and Japan, of 140 compounds in total, a majority (54%) are either natural products (14%), natural products derivatives (26%) of compounds made by total synthesis, but modeled on natural product leads (14%).

Accordingly, there is a considerable scientific and commercial interest in the continuing discovery of new anti-cancer agents from all natural product sources, inclusive of plant secondary metabolites (Kinghorn et al., 2003).

In the search for novel anti-cancer molecules, again the tropical rainforests have been privileged for two reasons:

1. The tropical forests sustain considerable biodiversity and in some of these, more tree species are found in 0.5 km

2 area than all of North America (Burslem et al., 2001) 2.

There is justifying concern about the impending loss of tropical species so some of these species may not be available to future generations of natural product drug discovery scientists (Cox, 2000).

It has been estimated that of the total number of higher plants on earth (310,000–422,000), about 120,000 of these are

Moreover, some biodiversity hot spots with high floristic diversity are undergoing major habitat loss (Pitman and Jorgensen

Catharanthus roseus (Apocynaceae).

Madagascar Periwinkle, Vinca Rosea

This plant had been used and patent medicines such as Vinculin in England and Covinca in South Africa have been

Experimental injections of a periwinkle extract have been effective in decreasing the symptoms in a group of diabetic

The Periwinkle has a long history of treating a wide variety of diseases and has also been used for centuries, in Europe, West Indies, Indian Ocean Islands against diabetes.

Its use as a source of anti-cancer alkaloids arose from its reputation as a cure for diabetes.

This traditional use resulted in preliminary laboratory investigations in 1950s.

Laboratory animals developed critically low counts of white blood cells leaving them defenceless against infections caused. Since then more than 150 alkaloids have been isolated and characterized, a number of which have been found to be indole alkaloids including dimeric and bis-indole alkaloids.

Thus bioassay-guided isolation of the extracts of the plant led to the characterization of the active complex alkaloidal compounds: Vincristine and Vinblastine.

They have proven to be effective agents against childhood leukaemia, breast cancer and Hodgkins disease (a cancer of the lymph nodes), choriocarcinoma respectively. Vincristine, R = CHO; Vinblastine, R = CH₃

The level of Vincristine in the plant is extremely low (0.0002%) and hence making it a very expensive anti-tumour agent.

Vincristine and Vinblastine exert their anti-cancer properties by inhibiting mitosis by binding to tubulin, thus preventing the cell from making spindles it needs to be able to move its chromosomes around as it divides.

Vinblastine is marketed as Velbeby Eli Lilly and is useful in treating Hodgkins disease, lymphomas, advanced testicular cancer and breast cancers as well as Kaposi sarcoma.

Nonetheless, the side effects are significant and include hair loss, nausea, lowered blood cell counts etc.

Vincristine is marketed as Oncovin by Eli Lilly and is used to treat acute leukaemia, Hodgkin's disease and other lymphomas.

The semi-synthetic vinca alkaloids—Vinde-sin (marketed under the name Eldisine), used to treat leukaemia and lung

Vinorelbine (marketed as Navelbine) by Glaxo Smith Kline is used to treat ovarian cancer.

Vinorelbine has a wider range of anti-tumour activity than the other vin-ca alkaloids and is used, in combination with cisplatin, in the treatment of patients with non-small-cell lung cancer (Heinrich et al., 2004).

Podophyllum peltatum

Podophyllum peltatum is commonly known as the Devils apple or May apple. This perennial plant is found growing in the woodland in Northern America. The rhizome, which is the most important part of the plant, is known to be toxic. The main components found therein are podophyllotoxin and a- and b-peltatin, all being toxic. The lignan, Podophyllotoxin is also found in other species of *Podophyllum*. These plants have a long history as a medicine, among native North American and Asian tribes (Hartwell, 1982). They used to gather the rhizomes in the autumn, dry them and grind them to a powder. They would eat or drink a brew of the powder as a laxative or to get rid of intestinal worms. Currently, the extracts are applied on genital warts and some skin cancers. Nonetheless, the extracts and compounds present therein are too toxic to

A close inspection of the structures of the active compounds belonging to these classes or compounds has revealed that the presence of some structural features e.g. a 5-membered lactone ring, a 3,4,5-trimethoxyphenyl group and a methylenedioxyphenyl group, are responsible for their activity (MacRae and Towers, 1984). This natural compound has been used to generate semi-synthetic derivatives namely—Etoposide and Teniposide. Etoposide is now marketed as Venesid for small cell lung cancer, testicular cancer and lymphomas while Teniposide is also used in treating brain

Podophyllotoxin

The mode of action of Podophyllotoxin is that it binds to tubulin and is a member of spindle poison group of agents and functions by preventing microtubule formation. Etoposide and Teniposide work via different mechanisms by inhibiting the enzyme topoisomerase II thus preventing DNA synthesis and hence replication.

The difference in mechanism is attributed to the presence of small changes in the stereo-chemistry of the molecules.

Taxus brevifolia

(*Taxaceae*) (*Pacific Yew tree*)

Another example of plant-derived anti-cancer drug is paclitaxel more commonly known by its trademark name—Taxol.

Taxol, a complex terpene-based molecule is derived from the Pacific Yew (*Taxus brevifolia*) and is both a generic and a The Taxol story started in the 1960s, when a project was undertaken by the National Cancer Institute (NCI), which was involved in the collection of a number of plants to be assessed for their anti-tumour activity.

One of them being the very slow-growing Pacific Yew, *Taxus brevifolia*.

Extracts of the Pacific Yew were found to stop the growth of several mouse tumours, a case in which ethnobotany provided

Nonetheless although, native Americans did not use the trees specifically for cancers or tumours, an early ethnobotany reference noted that the Bella Coola tribe of British Columbia used Pacific Yew for lung ailments.

This reference may have overshadowed the present as paclitaxel is now being used to treat lung cancers that do not

Paclitaxel, along with several key precursors (the baccatins) occur in the leaves (albeit in very low yields: 0.004% from 12 kg of plant material) of various *Taxus* species, and the ready semi-synthetic conversions of the relatively abundant baccatins to paclitaxel and active paclitaxel analogs, such as docetaxel (Cortes and Pazdur, 1995) has provided major. Cancer exhibit un-controlled cell division and paclitaxel stops malignant tumours from growing, by interfering with the micro-tubules that are responsible for dividing the chromosomes during cell division.

The microtubules do not disassemble after cell division is complete, and so many microtubules accumulate in the cell. Paclitaxel inhibits the separation of the tubulin molecules—the protein subunits that compose the microtubules—providing a unique method of interfering with cancerous growth.

Clinical trials during the 1980s revealed that paclitaxel could help in 30% of the advanced cases of ovarian cancer and the drug shows promise for other malignancies as well namely melanoma cell lines.

The activity of Taxol, its unusual and novel structure and the fact that it worked by a new mechanism, encouraged further research. This has resulted in the clinical trials and the development of analogues such as taxoteres.

Alternatives for getting significant amounts of this drug was envisaged seriously.

This was a significant breakthrough as the needles are a renewable resource and hence there was no need to destroy the trees by the removal of the bark especially as a tree can take up to 100 years to give a trunk of 4 inches in diameter. Research has also produced synthetic paclitaxel along with several similar analogs like Docetaxel, which was the latter may prove to be more effective in anti-tumour activity than paclitaxel itself.

The cost of synthetic drugs being high and coupled with the fact that the Pacific Yew is a slow growing species, this combination proved to be a challenge to the further development of Taxol.

It appeared that the fungus acquired copies of the genes for producing paclitaxel from its host tree.

Gene transfer from organism to organism does occasionally occur in nature and paclitaxel may benefit the fungus by inhibiting the growth of competing microorganisms.

Fungi grow rapidly and are easily cultured in large batches, this fungus now named *Taxomyces* and reanae (after its discoverer) may prove to be a better source of Taxol than either the Yew tree or synthesis.

Altering the growth conditions of the fungus or changing the fungus genetically may eventually result in paclitaxel that are sufficient for all patients and also protecting the Pacific Yew and its habitat from destruction.

Anti-drug discovery is targeting tubulin depolymerising protein as the major target.

As a result antimetabolic agents constitute an important class of the current anti-cancer drugs.

Hundreds of tubulin inhibitors naturally occurring, semi-synthetic or synthetic, have been reported.

Combretum caffrum (Combretaceae) (African Bush Willow)

The roots of the African Bush Willow (*Combretum caffrum*) from the Southern Africa region is commonly used in traditional medicine against body pain (Neuwinger, 2000).

The Combrestatins are a family of stilbenes, which act as anti-angiogenic agents causing vascular shutdown in tumours (Holwell et al., 2002) and resulting in tumour necrosis when tested against solid tumours (Cirila and Mann, 2003).

CA-4 shows strong cytotoxicity against a variety of cancer cells, including multi-drug resistant cancer cell lines.

It has also been demonstrated to exert highly selective effects in proliferating endothelial cells. CA-4 disodium phosphate (CA4DP), a water-soluble pro-drug of CA-4 shows potent anti-vascular and anti-tumour effects in a wide variety of tumours. Combrestatin A4 phosphate has undergone successful Phase I clinical trial and is currently in Phase II and has also exhibited the absence of cumulative toxicity (Young and Chaplin, 2004).

This has led to a significant number of compounds based up on the combrestatins skeleton to have been synthesized in the search for more effective anti-cancer agents (Li and Sham, 2002). CA4P also displayed significant cytotoxicity against ATC cell lines when compared to paclitaxel and these effects were longer lasting in two cell lines when compared to that

Combrestatin A4 phosphate

Camptotheca acuminata (Nyssaceae) (Xi Shu or Happy Tree)

The National Cancer Institute, in its search for anti-cancer agents had screened extracts of the wood bark of a native Chinese ornamental tree, *Camptotheca acuminata*, locally known as the Happy Tree.

Initial screening showed that the extracts were found to be active against mouse leukaemia assays.

Bioassay-guided isolation led to the isolation of the active agent—the quinoline alkaloid—Camptothecin.

This compound as its sodium salt, proved to be extremely active against leukaemia cells and solid tumour inhibitions.

The molecule has given rise to a host of other anti-cancer drugs including Topotecan, 9-aminocamptothecin and CPT-11.

Camptothecin and these analogues have been investigated to treat a wide variety of cancers but the compounds are quite

Among the other *Camptotheca* metabolites, is 10-hydroxycamptothecin, which has been found to be more active than

Camptothecin Hydroxycamptothecin

Interest in camptothecin grew as a result of its ability to inhibit topoisomerase I, which is the enzyme involved in many important cellular processes by interacting with DNA (Oberlies and Kroll, 2004).

With the structure of Camptothecin acting as template, several products have been developed namely topotecan (hycampta-mine) and irinotecan (CPT-11) (Friedman et al., 2003).

While camptothecin (as its sodium salt) was in clinical trials at the NCI in the 1970s but it had to be dropped because of Nonetheless, Irinotecan, being much less toxic than camptothecin, was approved in the US against metastatic colorectal cancer. Irinotecan has much greater water solubility and is a prodrug, being metabolized in vivo by hydrolysis to give topoisomerase I inhibitor which is 1000 times more active than the parent compound.

Topotecan has also been approved in the US for ovarian cancer and has been tested also among paediatric patients with resistant and recurrent solid tumours (Martinez et al., 2003).

Nowadays, the development of hairy root cultures and the cloning and characterization of genes encoding key enzymes of the pathway leading to Camptothecin formation in plants has opened new possibilities to propose alternative and more sustainable production systems for this important alkaloid (Lorence and Nessler, 2004).

Brucea antidysenterica (Simaroubaceae)

B. antidysenterica is a plant growing in the North Eastern part of Africa, particularly in Ethiopia.

This plant has been used by the local population against infectious diseases namely dysentery—hence its botanical name.

Further search into this plant has resulted in the isolation of the Quassinoid—Bruceantin.

The purified compound along with other related quassinoids were found to be toxic to *Entamoeba histolytica*, in vitro (IC₅₀ = 0.0181 µg/ml) (Gillin et al., 1982).

Bruceantin Me

Further testings were also being carried out for their anti-tumour properties.

This led to the isolation of the quassinoid glucosides Bruceantinoside-A and B (Okano et al., 1981, 1985) and bruceanic

Preliminary cytotoxicity tests effected showed the compounds to be active against five human tumour cell lines, malignant melanoma (RPMI-7951), lung carcinoma (A-549), ileocecal adenocarcinoma (HCT-8) epidermal carcinoma of the nasopharynx (KB) and medulloblastoma (TE-671) and against murine lymphomatous leukaemia (P-388) (Imamura et al., 1985). In vivo studies using RPMI 8226 human-SCID xenografts demonstrated that bruceantin induced regression in early as well as advanced tumours, and these significant anti-tumour responses were facilitated in the absence of overt toxicity.

Apoptosis were significantly elevated in tumours derived from animals treated with bruceantin and it was concluded that bruceantin interfered with the growth of leukaemia, lymphoma and myeloma cells in culture and xenograft models.

The clinical efficacy against haematological malignancies is being investigated (Cuendet and Pezzuto, 2004).

23. Plants used against infectious diseases

23.1. Anti-malarial properties

Throughout Man's troubled history, few diseases have played so tragic a role as malaria.

It has killed or incapacitated more people than all plagues, wars and auto-mobiles.

More than 10% of the US overseas armies in 1943 had malaria.

In 1596, the earl of Cumberland captured Spanish Puerto Rico but could not hold it because his forces were decimated. Alexander the Great died of it in June 323 B.P.

Untreated malaria may kill about 1% of those infected.

The survivors prone to relapse may suffer from anaemia, weakness, sexual impotence, chronic abortion and secondary infections—all of which lower the value of the individual to self, community, family. Malaria is believed to be the most serious and important parasitic disease in the world.

Malaria, nowadays, is the number one infectious disease in the world and over two million people die each year from malaria (Meshnick and Dobson, 2001) and the majority of the victims being young children.

The name malaria was coined in the 17th century by Dr. Francisco Torti by combining the Italian word for bad and air as it has been called the shakes, the fevers, theague and many other things, none affectionate.

Hippocrates had reported several cases of malaria. It was also known even at that time that swamps (Bruce-Chwatt, 1985) and mosquitoes were involved for malaria was rarely found in dry and windy places and disappeared in winter.

It was only during the middle of the 18th century that the relationship of mosquitoes to the fevers be accepted. In 1880, the French Physician, Charles Laveran, found microscopic parasites in red blood cells of human victims of malaria.

By 1899, the complete life cycle of the parasite, called Plasmodium was known.

There are four major species of malarial parasites, each causing different clinical types of the disease.

The need for mosquito control became obvious and marshes were drained and other control measures were adopted throughout the world. DDT, in spite of its almost criminal misuse, as an insecticide, saved millions of lives. Even as far back as the 15th century, physicians were dreaming of some medicine, which could cure the disease, what today is referred to as a chemotherapeutic agent—specific for the malarial parasite. One was found in a plant and its history started in Lima, Peru the capital of New Spain. After Lima was founded in 1520s, it became a proud and wealthy city and where business prospered.

The turn-over for business was high at a place where malaria was endemic.

The Church fathers noted that the Indians were not so much bothered by the disease and they attributed the cure to the fevers to the bark of a tree which when mixed with water, cured the fevers. The natives called the tree- the Quina or the Fever bark tree.

It was the Society of Jesus that recognized the political potential inherent in this powder and soon developed a monopoly. The Jesuits bark was used to cure and convert people.

In 1693, the Chinese emperor, the great Kang His, had bad malarial attack and the Jesuits in attendance at his court, introduced the bark and saved his life; King Kang His was grateful but he never became a convert.

However by the end of the 17th century, quinine powder no longer Jesuit Powder was the standard treatment for malaria. Spain still controlled trade through its exclusive mandates in Peru and Bolivia.

As demand increased, it became obvious that there weren't enough trees available to assure supplies.

Bark collectors had to go further and further into the mountainous bush to find the trees, getting lost and dying in the jungles with dysentery and the dart poisons of the Jivaro Indians. In the middle of the 18th century, a group of French. This information was later confirmed by Linnaeus who later gave the name Cinchona to the trees to honour the Viceroy of Peru in 1628–1639 (Potier, 2001).

Today, the disease has become very critical and widespread and one of the main reasons for this is that the anti-malarial drugs, including chloroquine, is no longer effective against the disease as its efficacy has been decreased by the spread of. This loss in efficacy has been a major barrier to the effective treatment of malaria and has posed an urgent challenge to discover new anti-malarial drugs.

Malaria is caused by four species of the genus Plasmodium, namely *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*.

Almost all fatalities are due to *P. falciparum* infections and therefore the most important species but *P. vivax* also causes. This shocking reality is largely due to the emergence of drug resistant strains of *Plasmodium falciparum*.

In the early days, quinine was the curative agent for malaria and subsequently, quinoline anti-malarials and related aryl alcohols were developed on the quinine prototype.

This led to the emergence of drugs such as chloroquine, and mefloquine.

With the rise of parasite-resistant to these anti-malarials, it became a necessity to search for other synthetic and natural. Another plant long used in the treatment of fevers in Chinese traditional medicine was considered.

The suggestion to investigate wormwood for anti-malarial activity came from Chinese herbal medicine as this herb—qing hao —has been prescribed for fevers by the Chinese physician Li Shizen in 1527.

Artemisia annua (Asteraceae)

Artemisia annua, also known in China as Qinghao, has a long history in Chinese medicine.

A. annua or Sweet Wormwood has yielded the agent Artemisinin and derivatives which are potent classes of anti-malarial. The Artemisinins are sesquiterpene lactones and are widely used to treat multi drug-resistant malaria and they act also on cerebral malaria-causing strains of *Plasmodium falciparum*.

The clinical efficacy of these drugs is characterized by an almost immediate onset and rapid clearance reduction of parasitemia (Eckstein-Ludwig et al., 2003; Jung et al., 2004).

Artemisinin is now used as an alternative to chloroquine in areas of China with resistant strains of *Plasmodium* and has been investigated in the United States by the military, since malaria can quickly debilitate troops.

In the meantime, in view of the fact that *A. annua* gives extremely low yields of Artemisinin (0.01–0.8%), the direct

Therefore the enhanced cell culture of artemisinin either in cell/tissue culture is highly desirable and are being tried (Abdin et al., 2003). First isolated in 1972, the sesquiterpene endoperoxide Artemisinin has been the basis for several semi-synthetic drugs, namely Artemether and Arteether, which have greater solubility in vaccines and greater anti-malarial

Artemisinin MeMeHHOR Artemether R

Arteether R = CH

Nonetheless while the synthetic and semi-synthetic analogues are being tested, malaria still poses a challenge to poorer countries where these modern anti-malarial drugs are often unavailable.

In these countries, randomized pilot trials have been effected so as to investigate the efficacy of traditional tea preparations of *A. annua* in the treatment of uncomplicated malaria.

After 7 day medication, cure rates were on average high (74%) but recrudescence was high which suggested that monotherapy with *A. annua* cannot be recommended as alternative to modern anti-malarials (Mueller et al., 2004; Willcox et al., 2004) but a combination with other anti-malarials, is being recommended (Balint, 2001).

The next question that remains is—How quickly malaria will evolve immunity to artemisinin? In fact the best defence

Quillaja saponaria

(*Rosaceae*) (*Soap bark tree*)

Several alternatives of vaccine are being worked upon.

The extracts from the South American tree, *Quillaja saponaria*, contain triterpenoid saponins (Guo and Kenne, 2000), which are ingredients in an experimental malaria vaccine (Bienzleet et al., 2004; Kirk et al., 2004).

Partial purification of the crude extract has resulted in the isolation of Quil A, later named Stimulon. Stimulon seems to work as an adjuvant, a pharmacological additive that improves the effectiveness of a vaccine in promoting the formation of antibodies. While searching for a vaccine, research going on in other parts of the world where malaria is endemic.

With the re-emergence of malaria in the central Highlands of Madagascar in the 1980s and coupled with the lack of inappropriate drugs, pushed the population towards traditional herbal remedies among them were the *Strychnos* species.

Strychnos myrtoides

(*Loganiaceae*) *Strychnos*

species are commonly used in the local pharmacopoeia in Madagascar as well as in mainland Africa.

The roots have been used against constipation, toothache, coughs as well as epilepsy.

The aerial parts also been used against malarial fever (Neuwinger, 2000). With the prevalence of quinine-resistant, *Plasmodium falciparum*, in Madagascar attention has been focused on medicinal plants that could reverse

Investigation into several plants led to the investigation of *Strychnos myrtoides* as the crude alkaloids were empirically used as an adjuvant to chloroquine in Malagasy herbal remedies.

When combined with chloroquine at a dose level lower than their IC value, they markedly enhanced in vitro, the effectiveness of the synthetic drug against a chloroquine-resistant strain of *P. falciparum*.

They also enhanced in vivo chloroquine activity against a resistant strain of *P. yoelii*. This led to the isolation of two major bioactive constituents—*Strychnobrasiline* and *Malagashanine* (Rasoanaivo et al., 1994) as well as four minor alkaloids.

Malagashanine, turned out to be the parent compound of a new subtype of *Strychnos* alkaloids, the C-21, Nb-secocuran indole alkaloids, isolated so far from the Malagasy

Strychnos (Rafatro et al., 2000; Rasoanaivo et al., 2001; Martin et al., 1999).

Strychnobrasiline and *Malagashanine* were devoid of both intrinsic anti-malarial activity both in vitro (IC₅₀/ml for *strychnobrasiline* and IC₅₀ A. Gurib-Fakim / Molecular Aspects of Medicine 27 (2006) 1–93 for *malagashanine* and in vivo

10 mg/kg conferred as a 5% suppression of parasitemia) and cytotoxicity (Rasoanaivo et al., 1996) but exhibited significant chloroquine-potentiating actions which could justify the empirical uses of *S. myrtoides* *Strychnobrasiline*

At present, the infusion of the stem barks of *S. myrtoides* in association with chloroquine has been successfully evaluated

The aim now is to develop purified and standardized extracts for clinical trial and to eventually develop efficient and

inexpensive drugs for the treatment of chloroquine-resistant malaria (Rasoanaivo et al., 1996).

It has a weak anti-plasmodial action, but when combined to chloroquine at concentrations much lower than required for anti-malarial effect, it enhanced in vitro and in vivo, chloroquine action against chloroquine-resistant strains of

Calophyllum sp. And Garcinia sp.

(*Clusiaceae* family)

Recently the xanthenes from the extracts of *Calophyllum caledonicum* and *Garcinia vieillardii* (*Clusiaceae*) have been tested for their anti-malarial activity against the chloroquine-resistant strains of *Plasmodium falciparum*.

The most potent xanthenes were found to be the following: demethylcalabaxanthone, calothwaitesixanthone and 6-deoxy-gamma-mangostin with an IC₅₀ value of 1.0 microg/ml (Hay et al., 2004).

23.2.

Plants and AIDS

Worldwide millions of people are infected and are being infected with the Human Immuno deficiency Virus (HIV), the pathogen that causes Acquired Immuno deficiency Syndrome (AIDS).

AIDS is a complex array of disorders resulting from the deterioration of the immune system and infected individual become susceptible to rare forms of cancer; common microbes become opportunistic pathogens.

HIV uses cells of the immune system (macrophages and helper T cells) as sites for reproduction and multiple copies of the viral genetic material (RNA) are made and packaged into new viral particles ready for dispersal into new viral hosts.

More cells of the immune system are killed or damaged with each round of infection, when millions of viral particles may

Despite the production of antibodies and helper T cells that fight the disease, eventually the virus prevails and the infections and cancer associated with AIDS begin to appear

With no known cure or vaccine against HIV, drugs slow the progression of the viral infection and the onset of AIDS.

New anti-HIV compounds from natural sources are reported almost daily, some essentially unproven and others with distinct promise based on in vitro research.

Secondary metabolites will play a significant role in combating viral infections along with the AIDS infections incurred by a compromised immune system.

More than 36,000 extracts have been tested by the National Cancer Institute of the USA and 10% of them have been reported to exhibit some anti-HIV activity.

One of the most promising anti-AIDS compounds is produced by the Malaysian tree, a member of the tropical *Garcinia* family (Guttiferae-Clusiaceae) that is valued both for its wood and resins.

A detailed survey of *C. lanigerum* and related species showed that latex of *Calophyllum teysmanii* yielded extracts with

The active constituent was found to be (-)-calanolide B, which was isolated in yields of 20–30%. Eight compounds have been isolated from *C. lagenarium* with Calanolide A showing anti-HIV activity and

C. teysmannii has yielded Calanolide B, equally found to be slightly less active than the (+)-Calanolide A, but it has the advantage of being readily available from the latex which is tapped in a sustainable manner by making small slash wounds in the bark of mature trees without causing any harm to the trees.

Chemically, Calanolide A is a coumarin and is now being tested in human trials. The drugs are being developed by Sarawak Medichem Pharmaceuticals, a joint venture company formed between the Sarawak State Government and Medichem Research, Inc. (+)-Calanolide A (which has been synthesized by Medichem chemists) is currently in Phase II. These two Calanolides can also be isolated from other *Calophyllum* species, namely from the leaves of *C. brasiliensis* (Huerta-Reyes et al., 2004) and exhibiting more or less the same pattern of activity. OOOOOHOO OOOH (+) - Calanolide. Eventually, it may be one of the antiviral ingredients included in the AIDS cock-tail that slowed the rate of AIDS progression and extended the lives of HIV-infected patients.

Another potential anti-HIV drug originated in Africa, comes from the woody vine *Ancistrocladus* species.

The crude extract from this plant has yielded Michellamine Ba new alkaloid, which in the initial trials have been shown to work against the HIV virus. Michellamine B is a chemically stable molecule found to be present in the leaves even after the *Michellamine B*

Based on the observed activity and the efficient formulation of the di-acetate salt, the NCI committed Michellamine B to advanced pre-clinical development, but continuous infusion studies in dogs indicated that in vivo effective anti-HIV concentrations could only be achieved close to neuro-toxic dose levels.

Thus, despite in vitro activity against an impressive range of HIV-1 and HIV-2 strains, the difference between the toxic dose level and the anticipated level required for effective antiviral activity was small, and NCI decided to discontinue. However, the discovery of novel anti-malarial agents, the korupensamines, from the same species (Hallock et al., 1994), adds further promise for this species.

Homalanthus nutans

(*Euphorbiaceae*) (*Mamala*)

Still in the search for new anti-AIDS compounds, Prostratin was isolated as the active constituent from an extract of the wood of the tree *Homalanthus nutans* (Gustafson et al., 1992) growing in Samoa.

This breakthrough came as a curiosity by ethnobotanist Paul Cox who was working in Samoa.

He observed that the inner bark of *Homalanthus nutans* was used to treat yellow fever, which is a clinical manifestation of. He carried out several interviews with traditional healers in Samoa, collected samples and subsequently sent the samples to the NCI for assessment of the antiviral activity in anti-AIDS assay.

Subsequent studies determined that prostratin is a relatively polar 12-deoxyphorbol ester.

When it was discovered that the main active compound was a phorbol ester, interest was greatly reduced because it is a known fact that phorbol esters are strong tumour-promoters.

Nonetheless, the extracts from this plant were tested for their tumour-promoting ability.

It was found that this compound did not promote tumour formation but instead prolonged the life of HIV-infected cells and stops the infection of healthy cells by HIV (Gustafson et al., 1992).

Prostratin is therefore, a potent activator of HIV expression in latently infected T-cell lines (Gulakowski et al., 1997), and its potential value in HIV therapy lies more in its possible utility as a viral activator rather than as an anti-HIV agent.

Prostratin

Several other botanical drugs may be useful in treating AIDS-related infections and cancers.

The alkaloid berberine, found in members of the Poppy family (Papaveraceae) has been used to treat infections caused by bacteria, fungi and protozoans.

As a broad-spectrum antibiotic with few side effects, berberine has potential for treating the various forms of severe Protozoans in particular cause gastrointestinal infections in people with damaged immune systems, and perhaps a maintenance dose of berberine would help to control such opportunistic pathogens.

Catharanthus roseus

(*Apocynaceae*) (*Madagascan Periwinkle*)

AIDS patients also find themselves at risk for cancers that are usually controlled by a normal immune system.

Vinorelbine, a semi-synthetic version of one anti-cancer alkaloid from the Madagascan Periwinkle (*Catharanthus roseus*, *Apocynaceae*) disrupts the spindle fibres that are responsible for separating chromosomes during cell division.

It works at lower concentrations and with fewer side-effects than the alkaloids derived directly from the plants and it could be useful in combating Kaposi sarcoma, a rare skin cancer.

253

Empty page

254

Medicinal plants, functional foods and nutraceuticals ...

Medicinal plants, functional foods and nutraceuticals ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of->

24. Medicinal plants, functional foods and nutraceuticals

24.1. The functional food concept

Over the past 15 years, the consumers interest in healthy nutrition has changed considerably.

Earlier, good nutrition meant avoiding products with high calorie, salt and fat content. Today, more attention is being paid to positive/preventive nutrition owing to the increased choice of food products with the desired functional components and Several reasons can be forwarded as to why this preventive concept has come to prevail.

Nutritional research is playing a leading role in emphasising on more preventive and public health aspects.

Furthermore, health professionals have learned through positive experience with fortified foods.

Currently, there is no legal definition for functional foods, either in Europe or in the US.

Only Japan has introduced an official definition for Foods for Specific Health Use (FOSHU) in 1991.

For the Food Industry, the working definition is as follows:

Functional Foods are foods and beverages with a specific health-promoting effect based on scientific proof.

In view of a lack of an unequivocal definition, problems arise with consequences for market research and legislation.

Confusions about the terms nutraceuticals and functional food arise especially as both terms are being used

Functional foods appear to be foods whereas nutraceuticals may be produced from foods but are marketed in concentrated form as pills, capsules, powders, tinctures etc. either as a single or mixed preparations.

In the US, this ambiguity still allows companies to distribute foods containing herbs that do not fulfill the GRAS (General Regarded As Safe) status under DSHEA (Dietary Supplement Health Education Act) as herbal supplements.

It is agreed nonetheless, that functional food ingredients, need to be GRAS.

This statement also covers botanical functional food ingredients.

The term botanical is generally used in the broader sense of the word as it would include herbal drugs/extracts and Phytochemicals are enriched or selected fractions of plant extracts.

Currently, the terms are being used for secondary metabolites of plants that may exert health-related effects.

Therefore, botanicals are the bioactive ingredients added to or already inherently present in foods and beverages, in order

The key driving forces for the functional food concept has been progress in nutritional science.

This coupled with the changes in lifestyle in industrialized countries where people have started to adopt a more active and

Added to this are health and educational campaigns as well as commercial advertising.

Prevention-oriented medicine and more self-responsibility in health issues are becoming a political necessity, especially

Value-addition to regular foods is gaining popularity rapidly, especially to an industry which has for long remained

24.2. *Categories of botanical functional food ingredients*

Antioxidants Antimutagenic and anticarcinogenic agents Antimicrobial and antiviral substances Enhancers of the gastrointestinal function Immune-modulators and stimulators Inflammation-inhibiting substances Cognitive enhancers (psychotropic/neuroregulatory substances) Oestrogen-modulators

Blood-pressure-reducing agents Cholesterol-reducing agents Anti-Allergenic Anti-Diabetics An ingredient may have beneficial effects in more than one category, whereas others react very specifically.

Furthermore, scientific evidence for efficacy and more importantly clinical proof is quite heterogeneous, both within a Traditional ingredients (such as soya proteins) have been re-discovered, phytochemicals in fruits and vegetables (e.g. resveratrol) are recent discoveries, as are innovative ingredients (e.g. phytosterols).

The complete mode of action has been elucidated only for a few ingredients.

The most widely used, as well as the most promising ingredients categories or plant origin are highlighted and emphasis is also placed on the commercial and marketing aspects.

It must be pointed out nonetheless that the functional food industry has focused mainly on those botanical ingredients that are inherent to vegetables, grains and fruit which are part of the normal human diet, their specific nutritional value and or/effective dose that often remained obscure. until recently when epidemiologists/clinical research have shed light on Ethnobotanical studies are also highlighting the applicability of other herbs and plant sources for more potent or even So far safety concerns, as well as time-consuming efficacy and toxicological studies have prevented a broader use of herbal ingredients in functional foods.

24.3. *Traditional 'functional foods' Soya proteins:*

The functional components of Soya extracts include proteins, isoflavones, oligosaccharides and phospholipids.

Soya proteins have been reported to have beneficial effects directed towards the most relevant diseases in industrialized countries, including cardiovascular disease, cancer and diabetes.

In Japan, Soya proteins have FOSHU status as an active ingredient in food to reduce blood pressure.

In 1999, the FDA released a health claim approval, which stated that: "25 g of soya proteins a day, as a part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease".

There is a major problem with Soya—especially among European consumers—is its lack of acceptance due to the fact that soya is a typical GM (Genetically Modified) crop.

In fact, in 2001, US soya bean farmers planted around 63% of their soya bean field with GM soya and also non-GM Organically grown soya for use as food ingredients is increasingly being imported from South America.

Phytosterols:

Phytosterols and stanols are currently among the most successful phytochemicals for the development of functional foods

Phytosterols have clinically proven cholesterol-lowering properties.

Prebiotics:

An alternative approach for dietary modulation of intestinal flora instead of oral administration of living bacteria ("probiotic") is to specifically stimulate the growth of endogenous microorganisms by prebiotics.

These are defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and this improves host health.

Prebiotics are basically non-digestible carbohydrates, mainly obtained by extraction from plants, followed by enzymatic The fructose-based disaccharide inulin and oligofructose are the most widely used as food ingredients, because of their technical (fat replacement, gelling) and nutritional (bifidogenic) properties.

Both are increasingly used in functional foods, especially in dairy and bakery products.

The primary source of inulin is the roots of the Chicory (70% of the dry materials).

Fibres:

Apart from prebiotic disaccharides inulin and oligofructose, there are other natural oligo- and polysaccharides, including pectins, gums and β -glucan, collectively called soluble dietary fibre, that exert beneficial effects on intestinal function by increasing the physical bulk in the bowel and stimulating intestinal transit.

In addition, the functional food concept makes use of the hypocholesterolaemic properties of water-soluble fibres.

Soluble fibres are already added to a variety of functional food products such as milk products, bakery goods, confectionery and soft drinks. Pectin, a structural component of plant cell walls is produced primarily from apple pomace

Psyllium seed husks had previously been recommended after having received approval for a health claim but commercially Gums, used in food processing are the exudates Gum Arabic.

Guar gum from *Cyamopsis tetragonolobus*, is an annual leguminose grown in India and Pakistan.

Increasingly seaweed gums such as Carrageenan (extracted from red seaweed) or al-gin (brown sea weed) are another Seaweeds are used extensively in Asian kitchen. It contains other interesting components or traditional medicinal value with curative powers for a variety of diseases (tuberculosis, arthritis, colds, influenza, cancer etc.).

Nori Porphyra sp.) a red alga popular in Japan and Korea has very high proteins, iodine and vitamin C content.

Nori is the most valuable single crop produced by aquaculture worldwide.

Phytoestrogens:

There are many plants that contain oestrogenic substances (phytoestrogens) and pharmacological and epidemiological evidence suggests that they act as mild oestrogens or, in some instances, can act as anti-oestrogens (in as much as they bind to oestrogen receptors and they prevent the occupation by natural oestrogens).

Phytoestrogens are gaining popularity for the development of functional food products targeted at women suffering from menopausal symptoms and to prevent osteoporosis.

They may also reduce the risk of hormone-dependent cancers, such as breast cancer in women and prostate cancer in men.

Because of the structural similarity to oestradiol and its binding ability to the human oestrogen receptor, they are suspected to act as natural SERMs (Selective Oestrogenic Receptor Modulators).

The three major classes of phytoestrogens are described—iso flavones, lignans and coumestrans.

Some species of Palm even contain similar hormones (e.g. estriol).

Soya is a particularly rich source of isoflavones, whereas flax has the highest known lignan content.

The common occurrence of these substances, has implications for men as well as for women, in that the incidence of benign prostatic hyperplasia is lower in men, and menopausal symptoms in women, in societies consuming significant amount of foods containing these substances in their normal diets.

Although it is known that they have beneficial effects, including chemopreventive activity, the full mechanism of action is

It is also worth pointing out that the efficacy and long-term safety need to be investigated more extensively before these purified phytoestrogens are more widely used commercially as functional ingredients.

Plant oils:

Polyunsaturated fatty acids (PUFAs) are basically divided into 2 families—the Omega-3 and the Omega-6 PUFAs.

Both are essential because the human body is not able to synthesize the double bonds in the molecule.

Clues to the risk-reducing properties of omega-3 PUFAs against coronary heart disease point back to epidemiological observations of Eskimos consuming a diet extremely rich in fatty fish.

Today, clinical evidence of protective effects of omega-3 PUFAs on conditions such as arteriosclerosis, thrombosis, blood pressure and cardiac function is available.

Further omega-3 PUFAs have significant anti-inflammatory properties, making them potentially useful for rheumatoid arthritis and inflammatory bowel diseases.

Intake of omega-3 PUFAs has also shown positive effects in the treatment of several psychiatric disorders.

Still, the primary commercial source of omega-3 PUFAs is fish oil.

However, vegetable oils and single-cell oils from marine algae (e.g. *Cryptocodium cohnii*) and fungi (e.g. *Mortierella alpina*) gain ground because of better acceptance by the consumer.

Flax seed and rapeseed oil, dark green leafy vegetable, legumes and nuts all contain considerable amounts of omega-3

The demand for fish oil alone has been forecast to reach 25,000 tons by 2010, making alternative sourcing mandatory.

Fish oil preparations are usually distributed as dietary supplements in the form of capsules.

Omega-6 PUFAs such as α -linolenic acid (GLA) have pronounced anti-inflammatory properties.

The major dietary sources of GLA are seed oils from Borage, Primrose and Blackcurrant.

Although they are currently only marketed as encapsulated supplements, stabilised powders for fortification of foods are

Phospholipids are another interesting group of plant lipid ingredients.

The main sources are common seeds such as Soya, Grapeseed and Sunflower.

Phospholipids (lecithin) have been primarily used as emulsifiers in the food industry.

However, there is now increasing evidence that they can lower elevated serum cholesterol levels and the balance of phospholipids. Moreover, phospholipids have been shown to have beneficial effects on age-related memory loss (phosphatidylserine in particular) and functional decline of the immune system (Gruenwald et al., 2002).

24.3.1. Vitamins

Vitamins are the only functional food ingredients category that has clear government recommendations.

Herbal supplements:

Herbal supplements is a very important segment for botanical use both in volume and diversity and accounts for about 25% of the total dietary supplements market.

It is nonetheless, becoming very difficult to establish boundaries between functional food products and herbal supplements as several enriched food products are marketed as dietary supplements rather than food.

While there has been a decline in the sales values among the top 10 selling supplements (kava kava, ginkgo, Echinacea, garlic, ginseng, St. Johns Wort, Saw Palmetto etc.), there has been some winners (soya, valerian, elderberry, guarana).

This decline may be explained to the negative media coverage about herbs.

25. The need for validation

25.1. Quality and safety:

Production, standardization and quality control

Plant drugs, also known as phytomedicines or phytopharmaceuticals are plant-derived medicines that contain a chemical compound or more usually mixtures of chemical compounds that act individually or in combination on the human body to Pure compounds or chemical entities are either isolated from natural products or made by synthesis in the laboratory.

Herbal teas, decoction, alcoholic extracts are also traditional ways of using medicinal plants.

Very often these plant materials are used in a non-standardised manner.

However, nowadays more and more emphasis is being put on the use of standardized materials.

Doses and efficacy

Two questions have confounded the first person who sampled a medicinal plant—

1 Do herbal remedies work ?

2 and How much should a patient ingest for an effective and safe cure?

If one goes back and reads about the history of Mankind, the battle against diseases in all the cultures of the world, the search for miracle cures for diseases like cancer, malaria and leukaemia etc., then the answer would be a resounding Yes. However, in many instances, scepticism about the efficacy of quite a few plants is also justified.

This scepticism has been growing as a result of the many unrealistic claims made by producer of herbal products.

Scientists have been proceeding in a systematic way in order to validate the claims of several medicinal plants.

For some symptoms and ailments, this may be fairly easy to prove but in more complex health conditions, the situation

Nonetheless, medicinal plant extracts are showing a great deal of promise even in instances of complexity of illnesses.

In order to proceed with the validation of the efficacy of medicinal plants, there are several levels of evidence that are taken into account (WHO Monographs, 1999, 2002).

1. The Ethnobotanical claims
2. Anecdotes
3. Pharmacological studies
4. Observational studies
5. Clinical studies

Millions of dollars are spent each year on herbal products that are marketed as food supplements but in reality very few know, chemically, what they are purchasing or using.

Very often the dosage varies from the different brands of the same herbal product.

In spite of these major shortcomings, there has been a phenomenal increase in the interest towards phytotherapies.

The chemistry and efficacy of many of these plants are relatively unknown and there is a chance of toxicity or overdose until the secondary compounds are known and understood.

There is a tendency in the US and in Europe to regulate and license this market and this has led to greater and more effective use of these important medicinal plants.

There is also general agreement that chemical standardization is the way forward in order for herbal remedies to be prescribed to patients who seek to be treated with medicinal plants.

Standardisation is a method of assuring a minimum level of active ingredients in the extract and is becoming increasingly important as a means of ensuring a consistent supply of high-quality phytopharmaceutical products.

It can be defined as the establishment of reproducible pharmaceutical quality by comparing a product with established reference substances and by defining minimum amounts of one or several compounds or groups of compounds.

In the field of phytomedicines, standardization only applies to extracts. Standards for active ingredients to be used in medicinal products may be found in monographs and/or pharmacopoeias.

25.3. Why is standardization important?

It is accepted that concentration or dosages are very important because herbal medicines (in common with conventional medicines) contain biologically active substances that may produce non-trivial side effects when taken in excessive doses. Very low doses, on the other hand, may have no therapeutic value.

In practice, plant material is often highly variable, so that a minimum concentration or a concentration range is often used.

An upper limit is necessary with highly active or potentially harmful ingredients, as most plants have a wide therapeutic window (e.g. a toxic compound is considerably higher than the therapeutic dose).

In the case of compounds with a narrow therapeutic window, chemical entities are favoured, as opposed to extracts.

These phytodrugs when they become registered become a medicine that needs to comply with the basic standards required. Standardisation also allows comparison of the clinical effectiveness, pharmacological effects and side effects of a series of products (e.g. against a placebo).

Standardised products provide more security and increase the level of trust people have in herbal drugs.

At the international level, the World Health Organisation has developed a strategy to review traditional medicines and included within this review is a programme to develop monographs for herbal ingredients.

Additionally, the European Scientific Cooperative on Phytotherapy (ESCOP) was established in 1989 to advance the scientific status of phytomedicine and to assist with the harmonization of their regulatory status at the European level.

ESCOP has already published 60 monographs on the medicinal uses of plant drugs that have been submitted to regulatory authorities across Europe and accepted by the Working Party on Herbal Medicinal Products of the European Agency for the Evaluation of Medicinal Products (EMA) as providing the basis for proposed core-SPCs for European decentralized. A Pharmacopoeia is a collection of quality standards for medicines and their components.

In order to obtain marketing authorization for a medical product, the ingredients or the medicinal product must generally comply with a pharmacopoeial standard.

Thus Pharmacopoeial standard may provide guidance on acceptable purity criteria for that ingredient.

25.4. Some of the existing Legal Framework for plant-derived ingredients with medicinal properties

25.4.1. The World Health Organisation (WHO)

The WHO views herbal medicines as herbs, herbal materials, herbal preparations and finished herbal products that contain active ingredients parts of plants, and other plant materials, or combinations.

The WHO recognizes that the traditional use of herbal medicines refers to the long historical use of these medicines and that they may be accepted by national authorities.

As a result of this view, the WHO Traditional Medicines Strategy 2001–2005 was developed to review a framework for action for WHO and its partners aimed at enabling TM/CAM to play a far greater role in reducing excess mortality and

25.4.2. European Union (EU)

The EU directives 2001/83/EC on the Community code relating to medicinal products for human use lays down a general framework for pharmaceutical products requiring pre-marketing approval before gaining access to the market and laying down the requirements for the documentation of quality, safety and efficacy, the dossier and expert reports.

This framework has effectively been in operation and additionally the European Agency for the Evaluation of Medicinal Plant Products (EMA), which acts as a central agency for single European medicines marketing authorizations operates a

However, individual Member States (UK, Germany, France, Italy etc.) have taken different approaches in reviewing herbal

25.4.3. *The United States (US)*

In the US, the Food and Drug Administration (FDA) has responsibility for food and drug products.

Drugs are regarded as products that claim to treat, cure, mitigate or prevent a disease.

Herbal medicines follow the same procedures as those for a chemical drug.

Otherwise natural products are regulated as foods under a requirement for ingredients to be generally recognized as safe

Natural products generally have GRAS status, provided that this is supported by expert consensus.

Hence dietary supplements and herbs are considered to be foods provided that they are generally regarded as safe and do

Furthermore, the ingredients and the plants or parts of the plants must be quantified and where, ingredients are listed with a pharmacopoeial reference, they must meet the standard laid down in the pharmacopoeia.

There are also specific requirements for food additives that do need a pre-market approval by the authority.

25.5. *Standardised extracts*

These extracts as mentioned above are those for which the active constituents (single or groups) are known.

They can thus be standardized to be a defined content of the active constituents giving a clearly defined amount of an

Onion bulbs

(*Bulbus Allii cepae*, Onion)

Ginkgo extracts

(*Folium Ginkgo*): Standardized extracts (dry extracts from dried leaves, extracted with acetone and water, drug: extract ratio 35–67:1) contain 22–27% flavone glycosides and 5–7% terpene lactones, of which approximately 2.8–3.4% consists of ginkgolides. The level of ginkgolic acids is below 5 mg/kg (WHO Monographs, 1999).

Groups of compounds likely to have the desired pharmacological activity are unknown, but are not solely responsible for the clinical efficacy of the extract.

The monograph must define a range of content of the selected constituent(s) some of which are lead compounds.

Standardisation by blending different batches of a herbal drug before extraction, or by mixing different lots of herbal drug preparation, is acceptable but adjustment using excipients is not acceptable (Heinrich et al., 2004).

Examples of Quantified Extract.

Ginkgo biloba leaves.

Ginkgo biloba leaves are used for improving cerebral and peripheral circulation among old people and also for cerebral

Ginkgo extracts are well-known for the two groups of compounds which are particularly relevant:

The Flavonoids (0.5–1%): flavone and flavonol glycosides, acetylated flavonol glycosides, biflavonoids.

Terpene lactones: (0.03–0.25%)

Although it is a well-known fact that these compounds are among the most important ones, other compounds are also important and their role and action must also be understood as they may well add to the pharmacological activity of the

25.7. *Quality control*

Microscopy is less important here as opposed to phytochemical methods.

In the case of the crude drug, Thin Layer Chromatography is only feasible for some components like the flavonoids.

The presence of vital minor compounds may be masked and may not be very visible.

It is in this particular instance that the complementarity of analytical methods like HPLC and GC are of paramount importance for analyzing both the lead and the minor compounds.

26. *Side-effects (toxicity) of plant extracts*

- 1 It would be naive on anybody's behalf to think that every plant extract is necessarily safe for human consumption.
- 2 It is precisely for these reasons that poison centers have been established across several continents.
- 3 Nonetheless, it would be difficult to distinguish between an effective medicine from a deadly poison.
- 4 The dosage is critical in these circumstances especially as some plants with a long history of use have been implicated as
- 5 Among such plants are, amongst others, the Comfrey (*Symphytum officinale*) which has been reported to cause acute liver damage; Yohimbe (*Corvnanthe vohimbe*) is used as a dietary supplement and aphrodisiac but at high doses, it is

Plants used for the endocrine system—diabetes ...

Plants used for the endocrine system—diabetes ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-17>. *Plants used for the endocrine system—diabetes*

Diabetes mellitus (DM) is the commonest endocrine disorder that affects more than 100 million people worldwide and in the next 10 years, it may affect about five times more people than it does now (ADA, 1997). History has recorded that as 700–200 BC, this disease was recognized and even distinguished into two types: a genetically based disorder and the This chronic and incurable disease is essentially, caused by lack of insulin, Type 1, or insulin resistance Type 2.

Both types are associated with short- and long-term complications that affect the individuals quality of life and often engender fear and powerlessness and can compromise physical and psychological functioning.

Complications are the major cause of morbidity and mortality in DM.

Complications arise because of a lack of good blood glucose control.

However, achieving good control is difficult for many individuals because the delicate balance hormonal balance that controls glucose homeostasis is disrupted by the disease.

Because of the potential threat to quality of life and the chronic nature of diabetes, many people are turning to complementary therapies to assist them to cope and control the disease.

Drugs have been derived either directly or indirectly from plants. Some plant products act by lowering the level of glucose in the blood while others act by inhibiting glucose absorption from the gut and hence prevent the surge in blood glucose. The ethnobotanical information reports about 800 plants that may possess anti-diabetic potential (Alarcon-Aguilera et al., Several such herbs have shown anti-diabetic activity when assessed using presently available experimental techniques.

A wide array of plant derived active principles representing numerous chemical compounds have demonstrated activity consistent with their possible use in the treatment of NIDDM (Marles and Farnsworth, 1995).

Among them are alkaloids, glycosides, galactomannan gum, polysaccharides, peptidoglycans, hypoglycans, guanidine, steroids, carbohydrates, glycopeptides, terpenoids, amino acids and inorganic ions.

Even the discovery of widely used hypoglycaemic drug—Metformin—came from the traditional approach of using

It can be concluded therefore that plants are a potential source of anti-diabetic drugs but this fact has not gained enough momentum in the scientific community.

Several reasons may be advanced for this:

lack of belief among the practitioners of conventional medicine over alternative medicine, alternative forms of medicine are not very well defined, possibly or quacks practising such medicines providing alluring and magical cures and natural drugs may vary tremendously in content, quality and safety.

Although oral hypoglycaemic agents/insulin are the mainstay of treatment of diabetes and are effective in controlling hyperglycaemia, they have prominent side effects and fail to significantly alter the course of diabetic complications (Rang

As the knowledge of the heterogeneity of this disease increases, there is a need to look for more efficacious agents with

Though development of modern medicine resulted in the advent of modern pharmacotherapeutics including insulin, biguanides, pharmacotherapeutics including insulin, biguanides, sulfonylureas and thiazolidinediones, there is still a need to look for new drugs as no drug (except strict glycaemic control with insulin) has been shown to modify the course or For most of them the findings have been based on the ethnobotanical claims.

The present non-exhaustive list gives an overview of some plants with well-known profiles of anti-diabetic claims.

Aegle marmelos (Rutaceae) (Bael fruit)

This plant originating from India is used against diabetes.

In Mauritius, the bark decoction, is drunk by people suffering from diabetes.

The tests effected on the aqueous extracts of the root bark, as used by people in India, (1 ml/100gm) showed hypoglycaemic effect which peaked (44%) at 3 h in normal fasted rats.

In addition, the same extract completely prevented peak rise or blood sugar at 1 h in OGTT.

The hypoglycaemic activity was reduced upon storage of the extract.

Aqueous extracts of the leaves (1 mg/kg for 30 days) significantly controlled blood glucose, urea, bodyweight, liver glycogen and serum cholesterol or alloxanized (60 mg/kg IV) rats as compared to controls and this effect was similar to When fed as aqueous leaf extract (1gm/kg/day) to STZ (45 mg/kgIV) diabetic rats for 2 weeks, it decreased malate dehydrogenase levels (an enzyme known to increase in diabetes) in comparison to diabetic controls.

The extracts were equi-effective in comparison to insulin in restoring blood glucose and body weight to normal levels (Seema et al., 1996). It must be reported that aqueous leaf extracts administered orally for 28 days also normalized STZ (45 mg/kg body weight) induced histo-pathological alterations in the pancreatic and kidney tissues of rats (Das et al., 1996).

Allium sativum (Liliaceae) (Garlic)

This perennial herb is cultivated almost throughout the world and is used as a food ingredient.

Experiments have shown that an oral administration of 0.25gm/kg of ethanol, petroleum ether, ethyl ether extract of *Allium sativum* cause 18.9, 17.9, 26.2% reduction of blood sugar in alloxan-diabetic rabbits (150 mg/kg).

Oral administration of 0.25gm/kg allicin (isolated from Garlic) produced hypoglycaemia comparable to tolbutamide in mildly diabetic rabbits (glucose level ranging from 180–300 mg%) while it showed no effect on severely diabetic animals

Aqueous homogenates of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10gm/kg/day) in water for 2 months) significantly increased hepatic glycogen and free amino acid contents, decreased fasting blood sugar, triglyceride levels in serum, liver and aorta and protein levels in serum and liver in comparison to sucrose controls.

It has been shown also that oral feeding of garlic extracts (100 mg/kg) increased cardiovascular functions in STZ rats, prevented abnormality in lipid profile and increased fibrinolytic activities with decreased platelet aggregation.

Plasma insulin level increased with concomitant decrease in plasma glucose levels.

In addition, daily oral feeding of the same dose for 16 weeks showed anti-atherosclerotic effects in STZ diabetic rats.

Thus garlic may prevent diabetic cardiovascular complications (Patumraj et al., 2000).

Aloe barbadensis (Asphodelaceae) (Aloe vera) This plant is cultivated widely as an ornamental locally but in many countries. Aloe vera is cultivated on commercial scale for its gel and plant extracts.

The latter are recommended in Ayurveda for managing painful conditions and it is also mentioned in other Pharmacopoeias, namely the Arabic Pharmacopoeia, as being useful in managing diabetes.

Extracts of aloe gum effectively increased glucose tolerance in both normal and diabetic rats.

Chronic but not single administration of the leaf exudates at a certain dose (500 mg/kg PO) showed significant hypoglycaemic effect in alloxan-diabetic mice.

Nonetheless, single as well as chronic administration of the bitter principle (5 mg/kg IP) showed significant hypoglycaemia

The hypoglycaemic effect of single dose of the bitter principle was extended over a period of 24 h with maximum hypoglycaemia observed at 8h while chronic administration (exudates twice daily and the bitter principle once a day for 4 days) showed maximum reduction in plasma glucose level at the 5th day.

Hypoglycaemic effect of aloe and its bitter principle is mediated through the stimulation of synthesis and/or release of insulin from the β -cells of Langerhans (Ajab-noor, 1990).

It has been shown that the dried sap of the plant (half a teaspoonful daily) for 4–14 weeks) has shown significant hypoglycaemic effect both clinically as well as experimentally

Catharanthus roseus (Apocynaceae) (Rosy Periwinkle)

Originating from Madagascar but now of wide distribution throughout the tropics, this plant is commonly used in

The oral administration of water-soluble fractions and ethanolic extracts of the leaves, have been tested and have been found to show significant dose-dependent reduction in the blood sugar at 4 h by 26.22, 31.39, 35.57 and 33.37% respectively in normal rats. In addition, oral administration of 500 mg/kg 3.5 h before OGTT (10 mg/kg) and 72 h after STZ No gross behavioural changes and toxic effects were observed up to 4 mg/kg IP (Grover et al., 2002).

Momordica charantia (Cucurbitaceae) (Karela, Bitter gourd)

The Karela fruit is eaten as a vegetable.

The leaf may be made into a tea called cerassie.

The juice, extracted from the various plant parts (fruit pulp, seeds, leaves and whole plant), is very common folklore

When tested on laboratory animals, *M. Charantia* has shown hypoglycaemic as well as anti-hyperglycaemic activity.

Polypeptide-p isolated from fruit, seeds and tissue of *M. charantia* showed potent hypoglycaemic effects when administered subcutaneously to gerbils, langurs and humans.

The aqueous extracts of *M. charantia* improved OGTT after 8 h in normal mice and reduced hyperglycaemia by 50% after 13 days. In addition, chronic oral administration of extract to normal mice for 13 days improved OGTT while no significant effect was seen on plasma insulin levels.

Another study carried out recently on *M. charantia* fruit extracts has shown that the latter had a direct impact on transport. Everted intestinal sacs from rats mounted in an organ bath containing Krebs solution was used.

It was observed that *M. charantia* extract had a direct impact on water transport with increasing inorganic phosphate concentration with or without D-glucose in the buffer.

In the control experiment, fluid intake was greatly enhanced at high inorganic phosphate concentration (8–10 mM) in the presence of 5.5 mM D-glucose.

The addition of 3.0 mg/ml *M. charantia* extract to the serosal side inhibits the uptake of fluid significantly.

It has been hypothesized that an increase in inorganic phosphate enhances oxidative phosphorylation thereby increasing the fluid uptake across everted intestinal sacs of rats. This would point to the fact that *M. charantia* extracts reduced fluid absorption capacity and this may be because of interference with the carrier-mediated coupled entrance of glucose and

Murraya koenigii (Rutaceae) (Curry leaf, Carripoule)

The Curry leaf is an inevitable ingredient in Indian recipes.

It is extensively used as a flavoring agent both in curries and chutney.

It has been shown that an oral feeding of

Murraya koenigii leaves diet (10% w/w) for 60 days to normal rats showed hypoglycaemic effect associated with increased hepatic glycogen content due to increased glycogenesis and decreased glycogenolysis and gluconeogenesis (Khan et al.). Dietary supplement with curry leaves has been shown to increase lecithin cholesterol acyl transferase activity (Khan et al.). Curry leaf powder supplementation (12 g providing 2.5 g fibre) for a period of 1 month in 30 NIDDM patients showed reduction in fasting and post-prandial blood sugar levels at 15-day period with no significant changes in serum glycosylated cholesterol fraction, serum lipids, lipoprotein cholesterol levels, uronic acid and total amino acids (Iyer and Ocimum sanctum (Lamiaceae) (Tulsi, Holy Basil)

This herb, considered to be sacred by Hindus, is commonly planted next to temples generally.

It is also an ornamental plant and is grown in gardens.

The traditional pharmacopoeia reports on the use of this plant against diabetes.

In 1968, Dhar et al. in Alarcon-Aguilera et al., 1998 reported hypoglycaemic effect of the ethanolic extracts of the leaf.

The ethanol (70%) leaves extract or *Ocimum sanctum* has been shown to cause significant reduction of blood glucose level in normal, glucose fed hyperglycaemic and STZ (50 mg/kg IP) induced diabetic rats.

This effect was 91.55 and 70.43% of that of Tolbutamide in normal and diabetic rats respectively.

Diet containing leaf powder (1%) fed to normal and diabetic rats for 1 month significantly reduced fast-ing blood sugar, uronic acid, total amino acids, total cholesterol, triglycerides and total lipids (Rai et al., 1997).

This plant has also demonstrated anti-oxidant and hypolipidemic effect (Kelm et al., 2000).

Syzygium cuminii (Syn. *Eugenia jambolana*) (Myrtaceae) (Jamblon, Java plum)

This herb, widely distributed throughout India and Africa, is commonly used against diabetes.

The decoction of the dried leaves and bark as well as the seeds, have shown hypoglycaemic effect.

Oral feeding of *S. cuminii* (170, 240, 510 mg/rat for 15 days) caused 50% reduction of blood glucose or normal fasted rats while chlorpropamide showed 52% reduction.

In addition, there was a 2.4, 6.8-fold and 9.2-fold increase in cathepsin B activity (proteolytic conversion of pro-insulin to insulin) by plant extract and chlorpropamide respectively (Bansal et al., 1981).

Oral administration of the fruit pulp extract to normoglycemic and STZ induced diabetic rats showed hypoglycaemic activity in 30 min possibly mediated by insulin secretion.

In addition, the extract inhibited insulinase activity from the liver and kidney.

Oral administration of the aqueous extract or the seeds (2.5 and 5.0 mg/kg for 6 weeks) showed hypoglycaemic

Daily administration of lyophilized powder of *E. jambolana* (200 mg/kg) showed maximum reduction of 73.51, 55.62 and 48.81 as compared to their basal values in mild (plasma sugar > 180 mg/dl, duration 21 days), moderate (plasma sugar > 280 mg/dl, duration 120 days) and severe (plasma sugar > 400 mg/dl, duration 60 days) diabetic rats. In addition, the treatment also partially restored altered hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, *Trigonella foenum-graecum* (Apiaceae) (Fenugreek seeds)

This plant is a very commonly used herb in Indian cooking. It is also popular in traditional medicine as a hypoglycaemic

This hypoglycaemic effect of fenugreek seeds has been demonstrated in experimentally induced diabetic rats, dogs, mice and healthy volunteers (both IDDM and NIDDM) (Alarcon-Aguilera et al., 1998).

The isolated fibres, saponins and other proteins from the seeds were given with meals for 21 days to alloxan-diabetic dogs. Significant anti-hyperglycaemic, anti-glycosuric effect along with reduction in high plasma glucagons and somastatin. Oral administration of 2 and 8 g/kg of plant extract produced fall ($p < 0.05$) in blood glucose both in the normal as well as 4-Hydroxyisoleucine, a novel amino acid, extracted and purified from fenugreek seeds, has been found to increase glucose-induced insulin release (ranging from 100fmol to 11fmol) through a direct effect on the isolated islets of Langerhans in both. The pattern of insulin secretion was biphasic, glucose-dependent, occurred in the absence of any change in pancreatic alpha and delta cell activity and without interaction with other agonists or insulin secretion (such as leucine, arginine). In clinical trials, administration of fenugreek seed powder (50gm each with lunch and dinner) in insulin-dependent (Type 1) diabetic patient for 10 days significantly reduces fasting blood sugar and improved OGTT along with 54% reduction in glycosuria. In addition, it also showed significant hypolipidemic effect (Sharma et al., 1990).

Erythroxylum macrocarpum (Erythroxylaceae) (Bois de ronde)

The validation of locally used indigenous plants, against diabetes has given some interesting results on the leaf extracts of *E. macrocarpum* of the Erythroxylaceae family.

The crude aqueous extract is commonly used in traditional medicine as a diuretic.

Experimental findings have shown that 6.0 and 12.0 mg/ml or the crude extract of *E. macrocarpum* had significant inhibitory effect on the absorption, transport and tissue swelling of the rat small intestine.

While D-glucose absorption and transport was not significantly affected ($p > 0.05$), L-tyrosine transport was inhibited at 6–

As water molecules (260) are directly coupled to each sugar molecule transported, it was observed that a high concentration of the extract (12 mg/ml), tended to inhibit the transport of glucose across rat everted intestinal sacs, in vitro. It was hypothesized that active phytochemicals such as tannins, phenols and alkaloids in the extract may decrease the permeability of the enterocyte membrane and the energy independent transport of fluid (Mahomoodally PhD the-

257

Plants used in cardiovascular ailments ...

Plants used in cardiovascular ailments ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of-18>. *Plants used in cardiovascular ailments*

Among the ills to which flesh is heir is cardiac insufficiency, a condition in which a weakened heart fails to pump enough. Cardiovascular disorders are responsible for many deaths throughout the world and this has been attributed to a large extent to a consequence of lifestyle, diet and heredity.

Progress has been made when there has been changes in diet, exercise along with treatment with conventional drugs or Cardiology has benefited greatly with the introduction of many drugs, some of them semi-synthetic based on natural

Among these compounds one notes the presence of anti-platelet agent (Aspirin), derived from the *Salix* sp., warfarin, an anticoagulant derived from dicoumarol.

Other cardiovascular conditions are arrhythmias (*Rauwolfia*), dropsy or oedema, heart failures (*Digitalis*, *Crataegus*, *Strophanthus*), anti-platelets and anti-sclerotic drugs (*Allium* sp.).

18.1. Arrhythmias and heart failures

Heartbeat is irregular and fluid collects in the arms, legs and abdomen because the kidney cannot perform their normal. The swelling is known as dropsy or more formally as oedema.

This disease syndrome is not new.

Ancient physicians knew of it but because they lacked knowledge of the circulation of blood (discovered by William Harvey in 1628) and information on the function of the kidneys, treatment was limited to usually unsuccessful attempts to reduce oedema with medicines which increased urine production (diuretic agents).

Rauwolfia serpentina (Apocynaceae) (Radix Rauwolfiae)

Snake-root (*Rauwolfia serpentina*, Apocynaceae) is a small shrub native to India, Sri Lanka and the East Indies that was used locally for mental illness and snakebite long before it was discovered by Western medicine.

More than a thousand years ago, the Indian Rig Veda mentioned snake-root in its verses that describe medicinal plants.

In Hindi, it is known as chandra or moon, a reference to its use for moon disease or lunacy.

The Dutch physician and botanist G.E. Rumpf (1627–1702) had observed that mongoose or weasel, before attacking a snake, fortifies itself by eating the leaves of the *Rauwolfia* plant.

Snake-root had been cultivated for medicinal use in tropical India, and the roots are dried and ground into a powder that contains more than 60 alkaloids out of which Reserpine and Rescinnamine are among the principal hypotensive alkaloids. This way, it can also be sold as *pagal ke dawa*—the traditional herb for insanity. It even resists the deadly bites of the Cobra—hence an antidote to the poisonous bites of poisonous snakes.

Snake-root had been cultivated for medicinal use in tropical India, and the roots are dried and ground into a powder that contains more than 60 alkaloids out of which Reserpine and Rescinnamine are among the principal hypotensive alkaloids.

Reserpine

Exploration in Africa revealed that the related species *R. vomitoria* had high concentrations of Reserpine and it is now the major commercial source of the alkaloid.

Several drug companies initiated action to cultivate the plant.

Exploration in Africa revealed that the related species *R. vomitoria* had high concentrations of Reserpine and it is now the major commercial source of the alkaloid.

A third species, *R. canescens* is also used in West Africa where it is also used to treat high blood pressure. Experimental pharmacology on small animals has shown that powdered *Radix Rauwolfiae* has shown to lower the blood pressure by

The major alkaloids lower high blood pressure by depleting tissue stores of catecholamines (epinephrine and

By contrast, their sedative and tranquilising properties are thought to be related to the depletion of catecholamines and serotonin (5-hydroxytryptamine) from the brain.

Following absorption from the gastro-intestinal tract, the active alkaloids concentrate in tissues with high lipid content.

They also pass the blood-brain barrier and the placenta.

Radix Rauwolfiae products are characterized by slow onset of action and sustained effect.

Both the cardiovascular and central nervous system effects may persist following withdrawal of the drug.

The active alkaloids are metabolized by the liver to inactive compounds, that are excreted primarily in the urine.

Toxicity

Radix Rauwolfiae are contraindicated in patients who have previously demonstrated hypersensitivity to the plant or its alkaloids, also those patients with a history of mental depression. During or shortly after therapy with monoamine oxidase *Radix Rauwolfiae* is known to interact with or be potentiated by some drugs (WHO, 1999).

The use of Reserpine to treat mental illness has now been eclipsed by synthetic drugs but its discovery by Western physicians remains an important milestone in the history of medicine.

18.2. Heart failure, dropsy or oedema

Crataegus monogyna (Rosaceae) (Folium cum Flore Crataegi)

The aerial parts of the plant including the flowers are used in traditional medicine in the treatment of asthma, to support cardiac and circulatory functions.

The main constituents of the fruit are reported to be flavonoids including hyperoside, vitexin-4-rhamnoside.

Other phytochemicals present are proanthocyanidins, flavonol glycosides mainly in the form of hyperoside, spiraeoside, and Epicatechin (epicatechol) and related proanthocyanidins, phenolic acids are also present.

The other characteristic component is Crataegolic acid. The active constituents have not been identified but it is thought that the therapeutic effects are due to the presence of a mixture of them together.

Clinical and pharmacological data indicate that the standardized extracts of *Folium cum Flore Crataegi*, standardized to 4–30 mg of flavonoids, increase myocardial performance, myocardial circulatory perfusion and tolerance in case of oxygen. Positive therapeutic effects have also been observed on patients suffering from congestive heart failure (Degenring et al., 2003), hypertension, tachycardia and arrhythmia.

The procyranidins inhibit angiotensin-converting enzyme. Although improvements were seen, no long-term trials have assessed the effects of *Folium Cum Flore Crataegi* on the mortality rates in patients with chronic congestive heart failure.

18.3. Venous insufficiency

Venous circulation is one of the many problems encountered by patients suffering from cardiac-related ailments.

Plant drugs with anti-inflammatory, antioxidant activity can bring relief to conditions like haemorrhoids, varicose veins and other conditions that involve a better flow of blood.

The anti-inflammatory activities are often attributed to the presence of saponins while the antioxidant activity attributed to the presence of flavonoids and other molecules having antioxidant activities.

Among the plants that have contributed shown prominence are:

Horse chestnut (*Aesculus castanea*) and Gingko (*Gingko biloba*) *Aesculus castanea* (*Hippocastanea*) (*Semen Hippocastani*)

A. castanea is commonly known as the Horse chestnut.

This tree, indigenous to western Asia, is commonly grown in many gardens and parks in Western Europe and in the United States. Traditionally, the dried ripe seeds have been used in the treatment of coronary heart disease.

The main constituents are the triterpene saponins (up to 10%) and are collectively known as Aescin (a-aescin, b-aescin and cryptoaescin) and they are considered to be the major therapeutic principles of the seeds.

b-Aescin is a mixture of more than 30 different glycosides derived from the triterpene aglycones protoaescigenin (also known as protoescigenin) and barrintogenol C.

Other constituents present include the flavonoids (e.g. quercetin, kaempferol and their glycosyl derivatives).

R = H = Barrintogenol R = OH = Protoaescigenin

Hydro-alcoholic extracts of the seeds have been tested in canine saphenous veins *in vitro*, and an intravenous bolus (25–30 mg) increased venous pressure in perfused canine saphenous veins, *in vivo*.

Placebo-controlled clinical trials have been carried out to assess the efficacy of oral administration of standardized extracts (250–600 mg) equivalent to 100–150 mg aescin daily, in the treatment of Chronic Venous Insufficiency (CVI).

Clinical studies have shown symptomatic improvement in skin colour, venous prominence, oedemas etc in treated patients.

Pregnancy-related varicose veins in women, swollen legs during long (15 h) flights also responded positively to treatment.

Double-blind placebo-controlled in healthy volunteers also showed improvement in capillary resistance (WHO, 2002).

18.4. Anti-platelet and anti-sclerotic drugs

Allium sativum (Liliaceae) Garlic

This perennial bulbous herb has been used since time immemorial as a culinary herb.

It is particularly notorious because of its characteristic and persistent pungent smell and acrid taste.

This is due to the number of sulphur compounds and the main one being alliin.

The latter undergoes enzymatic hydrolysis by alliinase to produce allicin when the garlic pod is crushed.

Allicin forms a wide range of compounds such as allyl methyl trisulphide, diallyl disulphide, ajoene and many others, which are volatile. Garlic has also been used in traditional medicine to treat asthma, bronchitis, as an expectorant.

Experimental pharmacology has shown that the essential oil, water and ethanol extracts of the garlic bulb extract exhibits a wide range of anti-bacterial and anti-fungal activity against a wide range of pathogens (WHO, 1999).

The antimicrobial and anthelmintic activities have been attributed to the presence of allicin.

Ajoene and diallyl trisulphide also have anti-bacterial and anti-fungal activities.

Allicin E-Ajoene Diallyl trisulphide

Several forms of standardized garlic extracts are available on the market but it is known that the sulphur-containing compounds are those that are responsible for the activity.

The properties for which garlic (both essential oil and extracts) is also well known for, are its ability to lower cholesterol and plasma lipids, lipid metabolism and atherogenesis, both *in vitro* and *in vivo*.

Anti-hypercholesterolaemic and anti-hyperlipidaemic effects have been observed in various animal models after

Clinical studies on serum lipids and lipoproteins reviewed 25 randomized controlled trials, with daily doses of garlic over a period of 12 weeks showed a 12% average reduction of the total cholesterol and 13% in serum triglycerides.

Meta analysis of the clinical studies confirmed the lipid-lowering and cholesterol actions of garlic.

During the administration of garlic extract, an increase in fibrinolytic activity of patients suffering from atherosclerosis.

Clinical studies have demonstrated that garlic activates endogenous fibrinolysis.

Randomized, double-blind and placebo-controlled, cross-over trials of garlic extracts have shown that they significantly increased the mean diameter of the arterioles and venules as opposed to the controls.

The acute and chronic effects of garlic on fibrinolysis and platelet aggregation were also studied in randomized and

A daily dose of 600–900 mg of garlic powder for 14 days significantly inhibited platelet aggregation, as compared with Allicin is also an antioxidant and garlic extract protect endothelial cells from oxidized LDL damage.

Diallyl sulphide is also thought to inhibit carcinogen activation via cytochrome P450-mediated oxidative metabolism and an epidemiological study carried out has shown that a diet rich in garlic reduces the incidence of cancer.

258

Plants used against problems of the CNS ...

Plants used against problems of the CNS ...

<http://www.scribd.com/doc/54197230/Medicinal-Plants-Traditions-of-Yesterday-and-Drugs-of->

19. Plants used against problems of the CNS

During the history of Mankind, drugs affecting the Central Nervous System(CNS) have focused essentially on those that bring relief to psychiatric disorders.

Recently, a lot of focus has been made on those likely to bring relief to those acting on Parkinsonism and epilepsy and

Drugs of plant origin are important in all these areas although not usually for self-medication.

Reserpine has been a classical example where this anti-psychotic drug has revolutionized the treatment of schizophrenia and has enabled patients to avoid hospitalization before the introduction of drugs such as chlorpromazine and olanzapine. Reserpine in the meantime has shown some side effects in depleting the neurotransmitter levels in the brain thus causing severe depression and has recently been involved in the development of breast cancer.

For milder psychiatric conditions, phytotherapy can still provide support when one takes into account the statistics whereby depression and anxiety still affects one in six persons and that 40% of the people having mental problems will

259

Plants used against the respiratory systems ...

Plants used against the respiratory systems ...

The latter is more prevalent in women than in men with associated problems like sleep disturbances etc.

It is in this context again that phytotherapy is called upon to re-establish a regular pattern of sleep.

Migraines, dementia, Alzheimer's disease are many of the problems associated with the CNS, which are being addressed

19.1. Hypnotics and sedatives

It has been reported that the difference between a sedative and a hypnotic agent depends on the dose.

Plant products used in this way are not as potent as synthetic drugs but they do not have as many disadvantages as their synthetic counterparts, which are often recommended for short-term use.

Valeriana officinalis

(Valerianaceae) (Radix Valerianae).

This plant has a long history in traditional medicine as a digestive aid, and as adjuvant in spasmolytic states of smooth muscle and gastrointestinal pains of nervous origin.

It has also been used to treat epilepsy, gum sores, headaches, nausea etc. This herbaceous plant is being cultivated in many European countries, in the US and also in Japan.

The parts used pharmaceutically are the root, rhizome and stolons.

Valerian has a characteristic smell, usually described as unpleasant and is attributed to the presence of iridoid valepotriate constituents and other volatile oils.

The main components of the volatile oils are monoterpenes and sesquiterpenes including valeranone, valerianol, valerenol, valeranal and valerenic acid and derivatives.

Among the valepotriate compounds are: valtrate, didrovaltrate and isovaltrate, which are highly unstable decomposing

The extracts of *Valeriana officinalis* also contain γ -aminobutyric acid (GABA), glutamine and tyrosine.

The pharmacological properties and clinical efficacy of extracts of *V. officinalis* are attributed to the valepotriates and valepotriate degradation products.

The sedative effects are due to a mixture of compounds namely valeranal and valerenic acid which are both constituents of the volatile oils and also of valepotriate compounds.

Valtrate Valerenic acid

Among the modern medicinal uses for Valerian roots are insomnia, stress and anxiety.

The sedative activity of *V. officinalis* has been demonstrated in vitro and in vivo.

In vitro studies have demonstrated the binding of valerian extracts to GABA, adenosine, barbiturate and benzodiazepine

In vivo studies suggest that the sedative properties of the drug may be due to high concentrations of glutamine in the Glutamine is able to cross the blood-brain barrier where it is taken up by nerve terminals and subsequently metabolized to Increased GABA concentrations are associated with decreased CNS activity, which may, at least, partly explain valerian's sedative activity (WHO, 1999).

Recently several preparations containing valerian root in combination with other herbs (e.g. Hops) reputed to have hypnotic and/or sedative effects have been tested (Abourashedet al., 2004).

Nonetheless the required therapeutic dosage, the type of valerian preparations and the optimum period of use for therapeutic effect still needs to be worked out (Diaper and Hindmarch, 2004).

The spasmolytic activity of the valepotriates is principally due to valtrate or dihydrovaltrate. These agents act on centres of the CNS and through direct relaxation of smooth muscles, apparently by modulating Ca^{2+} entry into the cells or by

Although the extracts have been clearly shown to depress CNS activity, the identity of the active constituents still remains Neither the valepotriates nor the sesquiterpenes valerinic acid and valeranone, nor the volatile oil alone can account for the overall sedative activity of the plant.

It has been suggested that the baldrinols, degradation products or the valepotriates may be responsible.

It is clear unknown whether the activity of *Valeriana officinalis* resides in one compound, some unknown compounds or the synergistic activity of several compounds.

Piper methysticum

(*Piperaceae*) (*Kava kava*, *Rhizoma Piperis methystici*)

In the Pacific Islands, the roots of Kava (*Piper methysticum*) have been chewed for hundreds of years.

This small shrub with heart-shaped leaves has a thick woody root, which is fermented to give the famous ceremonial drink, which has been offered to important visitors namely the Queen and even the Pope.

This drink is used to induce a relaxed sociable state and nowadays it is used medicinally for its tranquilising properties as well as for other disparate complaints.

Kava dietary products have been sold worldwide for the treatment of nervous anxiety, tension and restlessness.

Recent reports have showed the potential association of kava usage and liver injuries (Hu et al., 2005).

The main components of kava are the kavalactones (also known as kavapyrones) and include kawain, dihydrokawain, methysticin, yangonin and desmethoxyyangonin and dihydrokawain. Kawain $R = R' = H$ Methysticin $R, R' = O-CH$

Some of the medicinal uses have been supported by clinical data and these include symptomatic treatment of mild states of anxiety and insomnia due to nervousness, stress and tension.

In vitro studies had initially provided conflicting data on receptor interactions of kava extract and isolated kava lactones.

Current thinking is that kava lactones potentiate GABA A receptor activity.

Other receptor binding studies demonstrate no interaction with benzodiazepine receptors.

Studies involving laboratory animals given kava extract or purified kava lactones have demonstrated several activities including behavioural effects, analgesic activity, neurological effects, anti-convulsant and antispasmodic and anti-microbial Clinical trials have confirmed the efficacy of kava extracts at relieving anxiety in double-blind and placebo controlled

Overall the randomized controlled trials involving patients with anxiety have suggested that the kava extracts may be as effective as certain benzodiazepines, although further research is needed to confirm these observations.

Recently pharmacological investigations of kava and Passiflora extract combination have shown there was a significant decrease of the amphetamine-induced hypermotility and significant prolongation of the sleeping phase induced by subcutaneous injections or barbiturates (Capasso and Sorrentino, 2005).

Toxicity

Kava extracts must not be taken for more than the limited period without medical advice.

Nonetheless patients have been reported to complain about allergic reactions, hepatotoxicity, discoloration of the skin

Hypericum perforatum

(*Hypericaceae*) (*St. Johns Wort*, *Herba Hyperici*)

This plant has had a long history of medicinal use. This perennial, herbaceous plant native to Europe and Asia has been used traditionally as a nervine tonic and eventually in the treatment of nervous disorders.

In recent years, herbal preparations containing the aerial parts of St. Johns Wort, have been among the top selling herbal

The active constituents are thought to have been, initially, due to the presence of hypericin as the major anti-depressant

Experimentally and clinically, it emerged that hyperforin is a major component required for anti-depressant activity. The plant contains other biologically active constituents such as flavonoids, which may act in a synergistic manner with the above-mentioned constituents in acting as an anti-depressant.

Hyperforin Hypericin

Although the extracts of St. Johns Wort have manifested activity as a depressant, the exact mode of action is unclear. Biochemical and pharmacological studies have shown that the extracts inhibit the synaptosomal uptake of the neurotransmitters, serotonin (5-hydroxytryptamine, 5-HT), dopamine and noradrenaline (nor-epinephrine) and GABA. Other effects of the extract of *H. perforatum* include the ability to reduce the level of cholesterol in the blood of small animals. The flavonoid-rich extract has been shown to lower the serum triglycerides, total cholesterol and lipoprotein cholesterol as well as slow lipid peroxidation and enhance antioxidant enzyme activity (Zouet al., 2005).

Toxicity

Extracts of St. Johns Wort are usually well-tolerated by patients over a prescribed period of time. In vitro studies of the methanolic extracts show that there is intensive binding with oral contraceptives than the aqueous extracts. Other studies have shown that the extracts of St. Johns wort can interact with anti-convulsants, cyclosporins, digoxin, HIV protease inhibitors, oral contraceptives, selective serotonin re-uptake inhibitor etc. Functional medicine involves understanding the origins, prevention, and treatment of complex, chronic disease.

Hallmarks of a functional medicine approach include:

Patient-centred care. The focus of functional medicine is on patient-centred care, promoting health as a positive vitality, beyond just the absence of disease. By listening to the patient and learning his or her story, the practitioner brings the patient into the discovery process and tailors treatments that address the individual's unique needs.

An integrative, science-based healthcare approach. Functional medicine practitioners look "upstream" to consider the complex web of interactions in the patient's history, physiology, and lifestyle that can lead to illness. The unique genetic make-up of each patient is considered, along with both internal (mind, body and spirit) and external (physical and social)

Integrating best medical practices. Functional medicine integrates traditional Western medical practices with what are sometimes considered "alternative" or "integrative" medicine, creating a focus on prevention through nutrition, diet, and exercise; use of the latest laboratory testing and other diagnostic techniques; and prescribed combinations of drugs and/or botanical medicines, supplements, therapeutic diets, detoxification programs, or stress-management techniques.

260

Empty page

261

Traditional medicine

Traditional medicine

262

Empty page

263

Empty page

264

Functional Medicine

Functional Medicine

<http://www.integrativemedicine.co.za/functional-medicine.html>

Full Therapy Index :

<http://www.integrativemedicine.co.za/laser-therapy.html>

Functional Medicine

Integrative Concepts :

- 1 Chronic disease
- 2 Obstacles to cure
- 3 Detoxification
- 4 Leaky Gut Syndrome
- 5 Bio-identical hormones
- 6 Heavy Metal Toxicity
- 7 Vaccination Controversies

Health Systems within Integrative Medicine :

- 1 African Traditional medicine
- 2 Anthroposophical medicine
- 3 Anti-aging medicine
- 4 Ayurvedic medicine
- 5 Functional medicine
- 6 Herbal medicine
- 7 Homeopathy
- 8 Naturopathy
- 9 Orthomolecular medicine
- 10 Traditional Chinese Medicine
- 11 Unani Tibb medicine

Therapies & Modalities of Integrative Medicine :

- 1 Acupuncture
- 2 BEMER therapy
- 3 BEST therapy
- 4 Biopuncture
- 5 Chelation therapy
- 6 Energy healing
- 7 Flower Essence therapy
- 8 Homotoxicology
- 9 Hypnotherapy

- 10 Intramuscular stimulation therapy
- 11 Intravenous therapy
- 12 Kinesiology
- 13 Laser therapy
- 14 Lifestyle modification
- 15 Live blood analysis
- 16 Meditation & Visualisation
- 17 Mindfulness-based Interventions
- 18 Nutritional therapy
- 19 Ozone therapy
- 20 Prolotherapy
- 21 Psycho-Neuro-Immunology
- 22 Psychophonetics
- 23 Quantec therapy
- 24 Reiki
- 25 Rife Resonator therapy
- 26 SCIO therapy
- 27 Trauma releasing exercise
- 28 VoiceBio

WHAT IS FUNCTIONAL MEDICINE?

Functional medicine is an evolution in the practice of medicine that better addresses the healthcare needs of the 21st century. By shifting the traditional disease-centred focus of medical practice to a more patient-centred approach, functional medicine addresses the whole person, not just an isolated set of symptoms.

Functional medicine practitioners spend time with their patients, listening to their histories and evaluating the interactions among genetic, environmental, and lifestyle factors that can influence long-term health and complex, chronic disease. In this way, functional medicine supports the unique expression of health and vitality for each individual.

WHY DO WE NEED FUNCTIONAL MEDICINE?

Our society is experiencing a sharp increase in the number of people who suffer from complex, chronic diseases, such as diabetes, heart disease, cancer, mental illness, and autoimmune disorders like rheumatoid arthritis and fibromyalgia.

The system of medicine practised by most physicians is oriented toward acute care, the diagnosis and treatment of trauma or illness that is of short duration and in need of urgent care, such as appendicitis or a broken leg. Physicians apply specific, prescribed treatments such as drugs or surgery that aim to treat the immediate problem or symptom. Unfortunately, the acute-care approach to medicine lacks the proper methodology and tools for preventing and treating complex, chronic disease. In most cases it does not take into account the unique genetic make-up of each individual or factors such as environmental exposures to toxins and the aspects of today's lifestyle that have a direct influence on the

There's a huge gap between research and the way doctors practice. The gap between emerging research in basic sciences and integration into medical practice is enormous – as long as 50 years – particularly in the area of complex, chronic illness. Functional medicine's aim is to evaluate, assess, and carefully unfold emerging research in a practical, efficient. Most physicians are not adequately trained to assess the underlying causes of complex, chronic disease and to apply strategies such as nutrition, diet, and exercise to both treat and prevent these illnesses in their patients.

HOW IS FUNCTIONAL MEDICINE DIFFERENT?

265

Empty page

266

What are functional foods?

What are functional foods?

<http://www.mayoclinic.com/health/functional-foods/AN02088>

I've heard the term "functional foods," but I don't know what it means. Can you explain?

Answer from Jennifer K. Nelson, R.D., L.D.

Functional foods are foods that have a potentially positive effect on health beyond basic nutrition. Oatmeal is a familiar example of a functional food because it naturally contains soluble fibre that can help lower cholesterol levels. Some foods are modified to have health benefits. An example is orange juice that's been fortified with calcium for bone health.

Of course, all foods are functional because they provide varying amounts of nutrients and energy to sustain growth or support vital processes. However, functional foods are generally considered to offer additional benefits that may reduce the

Currently no legal definition exists for functional foods. The Food and Drug Administration (FDA) regulates claims that manufacturers make about functional foods' nutrient content and effects on disease, health or body function. The FDA regulates these types of foods according to whether a food is considered to be a conventional food, a food additive, a

If you want to try functional foods, choose wisely. And keep in mind that while functional foods may help promote wellness, they can't make up for poor eating habits. Your best bet is still to eat a balanced and varied diet.

267

Functional food

Functional food

http://en.wikipedia.org/wiki/Functional_food

Functional food is a food where a new ingredient(s) (or more of an existing ingredient) has been added to a food and the new product has an additional function (often one related to health-promotion or disease prevention).

The general category of functional foods includes processed food or foods fortified with health-promoting additives, like "vitamin-enriched" products. Products considered functional generally do not include products where fortification has been done to meet government regulations and the change is not recorded on the label as a significant addition ("invisible fortification"). An example of this type of fortification would be the historic addition of iodine to table salt, or Vitamin D to milk, done to resolve public health problems such as rickets. Fermented foods with live cultures are considered Functional foods are part of the continuum of products that individuals may consume to increase their health and/or contribute to reducing their disease burden.

"Functional Food is a Natural or processed food that contains known biologically-active compounds which when in defined quantitative and qualitative amounts provides a clinically proven and documented health benefit, and thus, an important source in the prevention, management and treatment of chronic diseases of the modern age". It was debated at the 9th International Conference on "Functional Foods and Chronic Diseases: Science and Practice" at the University of Nevada, Las Vegas on March 15-17, 2011. Functional Food Center has adopted a new definition of functional food Functional foods are an emerging field in food science due to their increasing popularity with health-conscious consumers and the ability of marketers to create new interest in existing products.

The term was first used in Japan in the 1980s where there is a government approval process for functional foods called Foods for Specified Health Use (FOSHU).

Industry

The functional food industry, consisting of food, beverage and supplement sectors, is one of the several areas of the food industry that is experiencing fast growth in recent years. It is estimated by BCC Research that the global market of functional food industry will reach 176.7 billion in 2013 with a compound annual growth rate (CAGR) of 7.4%. Specifically, the functional food sector will experience 6.9% CAGR, the supplement sector will rise by 3.8% and the functional beverage sector will be the fastest growing segment with 10.8% CAGR. This kind of growth is fueled not only by industrial innovation and development of new products that satisfy the demand of health conscious consumers but also by health claims covering a wide range of health issues. Yet, consumer scepticism persists mainly due to the fact that benefits associated with consuming the products may be difficult to be detected. The industry suggests the establishment of

268

Functional food

Functional food

269

Health claims ...

Health claims ...

http://en.wikipedia.org/wiki/Functional_food

Functional food products typically include health claims on their label touting their benefits: for example: "Cereal is a significant source of fibre. Studies have shown that an increased amount of fibre in one's diet can decrease the risk of Some countries, such as Canada, Sweden, the United States and the European Union, have specific laws concerning the labeling of such products. In the United States, the kinds of claims which are allowed are overseen and regulated by the Food and Drug Administration (FDA). However, some claims will fall outside of the purview of the FDA and be accompanied by the disclaimer: "These statements have not been evaluated by the Food and Drug Administration. This Such a disclaimer typically accompanies supplements rather than foods, but since the definition of functional food is still evolving and somewhat amorphous, a functional food may find itself bearing the warning.

Current research

The Richardson Centre for Functional Foods and Nutraceuticals, which is part of the University of Manitoba, is dedicated to the discussion, discovery, and development of functional foods and nutraceuticals, with a focus on the crops of the Canadian Prairies. Research involves candidates for functional food ingredients by examining the efficacy of novel bioactive materials such as plant sterols -- natural components found in plants which can act as cholesterol-lowering agents. Some researchers, however, have concerns that food supplements with plant sterol esters might increase New Zealand Institute for Plant and Food Research also have a dedicated research team that works on functional foods. Their focus is on both 'whole-foods' and food extracts - examining extracts from berries and their effect on sports performance and recovery, as well as the gut-health and immune function role of natural fruits and vegetables. The group also work with 'mood foods' and the delivery mechanisms behind components in foods and beverages designed to enhance The Functional Food Centre at Oxford Brookes University is the UK's first research centre dedicated to functional food. The centre is known internationally for its work on Glycaemic Index and is the largest testing centre in Europe. The centre provides customer-focused research and consultancy services to the food and nutrition industry, UN and government agencies in the UK and overseas. The research and consultancy portfolio not only concentrate on the scientific characteristics of food and nutrition. but also integrate both the science and social aspects of food. The centre also focuses

What are Functional Foods and Nutraceuticals?

<http://www4.agr.gc.ca/AAFC-AAC/display-afficher.do?id=1171305207040>

There is no universally accepted term for functional foods and nutraceuticals. According to Health Canada (Section 2.2)

A *functional food* is similar in appearance to, or may be, a conventional food that is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions.

A *nutraceutical* is a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with foods. A *nutraceutical* is demonstrated to have a physiological benefit or provide protection against chronic disease.

270

Categories of Functional Foods

Categories of Functional Foods/Nutraceuticals

http://en.wikipedia.org/wiki/Functional_food

Source: Shambrock Consulting Group Inc. and Kelwin Management Consulting

Basic Foods

Carrots (containing the natural level of the anti-oxidant beta-carotene)

Processed foods - oat bran cereal (containing the natural level of beta-glucan)

Processed Foods with Added Ingredients

Calcium-enriched fruit juice

Foods enhanced to have more of a functional component (via traditional breeding, special livestock feeding or

Tomatoes with higher levels of lycopene (an antioxidant carotenoid)

Oat bran with higher levels of beta glucan

Eggs with omega-3 from flax

Isolated, purified preparations of active food ingredients (dosage form)

Isoflavones from soy

Omega-3 from fish oils (DHA and ALA)

Other Definitions

Source: Shambrock Consulting Group Inc. and Kelwin Management Consulting

Bioactive Compounds are the naturally occurring chemical compounds contained in, or derived from, a plant, animal or marine source, that exert the desired health/wellness benefit (e.g. omega-

Functional Ingredients are the standardized and characterized preparations, fractions or extracts containing bioactive compounds of varying purity, that are used as ingredients by manufacturers in the food (human and pet) and preparations, fractions or extracts containing bioactive compounds of varying purity, which are used as ingredients by manufacturers in *Herbs* are the leaves, roots and flowers of plants grown and processed for culinary, cosmetic, industrial, medicinal, landscaping, decorative and fragrant purposes. Much of the early interest in functional foods and nutraceuticals was based *Industrial Ingredients* are the standardized and characterized preparations, fractions or extracts of agri-commodities of varying purity, that are used as ingredients by manufacturers of non-food products.

Natural Health Products (NHP) includes homoeopathic preparations; substances used in traditional medicines; minerals or trace elements; vitamins; amino acid; essential fatty acids; or other botanical, or animal or micro-organism derived substances. These products are generally sold in medicinal or "dosage" form to diagnose, treat, or prevent disease; restore or correct function: or to maintain or promote health. As a product group. NHPs include nutraceuticals.

Novel Foods are defined by Health Canada as: products that have never been used as food; foods that result from a process that has not previously been used for food; or, foods that have been modified by genetic manipulation. This last

Spices are seeds, root, bark and flowers of plants that are grown, harvested and processed for use as food or beverage flavouring. Examples include caraway, coriander, dill and mustard. Recently there has been interest in bioactive

Traditional Food Ingredients are the standardized and characterized preparations, fractions or extracts of agri-commodities of varying purity, that originate from plant, animal or marine sources and are used as ingredients by manufacturers in the food (human and pets) and NHP sectors. They are used for a variety of reasons in food products including consistency, adding flavour or colouring, modifying texture or stabilizing mixtures. They are not marketed on the

Traditional Processed Foods are the conventional foods that have been manufactured by the traditional food processing industry and sold to the public through established distribution systems for generations. These foods are consumed as part of a usual diet and are consumed primarily for basic nutritional purposes. Examples are processed meats, bottled fruit juice, yoghurt, and breakfast cereal. They are not marketed on the basis of any bioactive compounds that they may contain.

Traditional Whole Foods are the conventional foods that have been grown by agricultural producers for generations. They are subjected to minimal processing (e.g. sorting, cleaning and bulk packaging) before being sold to the public through established distribution systems. These foods are consumed as part of a usual diet and are consumed primarily for basic nutritional purposes. Examples include raw vegetables (broccoli and spinach), fresh fruit (blueberries and apples) and fresh

271

Nutraceuticals

Nutraceuticals

272

What are Functional Foods and Nutraceuticals?

What are Functional Foods and Nutraceuticals?

<http://www4.agr.gc.ca/AAFC-AAC/display-afficher.do?id=1171305207040>

Key Terms

There is no universally accepted term for functional foods and nutraceuticals. According to Health Canada (Section 2.2)

A *functional food* is similar in appearance to, or may be, a conventional food that is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions.

A *nutraceutical* is a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with foods. A *nutraceutical* is demonstrated to have a physiological benefit or provide protection against chronic disease.

Examples of Functional Food Components

Functional Components	Source	Potential Benefits
-----------------------	--------	--------------------

Source: International Food Information Council

Carotenoids

Alpha-carotene/	Carrots, Fruits,	Neutralize free Beta-carotene	Vegetables	radicals, which
		may cause		
		damage to cells		
Lutein	Green vegetables	Reduce the risk		
		of macular		
		degeneration		
Lycopene	Tomato products	Reduce the risk of		
	(ketchup, sauces)	prostate cancer		

Dietary Fibre

Insoluble Fibre	Wheat Bran	Reduce the risk of		
		breast or		
		colon cancer		
Beta-Glucan	Oats, barley	Reduce the risk of		
		cardiovascular disease.		
		Protect against		
		heart disease and		
		some cancers;		
		lowerLDL and		
		total cholesterol.		
Soluble Fibre	Psyllium	Reduce the risk of		
		cardiovascular disease.		
		Protect against		
		heart disease and		
		some cancers;		
		lower LDL and		
		total cholesterol.		

Fatty Acids

Long chain	Salmon and	Reduce the risk of		
omega-3	other fish oils	cardiovascular disease.		
Fatty Acids-		Improve mental,		
DHA/EPA		visual functions.		
Conjugated	Cheese,	Improve body		
Linoleic A	meat products	composition.		
(CLA)		Decrease the risk of		
		certain cancers.		

Phenolics

Anthocyanidins	Fruits	Neutralize free		
		radicals; reduce		
		the risk of cancer		

Catechins	Tea	Neutralize free radicals; reduce the risk of cancer
Flavonones	Citrus	Neutralize free radicals; reduce the risk of cancer
Flavones	Fruits/ Vegetables	Neutralize free radicals; reduce the risk of cancer
Lignans	Flax, rye, vegetables	Prevention of cancer, renal failure
Tan (proanthocyanidines)	Cranberries, cranberry products, cocoa, chocolate	Improve urinary tract health. Reduce the risk of cardiovascular disease.

Plant Sterols

Stanol ester	Corn, soy, wheat, wood oils	Lower blood cholesterol levels by inhibiting cholesterol absorption
--------------	-----------------------------------	---

Prebiotics/Probiotics

Fructo- oligosaccharides (FOS)	Jerusalem artichokes, shallots, onion powder	Improve quality of intestinal microflora; gastrointestinal health
Lactobacillus	Yogurt, Other dairy	Improve quality of intestinal microflora; gastrointestinal health

Soy Phytoestrogens

Isoflavones: Genistein	Soybeans and foods	Menopause symptoms, Protect against heart disease and lower LDL and total cholesterol.
---------------------------	-----------------------	---

Categories of Functional Foods/Nutraceuticals

Source: Shambrock Consulting Group Inc. and Kelwin Management Consulting

Basic Foods

Carrots (containing the natural level of the anti-oxidant beta-carotene)

Processed foods - oat bran cereal (containing the natural level of beta-glucan)

Processed Foods with Added Ingredients

Calcium-enriched fruit juice

Foods enhanced to have more of a functional component (via traditional breeding, special livestock feeding or

Tomatoes with higher levels of lycopene (an antioxidant carotenoid)

Oat bran with higher levels of beta glucan

Eggs with omega-3 from flax

Isolated, purified preparations of active food ingredients (dosage form)

Isoflavones from soy

Omega-3 from fish oils (DHA and ALA)

Other Definitions

Source: Shambrock Consulting Group Inc. and Kelwin Management Consulting

Basic Foods

Carrots (containing the natural level of the anti-oxidant beta-carotene)

Processed foods - oat bran cereal (containing the natural level of beta-glucan)

Processed Foods with Added Ingredients

Calcium-enriched fruit juice

Foods enhanced to have more of a functional component (via traditional breeding, special livestock feeding or

Tomatoes with higher levels of lycopene (an antioxidant carotenoid)

Oat bran with higher levels of beta glucan

Eggs with omega-3 from flax

Isolated, purified preparations of active food ingredients (dosage form)

Isoflavones from soy

Omega-3 from fish oils (DHA and ALA)

Other Definitions

Source: Shambrock Consulting Group Inc. and Kelwin Management Consulting

Bioactive Compounds are the naturally occurring chemical compounds contained in, or derived from, a plant, animal or marine source, that exert the desired health/wellness benefit (e.g. omega-

Industrial Ingredients are the standardized and characterized preparations, fractions or extracts of agri-commodities of varying purity, that are used as ingredients by manufacturers of non-food products.

Natural Health Products (NHP) includes homoeopathic preparations; substances used in traditional medicines; minerals or trace elements; vitamins; amino acid; essential fatty acids; or other botanical, or animal or micro-organism derived substances. These products are generally sold in medicinal or "dosage" form to diagnose, treat, or prevent disease; restore or correct function: or to maintain or promote health. As a product group, NHPs include nutraceuticals.

Novel Foods are defined by Health Canada as: products that have never been used as food; foods that result from a process that has not previously been used for food; or, foods that have been modified by genetic manipulation. This last

Categories of Functional Foods/Nutraceuticals

Source: Shambrock Consulting Group Inc. and Kelwin Management Consulting

Spices are seeds, root, bark and flowers of plants that are grown, harvested and processed for use as food or beverage flavouring. Examples include caraway, coriander, dill and mustard. Recently there has been interest in bioactive

Traditional Food Ingredients are the standardized and characterized preparations, fractions or extracts of agricultural commodities of varying purity, that originate from plant, animal or marine sources and are used as ingredients by manufacturers in the food (human and pets) and NHP sectors. They are used for a variety of reasons in food products including consistency, adding flavour or colouring, modifying texture or stabilizing mixtures. They are not marketed on the

Traditional Processed Foods are the conventional foods that have been manufactured by the traditional food processing industry and sold to the public through established distribution systems for generations. These foods are consumed as part of a usual diet and are consumed primarily for basic nutritional purposes. Examples are processed meats, bottled fruit juice, yoghurt, and breakfast cereal. They are not marketed on the basis of any bioactive compounds that they may contain.

Traditional Whole Foods are the conventional foods that have been grown by agricultural producers for generations. They are subjected to minimal processing (e.g. sorting, cleaning and bulk packaging) before being sold to the public through established distribution systems. These foods are consumed as part of a usual diet and are consumed primarily for basic nutritional purposes. Examples include raw vegetables (broccoli and spinach), fresh fruit (blueberries and apples) and fresh

273

Examples of Functional Food Components ...

Examples of Functional Food Components ...

http://en.wikipedia.org/wiki/Functional_food

274

Functional Foods: Their Role in Disease Prevention and Health Promotion

Functional Foods: Their Role in Disease Prevention and Health Promotion

<http://www.nutriwatch.org/04Foods/ff.html>

A Publication of the Institute of Food Technologists

Expert Panel on Food Safety and Nutrition

Claire M. Hasler, Ph.D.

The tenet "Let food be thy medicine and medicine be thy food," espoused by Hippocrates nearly 2,500 years ago, is receiving renewed interest. In particular, there has been an explosion of consumer interest in the health enhancing role of specific foods or physiologically-active food components, so-called functional foods (Hasler, 1998). Clearly, all foods are functional, as they provide taste, aroma, or nutritive value. Within the last decade, however, the term functional as it applies to food has adopted a different connotation -- that of providing an additional physiological benefit beyond that of This Scientific Status Summary reviews the literature for the primary plant and animal foods that have been linked with physiological benefits. Although a plethora of biologically-active compounds have been identified in this regard (Kuhn, 1998), this review focuses on foods, rather than specific compounds isolated from foods.

Defining Functional Foods

The term functional foods was first introduced in Japan in the mid-1980s and refers to processed foods containing ingredients that aid specific bodily functions in addition to being nutritious. To date, Japan is the only country that has formulated a specific regulatory approval process for functional foods. Known as Foods for Specified Health Use (FOSHU), these foods are eligible to bear a seal of approval from the Japanese Ministry of Health and Welfare (Arai, 1996). Currently, 100 products are licensed as FOSHU foods in Japan. Functional Foods: Their role in disease prevention and health promotion In the United States, the functional foods category is not recognized legally. Irrespective of this, many organizations have proposed definitions for this new and emerging area of the food and nutrition sciences. The Institute of Medicine's Food and Nutrition Board (IOM/FNB, 1994) defined functional foods as "any food or food

Functional Foods From Plant Sources

Overwhelming evidence from epidemiological, in vivo, in vitro, and clinical trial data indicates that a plant-based diet can reduce the risk of chronic disease, particularly cancer. In 1992, a review of 200 epidemiological studies (Block et al., 1992) showed that cancer risk in people consuming diets high in fruits and vegetables was only one-half that in those consuming few of these foods. It is now clear that there are components in a plant-based diet other than traditional nutrients that can reduce cancer risk. Steinmetz and Potter (1991a) identified more than a dozen classes of these

Health professionals are gradually recognizing the role of phytochemicals in health enhancement (ADA, 1995; Howard and Kritchevsky, 1997), aided in part by the Nutrition Labeling and Education Act of 1990 (NLEA). The NLEA required nutrition labeling for most foods and allowed disease- or health-related messages on food labels.

Oats. Oat products are a widely studied dietary source of the cholesterol-lowering soluble fiber β -glucan. There is now significant scientific agreement that consumption of this particular plant food can reduce total and low density lipoprotein (LDL) cholesterol, thereby reducing the risk of coronary heart disease (CHD). For this, the Food and Drug Administration (FDA) awarded the first food-specific health claim in January 1997 (DHHS/FDA, 1997), in response to a petition

In its health claim petition, the Quaker Oats Company summarized 37 human clinical intervention trials conducted between 1980 and 1995. The majority of these studies revealed statistically significant reductions in total and LDL-cholesterol in hypercholesterolemic subjects consuming either a typical American diet or a low fat diet. The daily amount of oat bran or oatmeal consumed in the above studies ranged from 34 g to 123 g. Quaker Oats determined that 3 g of β -glucan would be required to achieve a 5% reduction in serum cholesterol, an amount equivalent to approximately 60 g of oatmeal or 40 g of oat bran (dry weight). Thus, a food bearing the health claim must contain 13 g of oat bran or 20 g Soy. Soy has been in the spotlight during the 1990s. Not only is soy a high quality protein, as assessed by the FDA's "Protein Digestibility Corrected Amino Acid Score" method, it is now thought to play preventive and therapeutic roles in cardiovascular disease (CVD), cancer, osteoporosis, and the alleviation of menopausal symptoms.

The cholesterol-lowering effect of soy is the most well-documented physiological effect. A 1995 meta-analysis of 38 separate studies (involving 743 subjects) found that the consumption of soy protein resulted in significant reductions in total cholesterol (9.3%), LDL cholesterol (12.9%), and triglycerides (10.5%), with a small but insignificant increase (2.4%) in high density lipoprotein (HDL) cholesterol (Anderson et al., 1995). Linear regression analysis indicated that the threshold level of soy intake at which the effects on blood lipids became significant was 25 g. Regarding the specific component responsible for the cholesterol-lowering effect of soy, recent attention has focused on the isoflavones (Potter, 1998). Isoflavones, however, were not effective in lowering cholesterol in two recent studies (Hodson et al., 1998; Nestle). On May 4, 1998, Protein Technologies International (PTI, St. Louis, Mo.) petitioned the FDA for a health claim on soy protein containing products pertaining to reduced risk of CHD. Based on an effective daily level of 25 g soy protein, PTI proposed that the amount of soy protein required to qualify an individual food to bear the health claim is 6.25 g with a minimum of 12.5 mg of total isoflavones (aglycone form) per reference amount customarily consumed. On August 12, the Several classes of anticarcinogens have been identified in soybeans, including protease inhibitors, phytosterols, saponins, phenolic acids, phytic acid, and isoflavones (Messina and Barnes, 1991). Of these, isoflavones (genistein and daidzein) are particularly noteworthy because soybeans are the only significant dietary source of these compounds. Isoflavones are heterocyclic phenols structurally similar to the oestrogenic steroids. Because they are weak oestrogens, isoflavones may act as anti-oestrogens by competing with the more potent, naturally-occurring endogenous oestrogens (e.g., 17 β -estradiol) for binding to the oestrogen receptor. This may explain why populations that consume significant amounts of soy (e.g., South-east Asia) have reduced risk of oestrogen-dependent cancer. However, the epidemiological data on soy intake and cancer

Soy may also benefit bone health (Anderson and Garner, 1997). A recent clinical study involving 66 post-menopausal women conducted at the University of Illinois (Erdman and Potter, 1997) found that 40 g isolated soy protein (ISP) per day (containing 90 mg total isoflavones) significantly increased (approximately 2%) both bone mineral content and density in the lumbar spine after 6 months. The theory that soy may alleviate menopausal symptoms was prompted by the observation that Asian women report significantly lower levels of hot flashes and night sweats compared to Western women. Most recently, 60 grams of ISP daily for 3 months reduced hot flashes by 45% in 104 post-menopausal women (Albertazzi et al., 1998). Although these observations are exciting, there is a significant placebo effect in these studies, and Flaxseed. Among the major seed oils, flaxseed oil contains the most (57%) of the omega-3 fatty acid, α -linolenic acid. Recent research, however, has focused more specifically on fiber-associated compounds known as lignans. The two primary mammalian lignans, enterodiol and its oxidation product, enterolactone, are formed in the intestinal tract by bacterial action on plant lignan precursors (Setchell et al., 1981). Flaxseed is the richest source of mammalian lignan precursors (Thompson et al., 1991). Because enterodiol and enterolactone are structurally similar to both naturally-occurring and synthetic estrogens, and have been shown to possess weakly oestrogenic and anti-oestrogenic activities, they may play a role in the prevention of oestrogen-dependent cancers. However, there are no epidemiological data and Fewer studies have evaluated the effects of flaxseed feeding on risk markers for cancer in humans. Phipps et al. (1993) demonstrated that the ingestion of 10 g of flaxseed per day elicited several hormonal changes associated with reduced breast cancer risk. Adlercreutz et al. (1982) found that the urinary lignan excretion was significantly lower in post-

Consumption of flaxseed has also been shown to reduce total and LDL cholesterol (Bierenbaum et al., 1993; Cunnane et al., 1993), as well as platelet aggregation (Allman et al., 1995).

Tomatoes. Selected by Eating Well magazine as the 1997 Vegetable of the Year, tomatoes have received significant attention within the last three years because of interest in lycopene, the primary carotenoid found in this fruit (Gerster). In a prospective cohort study of more than 47,000 men, those who consumed tomato products 10 or more times per week had less than one-half the risk of developing advanced prostate cancer (Giovannucci et al., 1995). Interestingly, lycopene is the most abundant carotenoid in the prostate gland (Clinton et al., 1996). Other cancers whose risk have been inversely associated with serum or tissue levels of lycopene include breast, digestive tract, cervix, bladder, and skin (Clinton, 1998) and possibly lung (Li et al., 1997). Proposed mechanisms by which lycopene could influence cancer risk are related to its antioxidant function. Lycopene is the most efficient quencher of singlet oxygen in biological systems (Di Mascio et al., 1989). The antioxidant function of lycopene may also explain the recent observation in a multi-center European study that Garlic. Garlic (*Allium sativum*) is likely the herb most widely quoted in the literature for medicinal properties (Nagourney, 1998). Thus, it's not surprising that garlic has ranked as the second best selling herb in the United States for the past two years (Anon., 1998). The purported health benefits of garlic are numerous, including cancer chemopreventive, antibiotic,

The characteristic flavor and pungency of garlic are due to an abundance of oil- and water-soluble, sulphur-containing elements, which are also likely responsible for the various medicinal effects ascribed to this plant. However, intact, undisturbed bulbs of garlic contain only a few medicinally active components. The intact garlic bulb contains an odorless amino acid, alliin, which is converted enzymatically by allinase into allicin when the garlic cloves are crushed (Block, 1992). This latter compound is responsible for the characteristic odor of fresh garlic. Allicin then spontaneously breaks down into several sulfur-containing compounds. Garlic components have been shown to inhibit tumorigenesis in several experimental models (Reuter et al., 1996). However, additional reports have shown garlic to be ineffective. Inconclusive results are likely due to differences in the type of garlic compounds or preparations used by various investigators. Considerable variation in the quantity of organosulphur compounds available in fresh and commercially available garlic products has been demonstrated (Lawson et al., 1993). Several epidemiologic studies show that the garlic may be effective in reducing human cancer risk (Dorant et al., 1993). A relatively large case-control investigation conducted in China showed a strong inverse relationship between stomach cancer risk and increasing allium intake (You et al., 1988). More recently, in a study of more than 40,000 post-menopausal women, garlic consumption was associated with nearly a 50% reduction in colon cancer risk (Steinmetz et al., 1994). Not all epidemiological studies, however, have shown garlic to be protective against carcinogenesis. A 1991 review of 12 case-control studies (Steinmetz and Potter, 1991b), found that eight showed a negative association, one showed no association, and three studies showed a positive association. A more recent review of 20 epidemiological studies (Ernst, 1993) found that 12 showed a negative association, 5 showed no association, and 3 showed a positive association. Garlic has also been advocated for the prevention of CVD, possibly through anti-hypertensive properties. According to Silagy and Neil (1994a), however, there is still insufficient evidence to recommend it as a routine clinical therapy for the treatment of hypertensive subjects. The cardioprotective effects are more likely due to its cholesterol-lowering effect. In a meta-analysis, Warshafsky et al. (1993) summarized the results of five randomized, placebo-controlled clinical trials, involving 410 patients. They showed that an average of 900 mg garlic/day (as little as one half to one clove of garlic) could decrease total serum cholesterol levels by approximately 9%. In a second meta-analysis involving 16 trials, Silagy and Neil (1994b) reported that 800 mg garlic/day reduced total cholesterol levels by 12%. The validity of both of these reports, however, is reduced by methodological shortcomings, including the fact that dietary intake, weight, and/or other factors were not controlled. Broccoli and other Cruciferous Vegetables. Epidemiological evidence has associated the frequent consumption of cruciferous vegetables with decreased cancer risk. In a recent review of 87 case-control studies, Verhoeven et al. (1996) demonstrated an inverse association between consumption of total brassica vegetables and cancer risk. The percentages of case-control studies showing an inverse association between consumption of cabbage, broccoli, cauliflower, and Brussels sprouts and cancer risk were 70, 56, 67, and 29%, respectively. Verhoeven et al. (1997) attributed the anticarcinogenic activity of cruciferous vegetables to glucosinolates, a group of glycosides stored within cell vacuoles of all cruciferous vegetables. Myrosinase, an enzyme found in plant cells, catalyzes these compounds to a variety of hydrolysis products, including isothiocyanates and indoles. Indole-3-carbinol (I3C) is currently under investigation for its cancer chemopreventive properties, particularly of the mammary gland. In addition to the induction of phase I and II detoxification reactions, I3C may reduce cancer risk by modulating oestrogen metabolism. The C-16 and C-2 hydroxylations of oestrogens involve competing cytochrome P-450-dependent pathways, each sharing a common estrogen substrate pool. Studies suggest that the increased formation of 2-hydroxylated (catechol) oestrogen metabolites relative to 16-hydroxylated forms, may protect against cancer, as catechol oestrogens can act as antiestrogens in cell culture. In contrast, 16-hydroxyestrone is oestrogenic and can bind to the estrogen receptor. In humans, I3C administered at 500 mg daily (equivalent to 350-500 g cabbage/day) for 1 week reduced the formation of 16-hydroxylated oestrogen metabolites. Although a wide variety of naturally occurring and synthetic isothiocyanates have been shown to prevent cancer in animals (Hecht, 1995), attention has been focused on a particular isothiocyanate isolated from broccoli, known as sulforaphane. Sulforaphane has been shown to be the principal inducer of a particular type of Phase II enzyme, quinone reductase. Fahey et al., (1997) recently demonstrated that 3-day-old broccoli sprouts contained 10-100 times higher levels of glucoraphanin (the glucosinolate of sulforaphane) than did corresponding mature plants. However, in view of the importance of an overall dietary pattern in cancer risk reduction, the clinical implications of a single phytochemical in isolation has been questioned.

Citrus Fruits. Several epidemiological studies have shown that citrus fruits are protective against a variety of human cancers. Although oranges, lemons, limes, and grapefruits are a principal source of such important nutrients as vitamin C, folate, and fibre, Elegbede et al. (1993) have suggested that another component is responsible for the anticancer activity. Citrus fruits are particularly high in a class of phytochemicals known as the limonoids (Hasegawa and Mivake, 1996). Over the last decade, evidence has been accumulating in support of the cancer preventative effect of limonene (Gould, 1997). Crowell (1997) showed this compound to be effective against a variety of both spontaneous and chemically-induced rodent tumors. Based on these observations, and because it has little or no toxicity in humans, limonene has been suggested as a good candidate for human clinical chemoprevention trial evaluation. A metabolite of limonene, nerrillvl Cranberry. Cranberry juice has been recognized as efficacious in the treatment of urinary tract infections since 1914, when Blatherwick (1914) reported that this benzoic acid-rich fruit caused acidification of the urine. Recent investigations have focused on the ability of cranberry juice to inhibit the adherence of Escherichia coli to uroepithelial cells (Schmidt and Sobota, 1988). This phenomenon has been attributed to two compounds: fructose and a nondialyzable polymeric compound. The latter compound, subsequently isolated from cranberry and blueberry juices (Ofek et al., 1991), was found Avorn et al. (1994) published the results of the first randomized, double-blind, placebo-controlled clinical trial designed to determine the effect of a commercial cranberry juice beverage on urinary tract infections. One hundred-fifty three elderly women consuming 300 ml cranberry beverage per day had significantly reduced (58%) incidence of bacteriuria with nrvria compared to the control group after six months. Based on the results of these studies, prevailing beliefs about Tea. Tea is second only to water as the most widely consumed beverage in the world. A great deal of attention has been directed to the polyphenolic constituents of tea, particularly green tea (Harbowy and Balentine, 1997). Polyphenols comprise up to 30% of the total dry weight of fresh tea leaves. Catechins are the predominant and most significant of all tea polyphenols (Graham, 1992). The four major green tea catechins are epigallocatechin-3-gallate, epigallocatechin. In recent years, there has been a great deal of interest in pharmacological effects of tea (AHF, 1992). By far, most research on health benefits of tea has focused on its cancer chemopreventive effects, although the epidemiological studies are inconclusive at the present time (Katiyar and Mukhtar, 1996). In a 1993 review of 100 epidemiological studies (Yang and Wang, 1993), approximately 2/3 of the studies found no relationship between tea consumption and cancer risk, while 20 found a positive relationship and only 14 studies found that tea consumption reduced cancer risk. A more recent review suggests that benefits from tea consumption are restricted to high intakes in high-risk populations (Kohlmeier et al., 1997a). This hypothesis supports the recent finding that the consumption of five or more cups of green tea per day was In contrast to the inconclusive results from epidemiological studies, research findings in laboratory animals clearly support a cancer chemopreventive effect of tea components. In fact, Dreosti et al. (1997) stated that "no other agent tested for possible chemoprevention effects in animal models has elicited such strong activity as tea and its components at the There is some evidence that tea consumption may also reduce the risk of CVD. Hertog and co-workers (1993) reported that tea consumption was the major source of flavonoids in a population of elderly men in the Netherlands. Intake of five flavonoids (quercetin, kaempferol, myricetin, apigenin, and luteolin), the majority of which was derived from tea consumption, was significantly inversely associated with mortality from CHD in this population. Although several other prospective studies have demonstrated a substantial reduction in CVD risk with tea consumption, the evidence is not Wine and Grapes. There is growing evidence that wine, particularly red wine, can reduce the risk of CVD. The link between wine intake and CVD first became apparent in 1979 when St. Leger et al. (1979) found a strong negative correlation between wine intake and death from ischemic heart disease in both men and women from 18 countries. France in particular has a relatively low rate of CVD despite diets high in dairy fat (Renaud and de Lorgeril, 1992). Although this "French Paradox" can be partly explained by the ability of alcohol to increase HDL cholesterol, more recent The high phenolic content of red wine, which is about 20-50 times higher than white wine, is due to the incorporation of the grape skins into the fermenting grape juice during production. Kanner et al. (1994) showed that the black seedless grapes and red wines (i.e., Cabernet Sauvignon and Petite Sirah) contain high concentrations of phenolics: 920, 1800, and 3200 mg/L, respectively, while green Thomson grapes contain only 260 mg/kg phenolics. Frankel and co-workers (1993) attributed the positive benefits of red wine to the ability of phenolic substances to prevent the oxidation of LDL, a critical Although the benefits of wine consumption on CVD risk reduction seem promising, a recent prospective study of 128,934 adults in Northern California concluded that the benefits of alcohol consumption on coronary risk were not especially associated with red wine (Klatsky et al., 1997). Moreover, a note of caution is in order, as alcoholic beverages of all kinds have been linked to increased risk of several types of cancer, including breast cancer (Bowlin et al., 1997). Moderate wine consumption has also been associated with a decreased risk of age-related macular degeneration (Obisesan et al., 1998). Those who desire health benefits of wine without potential risk may wish to consider alcohol-free wine, which has been shown to increase total plasma antioxidant capacity (Serafini et al., 1998). Furthermore, Day et al. (1998) showed that commercial grape juice is effective in inhibiting the oxidation of LDL isolated from human subjects. Red wine is also a significant source of trans-resveratrol, a phytoalexin found in grape skins (Creasy and Coffee, 1988). Resveratrol has also been shown to have estrogenic properties (Gehm et al., 1997) which may explain in part the cardiovascular benefits of

Functional Foods From Animal Sources

Although the vast number of naturally occurring health-enhancing substances are of plant origin, there are a number of physiologically-active components in animal products that deserve attention for their potential role in optimal health. Fish. Omega-3 (n-3) fatty acids are an essential class of polyunsaturated fatty acids (PUFAs) derived primarily from fish oil. It has been suggested that the Western-type diet is currently deficient in n-3 fatty acids, which is reflected in the current estimated n-6 to n-3 dietary ratio of 20:25-1, compared to the 1:1 ratio on which humans evolved (Simopoulos, 1991). This has prompted researchers to examine the role of n-3 fatty acids in a number of diseases -- particularly cancer and heart disease. That n-3 fatty acids may play an important role in CVD was first brought to light in the 1970s when Bang and Dyerberg (1972) reported that Eskimos had low rates of this disease despite consuming a diet which was high in fat. The cardioprotective effect of fish consumption has been observed in some prospective investigations (Krumhout et al., 1985), but not in others (Ascherio et al., 1995). Negative results could be explained by the fact that although n-3 fatty acids have been shown to lower triglycerides by 25-30%, they do not lower LDL cholesterol. In fact, a recent review of 72 placebo-controlled trials found that although eating large amounts of fish has not unequivocally been shown to reduce CVD risk in healthy men, consumption of 35 g or more of fish daily has been shown to reduce the risk of death from non-sudden myocardial infarction in the Chicago Western Electric Study (Daviglus et al., 1997), and as little as one serving of fish per week was associated with a significantly reduced risk of total cardiovascular mortality after 11 years in more than 20,000 U.S. male physicians (Albert et al., 1997).

Dairy Products. There is no doubt that dairy products are functional foods. They are one of the best sources of calcium, an essential nutrient which can prevent osteoporosis and possibly colon cancer. In view of the former, the National Academy of Sciences recently increased recommendations for this nutrient for most age groups. In addition to calcium, however, recent research has focused specifically on other components in dairy products, particularly fermented dairy products known as probiotics. Probiotics are defined as "live microbial feed supplements which beneficially affect the host animal." It is estimated that over 400 species of bacteria, separated into two broad categories, inhabit the human gastrointestinal tract. The categories are: those considered to be beneficial (e.g., *Bifidobacterium* and *Lactobacillus*) and those considered detrimental (e.g., *Enterobacteriaceae* and *Clostridium* spp.). Of the beneficial micro-organisms traditionally used in food fermentation, lactic acid bacteria have attracted the most attention (Sanders, 1994). Although a variety of health benefits have been attributed to probiotics, their anti-carcinogenic, hypocholesterolemic and antagonistic actions against enteric pathogens are the most well-documented. The hypocholesterolemic effect of fermented milk was discovered more than 30 years ago during studies conducted in Maasai tribesmen in Africa (Mann et al., 1964). The Maasai have low levels of serum cholesterol and clinical coronary heart disease despite a high meat diet. However, they consume daily 4 to 5 L of fermented whole milk. Although a number of human clinical studies have assessed the cholesterol-lowering effects of fermented milk products (Sanders, 1994), results are equivocal. Study outcomes have been complicated by inadequate sample sizes, failure to control nutrient intake, and the use of different probiotic strains. More evidence supports the role of probiotics in cancer risk reduction, particularly colon cancer (Mital and Garg, 1995). This observation may be due to the fact that lactic acid cultures can alter the activity of fecal enzymes (e.g., β -glucuronidase, azoreductase, nitroreductase) that are thought to play a role in the development of colon cancer. Relatively less attention has been focused on the consumption of fermented milk products and breast cancer risk, although an inverse relationship has been suggested (Gibson et al., 1996). In addition to probiotics, there is growing interest in fermentable carbohydrates that feed the good micro-flora of the gut. These prebiotics, defined by Gibson and Roberfroid (1995) as "non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improves host health," may include starches, dietary fibers, other non-absorbable sugars, sugar alcohols, and oligosaccharides (Gibson et al., 1996). Of these, oligosaccharides have received the most attention, and numerous health benefits have been attributed to them (Tomomatsu, 1994). Oligosaccharides consist of short chain polysaccharides composed of three and 10 simple sugars linked together. They are found naturally in many fruits and vegetables (including banana, garlic, onions, milk, honey, artichokes). The prebiotic concept has been further extended to encompass the concept of conjugated linoleic acid (CLA). An anti-carcinogenic fatty acid known as conjugated linoleic acid (CLA) was first isolated from grilled beef in 1987 (Ha et al., 1987). CLA refers to a mixture of positional and geometric isomers of linoleic acid (18:2 n-6) in which the double bonds are conjugated instead of existing in the typical methylene interrupted configuration. Nine different isomers of CLA have been reported as occurring naturally in food. CLA is unique in that it is found in highest concentrations in fat from ruminant animals (e.g., beef, dairy, and lamb). Beef fat contains 3.1 to 8.5 mg CLA/g fat with the 9-cis and 11-trans isomers contributing 57- 85% of the total CLA (Decker, 1995). Interestingly, CLA increases in foods that are cooked. Over the past decade, CLA has been shown to be effective in suppressing fore stomach tumors in mice, aberrant colonic crypt foci in rats, and mammary carcinogenesis in rats (Ip and Scimeca, 1997). In the mammary tumor model, CLA is an effective anti-carcinogen in the range of 0.1-1% in the diet, which is higher than the estimated consumption of approximately 1 g CLA/person/day in the United States. These results are not due to displacement of linoleic acid in cells, suggesting that there may be unique mechanism(s) by which CLA modulates tumor development. Thus, there has been more recently, CLA has been investigated for its ability to change body composition, suggesting a role as a weight-reduction agent. Mice fed CLA-supplemented diets (0.5%) exhibited 60% lower body fat and 14% increased lean body mass relative to controls (Park et al., 1997), possibly by reducing fat deposition and increasing lipolysis in adipocytes.

Safety Issues

Although "increasing the availability of healthful foods, including functional foods, in the American diet is critical to ensuring a healthier population" (ADA, 1995), safety is a critical issue. The optimal levels of the majority of the biologically active components currently under investigation have yet to be determined. In addition, a number of animal studies show that some of the same phytochemicals (e.g., allyl isothiocyanate) highlighted in this review for their cancer-preventing properties have been shown to be carcinogenic at high concentrations (Ames et al., 1990). Thus, Paracelsus' 15th century doctrine that "All substances are poisons . . . the right dose differentiates a poison from a remedy" is even more applicable today. The benefits and risks to individuals and populations as a whole must be weighed carefully when considering the widespread use of physiologically-active functional foods. For example, what are the risks of recommending the increased intake of compounds (e.g., isoflavones) that may modulate oestrogen metabolism? Soy phyto oestrogens may represent a "double-edged sword" because of reports that genistein may actually promote certain types of tumors in animals (Rao et

Conclusion

Mounting evidence supports the observation that functional foods containing physiologically-active components, either from plant or animal sources, may enhance health. It should be stressed, however, that functional foods are not a magic bullet or universal panacea for poor health habits. There are no "good" or "bad" foods, but there are good or bad diets. Emphasis must be placed on over-all dietary pattern -- one that follows the current U.S. Dietary Guidelines, and is plant-based, high in fibre, low in animal fat, and contains 5-9 servings of fruits and vegetables per day. Moreover, diet is only one of many factors that influence health. Health-conscious consumers are increasingly seeking functional foods in an effort to control their own health and well-being. The field of functional foods, however, is in its infancy. Claims about health benefits of functional foods must be based on sound scientific criteria (Clydesdale, 1997). A number of factors complicate the establishment of a strong scientific foundation, however. These factors include the complexity of the food substance, effects on the food, compensatory metabolic changes that may occur with dietary changes, and, lack of surrogate markers of disease development. Additional research is necessary to substantiate the potential health benefits of those foods for which the diet. Research into functional foods will not advance public health unless the benefits of the foods are effectively communicated to the consumer. The Harvard School of Public Health (Boston, Mass.) and the International Food Information Council Foundation (Washington, D.C.) recently released a set of communication guidelines, aimed at scientists, journal editors, journalists, interest groups, and others for improving public understanding of emerging science. The guidelines are intended to help ensure that research results about nutrition, food safety, and health are communicated in a clear, balanced, and non misleading manner (Fineberg and Rowe, 1998). Finally, those foods whose health benefits are supported by sufficient scientific substantiation have the potential to be an increasingly important component of a healthy lifestyle and to

About the Author

Dr. Hasler is executive director of the Functional Foods for Health Program, Department of Food Science and Human Nutrition, University of Illinois, Urbana, Illinois. This article can be downloaded in PDF format as originally published in

Animal derived surfactant extract for treatment of respiratory distress syndrome

http://www.nichd.nih.gov/cochrane_data/Animal_derived_surfactant/Animal_derived_surfactant.HT

Authors

Nadine Seger¹, Roger Soll

Background

Respiratory distress syndrome (RDS) is caused by a deficiency or dysfunction of pulmonary surfactant. A wide variety of surfactant products have been formulated and studied in clinical trials. These include synthetic surfactants and animal derived surfactant extracts. Trials of surfactant replacement have either tried to prevent the development of respiratory distress in high-risk premature infants or treat established respiratory distress in premature infants.

Objectives

To assess the effect of administration of animal derived surfactant extract on mortality, chronic lung disease and other morbidities associated with prematurity in pre-term infants with established respiratory distress syndrome. Subgroup analysis were planned according to the specific surfactant product, the degree of prematurity, and the severity of disease.

Search methods

Searches were made of the Oxford Database of Perinatal Trials, MEDLINE, EMBASE, and CINAHL from 1975 through December 2008. In addition, searches were made of previous reviews including cross references, abstracts, conference and symposia proceedings, expert informants and journal hand searching in the English language.

Selection criteria

Randomized or quasi-randomized controlled trials that compared the effect of animal derived surfactant extract treatment administered to infants with established respiratory distress syndrome in order to prevent complications of prematurity and

Data collection and analysis

Data regarding clinical outcomes were excerpted from the reports of the clinical trials by the review authors. Data analysis was done in accordance with the standards of the Cochrane Neonatal Review Group.

Results

Thirteen randomized controlled trials were included in the analysis. The studies demonstrated an initial improvement in respiratory status (improved oxygenation and decreased need for ventilator support). The meta-analysis supports a significant decrease in the risk of any air leak (typical relative risk 0.47, 95% CI 0.39, 0.58; typical risk difference -0.16, 95% CI -0.21, -0.12), pneumothorax (typical relative risk 0.42, 95% CI 0.34, 0.52; typical risk difference -0.17, 95% CI -0.21, -0.13), and a significant decrease in the risk of pulmonary interstitial emphysema (typical relative risk 0.45, 95% CI 0.37, 0.55; typical risk difference -0.20, 95% CI -0.25, -0.15). There is a significant decrease in the risk of neonatal mortality (typical relative risk 0.68, 95% CI 0.57, 0.82; typical risk difference -0.09, 95% CI -0.13, -0.05), a significant decrease in the risk of mortality prior to hospital discharge (typical relative risk 0.63, 95% CI 0.44, 0.90; typical risk

Authors' conclusions

Infants with established respiratory distress syndrome who receive animal derived surfactant extract treatment have a decreased risk of pneumothorax, a decreased risk of pulmonary interstitial emphysema, a decreased risk of mortality, and a

Plain language summary

Animal derived surfactant extract treatment for respiratory distress syndrome

Respiratory distress syndrome (RDS) is caused by a deficiency or dysfunction of the lining chemicals of the lung known as pulmonary surfactant. A wide variety of surfactant products have been formulated and studied in clinical trials. These include synthetic surfactants and animal derived surfactant extracts. Animal derived surfactant extracts are obtained from animal or human sources. Trials of surfactant replacement have either tried to prevent the development of respiratory distress in high-risk premature infants or treat established respiratory distress in premature infants. Infants with established respiratory distress syndrome who receive animal derived surfactant extract treatment have a decreased risk of lung rupture (pneumothorax), a decreased risk of lung injury (pulmonary interstitial emphysema), a decreased risk of dying, and a

Background

Description of the condition

Respiratory distress syndrome (RDS) is caused by a deficiency or dysfunction of pulmonary surfactant. Surfactant lines the alveolar surface and prevents atelectasis at end expiration. Pulmonary surfactant is predominantly dipalmitoylphosphatidylcholine with lesser amounts of other phospholipids including phosphatidylglycerol (PG), phosphatidylethanolamine, and phosphatidylinositol. Pulmonary surfactant also contains neutral lipids and four distinct surfactant proteins (SP-A, SP-B, SP-C and SP-D). Surfactant proteins may play a role in surfactant secretion, recycling, cooperative functioning with other surfactant proteins and phospholipids (Schurch 1992; Possmayer 1990), and innate host defense of the lung (Wright 1997). The physiologic functions of surfactant include the ability to lower surface tension, and

Description of the intervention

Investigators in the 1960s attempted to aerosolize dipalmitoylphosphatidylcholine (DPPC) to infants with established respiratory distress syndrome. These investigators could not demonstrate any beneficial effect of surfactant replacement (Robillard 1964; Chu 1967). The poor results were, in part, due to an incomplete understanding of what constitutes pulmonary surfactant. The first successful animal model of surfactant replacement therapy was conducted by Enhorning and co-workers (Enhorning 1972). Enhorning administered a crude animal derived surfactant extract obtained from lavage of the lungs of mature rabbits directly into the trachea of immature rabbits. Improvement in lung compliance and alveolar expansion was noted. Success in animal models led to clinical trials in newborn infants. The first successful experience with surfactant replacement therapy treated infants with established respiratory distress syndrome. Fujiwara 1980 studied a

How the intervention might work

A wide variety of surfactant products have been formulated and studied in clinical trials. These include synthetic surfactants and animal derived surfactant extracts. Animal derived surfactant extracts are derived from biologic sources including cows, pigs and humans. They are obtained by organic extraction of lavage fluid or minced lung. As currently formulated, animal derived surfactants contain surfactant proteins SP-B and SP-C. SP-A and SP-D, are extremely hydrophilic and do not remain in the preparation of any commercial natural surfactant. SP-B and SP-C are markedly hydrophobic and are thought to be crucial in promoting the adsorption and spread of monolayers of surfactant. Animal derived surfactant extracts can be further classified as either modified or unmodified surfactant extracts; modified animal derived surfactant extract is supplemented with phospholipids or other surface active material while unmodified animal derived surfactant extract contains only the components remaining after the extraction process. Trials of surfactant replacement have either tried to prevent the development of respiratory distress in high-risk premature infants or treat

Why it is important to do this review

Multiple systematic reviews have addressed the use of animal derived surfactant preparations or synthetic surfactant preparations in the prevention or treatment of respiratory distress syndrome (Soll 1997a; Soll 1998a; Soll 1998b). Systematic reviews have also addressed the benefits of preventive or early treatment and the benefits of different specific surfactant products (Yost 1999; Soll 2001a; Soll 2001b; Pfister 2007; Stevens 2007). Our analysis will include randomized controlled trials of animal derived surfactant extracts in the treatment of established respiratory distress syndrome. Although animal derived surfactant products are now widely used this review will allow for more precise estimates of

Objectives

To assess the effect of administration of animal derived surfactant extract compared to placebo or no treatment on the risk of mortality, chronic lung disease and other morbidities associated with prematurity in pre-term infants with established respiratory distress syndrome. Subgroup analysis were planned according to the specific surfactant product, the degree of prematurity, and the severity of

Methods

Criteria for considering studies for this review

Types of studies

Only randomized or quasi-randomized controlled clinical trials were considered for this review.

Types of participants

Preterm infants (less than 37 weeks gestation) with clinical and/or radiologic evidence of respiratory distress syndrome

Types of interventions

All included studies utilized surfactant products derived from mammalian sources (human amniotic fluid extract, calf lung surfactant extract, and modified bovine surfactant extract, porcine surfactant extract). Infants with established respiratory distress syndrome randomized to receive animal derived surfactant extract vs. control treatment (intra-tracheal administration of normal saline or air placebo, or no treatment).

Types of outcome measures

Primary Outcomes

Neonatal mortality (mortality < 28 days of age) from any cause

Mortality prior to hospital discharge (from any cause)

Bronchopulmonary dysplasia (oxygen requirement at 28 to 30 days of age)

Bronchopulmonary dysplasia or death prior to 28 days of age

Chronic lung disease (use of supplemental oxygen at 36 weeks post-menstrual age)

Chronic lung disease (use of supplemental oxygen at 36 weeks post-menstrual age) or death prior to 36 weeks post-

Secondary Outcomes

Any air leak syndromes (including pulmonary interstitial emphysema, pneumothorax, pneumomediastinum)

Any pneumothorax

Pulmonary Interstitial emphysema

Any pulmonary haemorrhage

Patent ductus arteriosus (PDA that has been treated with cyclo-oxygenase inhibitor or surgery)
Any culture proven bacterial sepsis
Any culture proven fungal sepsis
Necrotizing enterocolitis (defined as Bell Stage II or greater)
Periventricular leukomalacia
Retinopathy of prematurity [all stages and severe (stage 3 or greater)]
Intraventricular haemorrhage [any grade and severe (grade 3 to 4)]

Cerebral palsy

Neurodevelopmental outcome at approximately two years corrected age (acceptable range 18 months to 28 months) including: cerebral palsy, mental retardation (Bayley Scales of Infant Development Mental Developmental Index < 70), legal blindness (< 20/200 visual acuity), and hearing deficit (aided or < 60 dB on audiometric testing). The composite outcome "neurodevelopmental impairment" will be defined as having any one of the aforementioned deficits. Post hoc analyses will be considered for any unexpected adverse effects reported by the studies.

Search methods for identification of studies

See : Collaborative Review Group search strategy. The standard search method of the Cochrane Neonatal Review Group

Published manuscripts:

Search included PubMed (1966 to December 2008), CINAHL, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library Issue 4, 2008). All languages were included. Search terms: {surfactant OR pulmonary surfactant}, limited to humans and further limited to the age group of newborn infants (infant, newborn) and type of publication (clinical trial). From the resulting studies, randomized controlled trials and quasi-randomized controlled trials that fulfilled the inclusion criteria were selected. To identify long-term neurodevelopmental sequelae, a search using the following keywords was performed: (outcome OR sequelae OR follow-up OR mental retardation OR cerebral palsy OR hearing OR visual OR motor OR mental OR psychological) AND (surfactant OR pulmonary surfactant)

Published abstracts:

The abstracts of the Society for Paediatric Research (USA) (published in Paediatric Research) for the years 1985 to 2008 were searched by hand using the following key words: {surfactant OR pulmonary surfactant} AND {respiratory distress syndrome}. For abstract books that do not include keywords, the search was limited to relevant sections such as pulmonary

Data collection and analysis

For each included study, information was collected regarding the method of randomization, blinding, drug intervention, stratification, and whether the trial was single or multi-centre. Information regarding trial participants including gestational age criteria, birth weight criteria, and other inclusion or exclusion criteria was noted. Information on clinical outcome was analyzed including pneumothorax, pulmonary interstitial emphysema, patent ductus arteriosus, necrotizing enterocolitis, intraventricular haemorrhage (any intraventricular haemorrhage and severe intraventricular hemorrhage), bronchopulmonary dysplasia, retinopathy of prematurity, neonatal mortality, mortality prior to hospital discharge, and bronchopulmonary dysplasia or death. All of these outcomes were analyzed for the entire population of enrolled infants. The standard methods of the Cochrane Neonatal Review Group Guidelines were employed.

Selection process:

All randomized and quasi-randomized controlled trials fulfilling the selection criteria described in the previous section were included. Both review authors reviewed the results of the search and separately selected the studies for inclusion. The review authors resolved any disagreement by discussion.

Criteria for assessing the methodological quality of the studies:

The standard method of the Cochrane Neonatal Review Group were employed. The methodological quality of the studies will be assessed using the following key criteria: allocation concealment (blinding of randomization), blinding of intervention, completeness of follow-up, and blinding of outcome measurement/assessment. For each criteria, assessment will be yes, no, can't tell. Both review authors separately assessed each study. They resolved any disagreement by

Data extraction and entry:

Both review authors separately extracted, assessed and coded all data for each study, using a form that was designed specifically for this review. Any standard error of the mean was replaced by the corresponding standard deviation. We resolved any disagreement by discussion. For each study, final data was entered into RevMan by one reviewer (RS) and

Statistical analyses were performed using Review Manager software. Categorical data was analyzed using relative risk (RR), risk difference (RD) and the number needed to treat (NNT). Continuous data was analyzed using weighted mean difference (WMD). The 95% Confidence interval (CI) was reported on all estimates. We estimated the treatment effects of individual trials and examined heterogeneity between trials by inspecting the forest plots and quantifying the impact of heterogeneity using the I-squared statistic. If noted, the possible causes of statistical heterogeneity were explored (for example, differences in study quality, participants, intervention regimens, or outcome assessments) using post hoc sub

Subgroup analyses:

Surfactant product: bovine extract, modified bovine extract, porcine extract, human amniotic fluid extract

Gestational age (infants born at < 30 weeks gestation)

Birthweight (< 1000 g, ≥ 1000 g)

Moderate to severe respiratory disease (moderate to severe disease defined as need for assisted ventilation and supplemental oxygen greater than 0.60 necessary to maintain adequate oxygenation)

Results

Description of studies

Studies included in this review include studies of human amniotic fluid surfactant extract (Hallman 1985; Lang 1990), bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Gitlin 1987; Raju 1987; Soll 1988; Horbar 1989; Gortner 1990; Horbar 1990; Liechty 1991; Fujiwara 1990; Chen 1990) and porcine surfactant extract (Svenningsen). Details of each study are given in the table "Characteristics of Included Studies" and references and are discussed below:

Bovine Surfactant Extract:

Gortner 1990: In a multi-centre, randomized controlled trial, Gortner and colleagues (Gortner 1990; Gortner 1992 German) studied multiple doses of a bovine lung extract (SF-RI1, Alveofact). Infants between 25 to 30 weeks gestation were enrolled. Although described in the manuscript as a "prevention trial", in fact, infants were eligible only if they were intubated and on assisted ventilation at one hour of life. Thirty-four infants [GA 28.0 +/- 1.5 SD weeks, birth weight (BW), 1,048 +/- 299 g] received 50 mg/kg BW surfactant, whereas 35 infants (GA, 27.6 +/- 1.5 weeks, BW 969 +/- 269 g) served as controls. Retreatment with surfactant (up to three identical doses) 12 - 24 hours after the previous dose was permitted if FiO₂ was greater than 0.5. The primary outcomes studied were the effects of surfactant administration on gas exchange and survival without RPD. In addition, Gortner et al investigated the incidence of bronchopulmonary dysplasia.

Modified Bovine Surfactant Extract:

Modified Bovine Surfactant Extract - Surfactant TA

Gitlin 1987: Gitlin and co-workers (1987) conducted a prospective, randomized, unblinded, controlled trial of modified bovine surfactant extract (Surfactant TA) in premature infants requiring ventilator support for the treatment of severe hyaline membrane disease. Forty-one low birth weight infants weighing between 1000 - 1500 g with severe hyaline membrane disease (on assisted ventilation and supplemental oxygen > 40%) were randomly assigned to a single dose of Surfactant TA. Ware and colleagues (1990) reported the results of health and development assessment at one and two years of age in 32 survivors of a total of 41 premature infants enrolled in a randomized clinical trial of bovine surfactant therapy Gitlin 1987. Raju 1987: Raju and co-workers (1987) conducted a double-blind controlled trial of the effects of a single dose of modified bovine surfactant extract (Surfactant TA) in 30 premature infants (birth weight 751 - 1750 g) with severe hyaline membrane disease. 17 infants had a sonicated saline suspension of 100 mg/kg surfactant phospholipid instilled into the trachea at 5.0 (SD 0.7) hours of age and 13 infants received saline by the same route at 4.3 (1.1) hours of age. Soll 1988: Soll and co-workers (1988) conducted a small pilot study of modified bovine surfactant extract (Surfactant TA) at five European centers. 31 infants weighing 750 - 1750 g with respiratory distress syndrome requiring assisted ventilation were enrolled. Chen 1990: Chen and colleagues (1990) conducted a prospective, randomized, controlled trial to evaluate the efficacy and safety of modified bovine surfactant extract (Surfactant TA) in the treatment of respiratory distress syndrome (RDS). Eighteen premature infants with RDS were studied. Group I consisted of nine premature infants with a mean birth weight of 1,455 +/- 265.9 g and a mean gestational age of 31.4 +/- 1.3 weeks. Group II consisted of nine premature infants with a mean birth weight of 1,411 +/- 379.0 g and a mean gestational age of 30.6 +/- 1.7 weeks. Reconstituted bovine surfactant (Surfactant TA, Tokyo Tanabe Co., Japan), 120 mg/kg body weight was suspended in 4 ml normal saline and delivered to the lungs of the patients in group I through an endotracheal tube via a catheter in five divided doses (mean age at this point

Fujiwara 1990 conducted a multi-centre randomized controlled trial of a modified bovine surfactant extract (Surfactant TA) at 21 centers in Japan. Infants weighing 750 - 1750 g were enrolled if they had RDS requiring assisted ventilation and supplemental oxygen > 40%. Only neonates with surfactant deficiency and without ultra-sonographic evidence of intracranial haemorrhage greater than or equal to grade II were enrolled. Fifty-four patients received a single dose of modified bovine surfactant extract (Surfactant TA 100 mg of phospholipid/kg) and 46 patients received an air placebo within eight hours of life. The severity of RDS was categorized based on radiographic findings and the ventilatory index (VI). In addition, secondary outcome data was collected looking at the impact of surfactant TA use on other common

Modified Bovine Surfactant Extract- Survanta

Two identical single dose trials of modified bovine surfactant extract (Survanta) in the treatment of established respiratory distress syndrome have been reported (Horbar 1989; Horbar 1990).

Horbar 1989: Horbar and co workers (1989) conducted a multi-centre randomized, placebo-controlled trial to evaluate the efficacy and safety of surfactant in the treatment of respiratory distress syndrome. The study population was made up of 159 premature infants (78 treated and 81 controls) weighing 750 to 1750 g who were receiving assisted ventilation with 40% oxygen. The eligible infants received a single dose of either modified bovine surfactant extract [Survanta 100 mg of phospholipid/kg (4 ml per kilogram)] or an air placebo (4 ml/kg), administered into the trachea within eight hours of birth by an investigator not involved in the clinical care of the infant. The study evaluated the effect of a single dose of surfactant on the requirement for supplemental oxygen and clinical status at one week of age. In addition, the study

Horbar 1990: Horbar and colleagues (Horbar 1990) performed a similar multi-centre prospective randomized controlled trial to determine the efficacy and safety of the modified bovine surfactant preparation, Survanta (Abbott Laboratories, Chicago, USA), for 750 - 1750 g infants with respiratory distress syndrome receiving assisted ventilation with 40% oxygen. One hundred and six eligible infants from the eight participating centers were randomly assigned between March 1986 and June 1987 to receive either modified bovine surfactant (Survanta 100 mg phospholipid/kg, 4 ml/kg) or air (4 ml/kg) administered into the trachea within eight hours of birth (median time of treatment 6.2 h, range 3.2 - 9.1 h). The study was stopped before enrolment was completed at the request of the United States Food and Drug Administration

Liechty 1991: Liechty and colleagues (1991) reported on a large multi-centre trial using multiple doses of modified bovine surfactant extract (Survanta) in the treatment of established respiratory distress syndrome. Infants with birth weights between 600 and 1750 g were enrolled if they had respiratory distress syndrome requiring assisted ventilation and supplemental oxygen of 40% or greater. 798 infants (403 treated and 395 controls) were randomized to multiple doses of Survanta or sham air treatment prior to eight hours of age. The primary outcome was the incidence of death secondary to respiratory distress as well as the incidence of death and bronchopulmonary dysplasia. Secondary outcomes included respiratory function and ventilatory requirements, pulmonary air leaks, periventricular/intraventricular haemorrhage, PDA

A follow-up study of the Survanta Multidose Study Group published in 1994 reported data on the clinical status of over 900 surviving infants who were subjects in four double-blind, controlled clinical trials on multiple dosing of bovine surfactant in the prevention and treatment of RDS. Health and developmental status was evaluated at 6, 12, and 24 months

Porcine Surfactant Extract:

Svenningsen 1987: Svenningsen and co-workers (1987) studied whether the ventilatory maneuvers associated with surfactant replacement would influence oxygenation in newborn infants with severe respiratory distress syndrome. Eight patients (700 to 1400 g), all requiring mechanical ventilation with fraction of inspired oxygen greater than 0.6, were included in the trial; four were randomized to receive surfactant, and the others served as controls. Porcine surfactant (2 ml/kg; phospholipid concentration, 100 mg/ml) was instilled via a naso-endotracheal tube at end-expiration and dispersed into the lungs during a period of standardized "sighing" mediated by the ventilator: two prolonged ventilatory cycles (10 sec each) with an inspiration/expiration ratio of 4:1 followed by a 6-min ventilation with a frequency of 60 breath/min and

European 1988. The Collaborative European Multicenter Study Group (European 1988) conducted a randomized multi-centre trial of porcine surfactant extract (Curosurf) involving the collaboration of eight European neonatal intensive care units. Infants with birth weight 700 - 2000 g were studied if they had RDS requiring assisted ventilation and supplemental oxygen of > 60%. 146 infants (x surfactant, y control) were randomized to be given either a single large dose of porcine surfactant extract (Curosurf 200 mg/kg) or sham treatment. The median age of treatment was nine hours (range 2 - 15

Robertson and co-workers (1992) examined the postnatal growth, respiratory status, and neuro-developmental outcome of surviving infants enrolled in a European multi-centre trial of porcine surfactant replacement treatment for severe respiratory distress syndrome

European 1988. The infants were assessed at corrected ages of one and two years.

Human Amniotic Fluid Surfactant Extract:

Hallman 1985: Hallman and co-workers (1985) performed a randomized, prospective clinical trial comparing intra-tracheal administration of human amniotic fluid surfactant extract with conventional ventilatory treatment with intermittent mandatory mechanical ventilation alone for treatment of severe respiratory distress syndrome in pre-term infants of less than 30 weeks gestation. Fifty-three infants weighing < 1500 g with severe RDS who required assisted ventilation and supplemental oxygen of > 60% were enrolled at two centers. Twenty-two infants (mean gestational age 27.0 weeks, mean birth weight 987 g) were given surfactant, and 23 infants (mean gestational age 27.2 weeks, mean birth weight 1055 g) were given conventional treatment. Vaucher (1988) assessed postnatal growth, neurodevelopmental outcome, and occurrence of respiratory illnesses at 12 to 24 months in 46 infants enrolled in this trial. In a second study published in 1993, Vaucher et al compared the neurodevelopmental outcome of extremely premature infants who received either prophylactic surfactant, rescue surfactant after birth, or no surfactant. Lang 1990 studied human amniotic fluid extract in a population similar to the infants studied by Hallman 1985. In infants with severe respiratory distress syndrome who were born at 24 to 32 weeks of gestation weighing less than or equal to 1500 g, Lang and colleagues (1990) randomly assigned infants to receive human surfactant derived from amniotic fluid (N = 28) or control treatment (N = 31) within 12 hours of birth. A second dose of surfactant was given to patients in the control group. There are many case series of surfactant treatment of infants with respiratory distress syndrome. These are not listed in the section on excluded studies. Studies in which it was more difficult to determine how treatment assignment was made or had other reasons for exclusion are noted in the table "Characteristics of Excluded Studies".

Risk of bias in included studies

Randomized controlled trials that compared the effect of natural surfactant extract treatment of established respiratory distress syndrome compared to control treatment are included in the analysis. The 12 studies are of high methodological quality. Randomization: All included studies allocated assigned treatment by randomization. In all of the studies, sealed envelopes with randomly allocated treatment assignments were provided to participating centers.

Blinding of the treatment: Approximately half of the studies attempted to blind clinicians from knowing treatment assignment by having the treatment administered by "dosing investigators" who did not participate in the infant's ongoing care or assessment. These studies include Fujiwara 1990; Raju 1987; Soll 1988; Horbar 1989; Horbar 1990.

Blinding of outcome assessment: Investigators who were not involved with treatment assignment or administration

Exclusions after randomization: Minimal exclusions were noted after randomization. Hallman 1985 excluded eight of the 53 infants initially enrolled due to sepsis or cardiac disease mimicking RDS. Other studies allowed for exclusion of infants

Effects of interventions

ANIMAL DERIVED SURFACTANT EXTRACT VS. CONTROL IN THE TREATMENT OF RESPIRATORY DISTRESS SYNDROME IN NEONATES (Comparison 1):

Multiple randomized controlled trials have demonstrated that animal derived surfactant extract treatment of premature infants with established respiratory distress syndrome improves oxygenation (improved arterial/alveolar oxygen ratio, decreased inspired oxygen concentration) and ventilation (decreased mean airway pressure, improved ventilator efficiency index) during the first 48 - 72 hours of life. These short-term outcomes are not reviewed in the following analysis.

Animal derived surfactant extract treatment of established RDS has the following clinical impact:

Air leak (Outcome 1.1): Studies of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Horbar 1989; Horbar 1990; Liechty 1991), porcine surfactant extract (European 1988) and human amniotic surfactant extract (Hallman 1985; Lang 1990) all reported on the effect of animal derived surfactant extract on the risk of air leak. Overall, there is a highly significant decrease in the risk of air leak associated with animal derived surfactant extract treatment (typical relative risk 0.47, 95% CI 0.39, 0.58; typical risk difference -0.16, 95% CI -0.21, -0.12). The number needed to treat is 10. In the subgroups based on type of animal derived surfactant extract, significant decreases were noted in the risk of air leak in the studies that evaluated modified bovine surfactant extract (typical relative risk 0.44, 95% CI 0.34, 0.58; typical risk difference -0.16, 95% CI -0.20, -0.11), porcine surfactant extract (relative risk 0.60, 95% CI 0.36, 0.99; risk difference -0.16, 95% CI -0.31, -0.01) and human amniotic fluid surfactant extract (typical relative risk 0.45, 95% CI 0.26, 0.78).

Pneumothorax (Outcome 1.2): Studies on bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Chen 1990; Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987; Soll 1988), porcine surfactant extract (European 1988, Svenningsen 1987) and human amniotic fluid surfactant extract (Hallman 1985) all reported on the effect of animal derived surfactant extract treatment on the risk of pneumothorax. Overall, there is a highly significant reduction in the risk of pneumothorax associated with animal derived surfactant extract treatment (typical relative risk 0.40, 95% CI 0.32, 0.51; typical risk difference -0.18, 95% CI -0.22, -0.14) as well as the studies of porcine surfactant extract (typical relative risk 0.58, 95% CI 0.34, 1.00).

Pulmonary interstitial emphysema (Outcome 1.3): Studies with using bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Chen 1990; Fujiwara 1990; Gitlin 1987; Liechty 1991; Raju 1987), porcine surfactant extract (European 1988), and human amniotic surfactant extract (Hallman 1985) reported on pulmonary interstitial emphysema. Overall, there was a highly significant reduction in the risk of pulmonary interstitial emphysema (typical relative risk 0.45, 95% CI 0.37, 0.55; typical risk difference -0.20, 95% CI -0.25, -0.15). The number needed to treat to prevent one case of In the subgroup analysis, studies using modified bovine surfactant extract (typical risk ratio 0.43, 95% CI 0.35, 0.54) and the one study using porcine surfactant extract (relative risk 0.60, 95% CI 0.36, 0.99) demonstrated a reduction in the risk Pulmonary haemorrhage (Outcome 1.4): Fewer studies reported on the effect of animal derived surfactant extract treatment on pulmonary haemorrhage. Only studies using modified bovine surfactant extract treatment prospectively reported on this outcome (Fujiwara 1990; Liechty 1991). In this subgroup of studies, there was no evidence of effect on pulmonary haemorrhage (typical relative risk 1.29, 95% CI 0.77, 2.15; typical risk difference 0.02, 95% CI -0.02, 0.05).

Patent ductus arteriosus (Outcome 1.5): Studies of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Chen 1990; Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987; Soll 1988), porcine surfactant extract (European 1988; Svenningsen 1987), and human amniotic fluid surfactant extract (Hallman 1985; Lang 1990) reported on the effect of animal derived surfactant extract treatment on patent ductus arteriosus. In the overall analysis of all studies, no effect was demonstrated (typical relative risk 0.98, 95% CI 0.89, 1.08; typical risk difference - None of the subgroups based on surfactant type demonstrated an impact on the risk of patent ductus arteriosus. Some heterogeneity was noted between the studies (I-squared statistic = 27%).

Necrotizing enterocolitis (Outcome 1.6): Studies of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Fujiwara 1990, Gitlin 1987, Horbar 1989, Horbar 1990, Liechty 1991, Raju 1987), and human amniotic fluid surfactant extract (Hallman 1985) reported on the risk of necrotizing enterocolitis. Overall, no effect on the risk of necrotizing enterocolitis was demonstrated (typical relative risk 1.13, 95% CI 0.70, 1.82; typical risk difference 0.01, 95% CI -0.02, 0.04). None of the individual studies of bovine surfactant extract, modified bovine surfactant extract, or human amniotic fluid extract demonstrated an impact on necrotizing enterocolitis).

Sepsis (Outcome 1.7): Fewer studies reported on sepsis in newborns treated with animal derived surfactant extract. One study of bovine surfactant extract (Gortner 1990), two studies of modified bovine surfactant extract (Fujiwara 1990; Liechty 1991), and one study of human amniotic fluid surfactant extract (Hallman 1985) reported on sepsis in these infants. Overall, no impact on the risk of sepsis was demonstrated (typical relative risk 1.14, 95% CI 0.87, 1.48; typical risk difference 0.02, 95% CI -0.02, 0.07). None of the individual studies nor any of the subgroup analyses demonstrated an impact on the risk of sepsis.

Periventricular/intraventricular haemorrhage (Outcome 1.8): Studies of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987; Soll 1988), porcine surfactant extract (European 1988), and human amniotic fluid surfactant extract (Hallman 1985) reported on the effect of animal derived surfactant extract treatment on periventricular/intraventricular haemorrhage. Overall, no significant effect was noted on the risk of periventricular/intraventricular haemorrhage (typical relative risk 0.97, 95% CI 0.87, 1.07; typical risk difference -0.02, 95% CI -0.07, 0.03). A fair degree of heterogeneity was noted in these studies (I-squared = 65%). Some individual trials demonstrated a decrease in periventricular/intraventricular haemorrhage (Fujiwara 1990; Liechty 1991).

Severe periventricular/intraventricular haemorrhage (Outcome 1.9): Studies of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987), porcine surfactant extract (European 1988), and human amniotic fluid surfactant extract (Hallman 1985; Lang 1990) all reported on the effect of animal derived surfactant extract treatment on severe periventricular/intraventricular haemorrhage. Overall, no significant impact was noted on severe periventricular/intraventricular haemorrhage (typical relative risk 0.93, 95% CI 0.79, 1.10; typical risk difference -0.02, 95% CI -0.06, 0.02). Although certain individual studies reported on an increase in the risk of severe periventricular/intraventricular haemorrhage (Horbar 1990) the overall analysis demonstrated no significant impact.

Bronchopulmonary dysplasia (Outcome 1.10): Bronchopulmonary dysplasia was defined as a requirement for supplemental oxygen at 28 to 30 days of life. Studies of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Chen 1990; Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987; Soll 1988), porcine surfactant extract (European 1988), and human amniotic fluid surfactant extract (Hallman 1985; Lang 1990) all reported on the risk of bronchopulmonary dysplasia. In the overall analysis, no significant impact of animal derived surfactant extract treatment was noted (typical relative risk 0.95, 95% CI 0.84, 1.08; typical risk difference -0.02, 95% CI -0.07, 0.03). Chronic lung disease: No studies reported on the outcome of chronic lung disease (defined as need for supplemental oxygen at 36 weeks post-menstrual age).

Neonatal mortality (Outcome 1.11): Trials of modified bovine surfactant (Chen 1990; Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987; Soll 1988), porcine surfactant extract (European 1988), and human amniotic fluid surfactant extract (Hallman 1985) all reported on neonatal mortality. Overall, the meta-analysis demonstrates that animal derived surfactant extracts decreased the risk of neonatal mortality (typical relative risk 0.68, 95% CI 0.57, 0.82; typical risk difference -0.09, 95% CI -0.13, -0.05). The number needed to treat to prevent one neonatal death is 11 (95% CI 7, 17). The individual trial of porcine surfactant extract (European 1988) demonstrated a decrease in the risk of mortality (relative risk 0.61, 95% CI 0.41, 0.92). In the subgroup of trials using modified bovine surfactant extract, a significant decrease in the risk of neonatal mortality was noted (typical relative risk 0.70, 95% CI 0.57, 0.86; typical risk difference -0.08, 95% CI -0.13, -0.03).

Mortality prior to hospital discharge (Outcome 1.12): Trials of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Chen 1990; Gitlin 1987; Horbar 1989; Raju 1987), and trials of human amniotic fluid surfactant extract (Hallman 1985; Lang 1990) reported on mortality prior to hospital discharge. Overall, a significant decrease in the risk of mortality prior to hospital discharge was noted (typical relative risk 0.63, 95% CI 0.44, 0.90; typical risk difference -0.10. None of the individual trials nor the subgroup analyses demonstrated a significant decrease on the risk of mortality prior to hospital discharge. Reported mortality (Outcome 1.13): Trials of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Chen 1990; Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987; Soll 1988), porcine surfactant extract (European 1988; Svenningsen 1987), and human amniotic fluid surfactant extract (Hallman 1985; Lang 1990) all reported mortality at some time during the study or at hospital discharge. Overall, a significant decrease in the risk of mortality was noted (typical relative risk 0.68, 95% CI 0.57, 0.80; typical risk difference -0.10, 95% CI -0.14, -0.06). In the subgroup analysis of modified bovine surfactant extract and porcine surfactant extract, overall mortality was noted to be decreased. For modified bovine surfactant extract, the typical relative risk was 0.70 (95% CI 0.57, 0.86); for trials of porcine surfactant extract, the typical relative risk was 0.66 (95% CI 0.45, 0.97).

Bronchopulmonary dysplasia or death (Outcome 1.14): Trials of bovine surfactant extract (Gortner 1990), modified bovine surfactant extract (Chen 1990; Fujiwara 1990; Gitlin 1987; Horbar 1989; Horbar 1990; Liechty 1991; Raju 1987; Soll 1988), porcine surfactant extract (European 1988), and human amniotic fluid surfactant extract (Hallman 1985; Lang 1990) all reported on the combined outcome of bronchopulmonary dysplasia or death. Overall, a significant decrease in the risk of bronchopulmonary dysplasia or death was noted with treatment with animal derived surfactant extract (typical relative risk 0.83, 95% CI 0.77, 0.90; typical risk difference -0.11, 95% CI -0.16, -0.06). The number needed to treat to prevent one infant from either dying or having bronchopulmonary dysplasia is 9 (95% CI 6, 17). A moderate amount of the individual trial of bovine surfactant extract (Gortner 1990) demonstrated a decrease in the risk of bronchopulmonary dysplasia or death (relative risk 0.39, 95% CI 0.20, 0.76). The lone trial that reported on bovine surfactant extract (European 1988) also demonstrated a decrease in the risk of bronchopulmonary dysplasia or death (typical relative risk 0.61, 95% CI 0.46, 0.82). The individual trials of Fujiwara (Fujiwara 1990) and Liechty (Liechty 1991) both showed a decrease in the risk of bronchopulmonary dysplasia or death with modified bovine surfactant extract. In the subgroup analysis of all trials with modified bovine surfactant extract, a decrease in the risk of bronchopulmonary dysplasia or death was noted (typical relative risk 0.70, 95% CI 0.57, 0.86).

Retinopathy of prematurity (Outcome 1.15): Studies of modified bovine surfactant extract (Fujiwara 1990; Gitlin 1987; Raju 1987) and studies of human amniotic fluid surfactant extract (Hallman 1985) reported on retinopathy of prematurity. None of the individual trials nor the meta-analysis demonstrated an impact on retinopathy of prematurity. The overall estimate from the trials is still broad and consistent with a significant worsening or a significant improvement in retinopathy of prematurity. Severe retinopathy of prematurity (Stage 3 or greater) (Outcome 1.16): Few studies reported on severe retinopathy of prematurity. In a study of modified bovine surfactant extract, Raju and co-workers (Raju 1987) reported a non-significant increase in the risk of retinopathy of prematurity (relative risk 1.53, 95% CI 0.15, 15.09). In a study of human amniotic fluid surfactant extract, Lang and co-workers (Lang 1990) reported a non-significant risk increasing the risk of retinopathy of prematurity (relative risk 1.11, 95% CI 0.07, 16.88). The meta-analysis including these two studies demonstrates no significant impact of animal derived surfactant extract on severe retinopathy of prematurity (typical relative risk 1.34, 95% CI 0.15, 15.09).

Cerebral palsy (Outcome 1.17): Only one follow up study reported on the incidence of cerebral palsy. The European Collaborative Study (European 1988) reported on one and two year follow-up (Robertson 1992). No difference in the risk of cerebral palsy is noted in this study (relative risk 0.88, 95% CI 0.34, 2.27; risk difference -0.03, 95% CI -0.21, 0.16).

Visual impairment in survivors (Outcome 1.18): No studies reported on visual impairment as defined in the review protocol (visual acuity < 2/200). Two studies reported on visual impairment (undefined) (European 1988; Gitlin 1987). One study of modified bovine surfactant extract (Gitlin 1987) demonstrated a non-significant reduction in visual impairment in survivors (relative risk 0.38, 95% CI 0.02, 8.59). The one study of porcine surfactant extract (European 1988) did not show any impact on visual impairment. No infants were reported in either group (relative risk not estimable; risk difference 0.00, 95% CI -0.04, 0.04). The meta-analysis does not suggest any effect of animal derived surfactant on visual impairment in survivors.

Major developmental disability in survivors (Outcome 1.19): No studies reported on major neuro-developmental disability in survivors as defined in the review protocol. The European study (European 1988) reported on major neuro-developmental disability defined as severe forms of cerebral palsy, blindness, deafness requiring hearing aids or a Griffiths Developmental Quotient < 70. There is no evidence of an effect on major neuro-developmental disability. Given the small

275

Empty page

276

Probiotics and Prebiotics

Probiotics and Prebiotics

Straight Facts on Probiotics and Prebiotics

Straight Facts on Probiotics and Prebiotics

http://www.beta-glucan-info.com/probiotic_facts.htm

Whether you've heard about them yet or not, probiotics and prebiotics are rapidly gaining scientific popularity as safe and effective agents that help regulate the body's micro-environment. The micro-environment of your body varies from place to place but is ideally made up of healthy micro-organisms that not only thrive in a healthy ecosystem with us but are sometimes as beneficial to us as we are to them. But the market is full of probiotics and prebiotics supplements so how do you know which ones work and which ones don't? In this series of articles we will help you learn how to identify which

How to compare probiotics and prebiotics:

When our healthy micro-environment is nearly perfect, it contains colonies of bacteria and a few yeast organisms that live together without harming us, and without our body working to fight off the organisms as it does whenever we have an infection. The primary sites of colonization are the mouth, the skin, the genital organs and the intestinal tract. While each site is colonized a bit differently, the composition of one site can influence the types of micro-organisms living on another. When the micro-environment gets disrupted, such as when the immune system is low or when a person takes antibiotics, the healthy micro-organisms can drastically reduce in numbers so that unhealthy or "pathogenic" organisms can take their place. Yeast, particularly, can become overgrown as they are not killed off when someone takes an antibiotic and in the

any time pathogenic organisms become a big part of our micro-environment, we can develop colon problems, allergies, local infections of the skin or genital area and other problems related to the immune system. Some types of colitis, fibromyalgia and chronic fatigue syndrome have, in some cases, been found to be attributed to an imbalance of

This is where a diet supplemented with combinations of probiotics and prebiotics becomes extremely valuable to your health. Probiotics are strains of living bacteria in their natural state or in their spore form, which is the form bacteria choose to be in when conditions are harsh. The spore form of bacteria has a longer shelf life and survives the trip through the stomach until it reaches the colon and begins to further grow and develop into healthy colonies of bacteria, attached to

Probiotics

Probiotics: The most common types of probiotic bacteria are strains of Lactobacilli and Bifidobacteria. The body has a mechanism whereby it can tell the difference between healthy bacteria and unhealthy bacteria. Inside the intestine, the unhealthy or pathogenic bacteria create an immune response against the unhealthy bacteria, leading to diarrhoea, cramps and abdominal pain. Clostridium difficile is one of those pathogenic bacteria and is a complication of prolonged or repetitive antibiotic use. Giardia is a parasitic infection that leads to chronic diarrhoea. Each of these pathogens can be

Prebiotics

Prebiotics: these are best described as the nourishment the probiotic bacteria need to grow and colonize the bowels. They are more commonly referred to as Synbiotics. The most common kind of prebiotic is made of fructo-oligosaccharide molecules. These are short-chain sugar molecules containing fructose. The exciting thing about prebiotics is that, while traveling through our stomach and small intestines, we haven't the ability to take prebiotic molecules and digest them ourselves. The molecules, therefore, pass through untouched and are available for probiotic bacteria to use as nutrition for their own purposes. Ideal nutrition plus healthy bacteria make for a perfect environment inside the colon for these bacteria

While probiotics and prebiotics are taken by mouth in capsule or tablet form, they do not simply stop doing an effective job of recolonizing the body's micro-environment by colonizing the colon. Scientific research has shown that colonizing the colon with healthy bacteria also alters the colonization of the micro-environments of the genital areas, the mouth and the skin. By using probiotics and prebiotic supplements, the micro-environment of the entire body can be optimized and

Because probiotics come in several strains and because science has discovered that different strains of probiotic bacteria have different effects on the body, using a combination of probiotic strains is likely the best way to go. Simply picking a strain of probiotic that is advertised as being healthy doesn't mean it will help you in the way that you would like. The colon, for example, contains over 400 strains of different micro-organisms. It is unlikely that only one strain will be able to

Let's look at an example of a situation in which a probiotic and prebiotic combination can have a remarkable effect on the entire body. For example, consider an individual with diabetes who takes several courses of an antibiotic for a bladder infection that just won't go away. Before too long, she is likely to get a vaginal yeast infection and that, about the same

Given her uncomfortable situation, she has two choices. She could double up on the allergy medicine which may make her more tired than she already feels. Along with that she could see her doctor or go to the pharmacy and get something for the yeast infection. The problem is that she's diabetic so that getting rid of the yeast infection won't be that easy.

Her other alternative is to do some, all or none of the above treatments along with getting a good probiotic/prebiotic combination supplement and to tackle the problem by using a different approach. You see, what has likely happened to her is that she has destroyed the micro-environment of her intestines and her vaginal tract. Both have become overrun with yeast. Treating just her vaginal yeast infection won't get rid of the yeast overgrowth that is inside her colon.

The yeast in her colon has caused her colonic wall to become more permeable (or leaky) so that yeast toxins, other toxins and undigested molecules to get into her system and trigger an immune reaction, making her tired and increasing her allergy symptoms. The same yeast has overgrown inside her vaginal tract, causing an uncomfortable infection that thrives

A diet supplemented with a probiotic/prebiotic combination can alter the unhealthy micro-environmental situation she's in. Treating the allergies and the yeast infection alone does not treat the underlying condition. By eliminating the unhealthy ecology of her bowels and her vaginal tract, she properly addresses the situation.

The point to really think about is that situations similar to the one above happens more often and to more people than one would think. Many bowel conditions have unhealthy micro-environments that are contributing to them. Some systemic conditions, like fibromyalgia and chronic fatigue syndrome, have been found to be related to unhealthy microflora in the body. Researchers are beginning to find a connection between an unhealthy colonic environment and the development of

Perhaps it would be best to summarize the benefits of supporting your diet with safe and effective probiotics by listing the various body systems and conditions in which intestinal floral imbalance can lead to:

Infant allergies and infections (when used in formula)

Inflammatory colitis

Candida yeast infections (in all body areas)

Atopic dermatitis

Bladder infections

Vaginal infections

Acute pancreatitis

Indigestion

High cholesterol

Crohn's Disease

Non-alcoholic fatty liver disease

Ulcerative colitis

Antibiotic-induced diarrhoea

Gastroenteritis (stomach flu)

Diarrhoea

Risk of colon cancer

Gastric ulcers

Duodenal ulcers

Helicobacter pylori infections

Post-operative bowel infections

Clostridium difficile infections

Complications of prematurity

Abdominal radiation

Keeping your micro-environment healthy on a daily basis prevents the many unwanted effects that can occur whenever your system gets out of balance. Probiotic and prebiotic combinations can regulate your body micro-environment in a safe

What Is Respiratory Distress Syndrome?

<http://www.nhlbi.nih.gov/health/health-topics/topics/rds/>

Respiratory distress syndrome (RDS) is a breathing disorder that affects newborns. RDS rarely occurs in full-term infants. The disorder is more common in premature infants born about 6 weeks or more before their due dates. RDS is more common in premature infants because their lungs aren't able to make enough surfactant (sur-FAK-tant). Surfactant is a liquid that coats the inside of the lungs. It helps keep them open so that infants can breathe in air once Without enough surfactant, the lungs collapse and the infant has to work hard to breathe. He or she might not be able to breathe in enough oxygen to support the body's organs. The lack of oxygen can damage the baby's brain and other organs Most babies who develop RDS show signs of breathing problems and a lack of oxygen at birth or within the first few hours

Overview

RDS is a common lung disorder in premature infants. In fact, nearly all infants born before 28 weeks of pregnancy develop RDS might be an early phase of bronchopulmonary dysplasia (brong-ko-PUL-mo-nar-e dis-PLA-ze-ah), or BPD. This is another breathing disorder that affects premature babies. RDS usually develops in the first 24 hours after birth. If premature infants still have breathing problems by the time they reach their original due dates, they may be diagnosed with BPD. Some of the life-saving treatments used for RDS may Some infants who have RDS recover and never get BPD. Infants who do get BPD have lungs that are less developed or more damaged than the infants who recover.

Infants who develop BPD usually have fewer healthy air sacs and tiny blood vessels in their lungs. Both the air sacs and the tiny blood vessels that support them are needed to breathe well.

Outlook

Due to improved treatments and medical advances, most infants who have RDS survive. However, these babies may need extra medical care after going home. Some babies have complications from RDS or its treatments. Serious complications include chronic (ongoing) breathing problems, such as asthma and BPD; blindness; and brain damage.

Other Names for Respiratory Distress Syndrome

Hyaline membrane disease
Neonatal respiratory distress syndrome
Infant respiratory distress syndrome
Surfactant deficiency

What Is Respiratory Distress Syndrome?

Respiratory distress syndrome (RDS) is a breathing disorder that affects newborns. RDS rarely occurs in full-term infants. The disorder is more common in premature infants born about 6 weeks or more before their due dates. RDS is more common in premature infants because their lungs aren't able to make enough surfactant (sur-FAK-tant). Surfactant is a liquid that coats the inside of the lungs. It helps keep them open so that infants can breathe in air once Without enough surfactant, the lungs collapse and the infant has to work hard to breathe. He or she might not be able to breathe in enough oxygen to support the body's organs. The lack of oxygen can damage the baby's brain and other organs Most babies who develop RDS show signs of breathing problems and a lack of oxygen at birth or within the first few hours

Overview

RDS is a common lung disorder in premature infants. In fact, nearly all infants born before 28 weeks of pregnancy develop RDS might be an early phase of bronchopulmonary dysplasia (brong-ko-PUL-mo-nar-e dis-PLA-ze-ah), or BPD. This is another breathing disorder that affects premature babies. RDS usually develops in the first 24 hours after birth. If premature infants still have breathing problems by the time they reach their original due dates, they may be diagnosed with BPD. Some of the life-saving treatments used for RDS may Some infants who have RDS recover and never get BPD. Infants who do get BPD have lungs that are less developed or more damaged than the infants who recover. Infants who develop BPD usually have fewer healthy air sacs and tiny blood vessels in their lungs. Both the air sacs and the tiny blood vessels that support them are needed to breathe well.

Outlook

Due to improved treatments and medical advances, most infants who have RDS survive. However, these babies may need extra medical care after going home.

Some babies have complications from RDS or its treatments. Serious complications include chronic (ongoing) breathing problems, such as asthma and BPD; blindness; and brain damage.

What Causes Respiratory Distress Syndrome?

The main cause of respiratory distress syndrome (RDS) is a lack of surfactant in the lungs. Surfactant is a liquid that coats a fetus's lungs start making surfactant during the third trimester of pregnancy (weeks 26 through labor and delivery). The substance coats the insides of the air sacs in the lungs. This helps keep the lungs open so breathing can occur after birth. Without enough surfactant, the lungs will likely collapse when the infant exhales (breathes out). The infant then has to work harder to breathe. He or she might not be able to get enough oxygen to support the body's organs. Some full-term infants develop RDS because they have faulty genes that affect how their bodies make surfactant.

Who Is at Risk for Respiratory Distress Syndrome?

Certain factors may increase the risk that your infant will have respiratory distress syndrome (RDS). These factors include:

Premature delivery. The earlier your baby is born, the greater his or her risk for RDS. Most cases of RDS occur in babies born before 28 weeks of pregnancy.

Stress during your baby's delivery, especially if you lose a lot of blood.

Infection.

Your having diabetes.

Your baby also is at greater risk for RDS if you require an emergency Caesarean delivery (C-section) before your baby is full term. You may need an emergency C-section because of a condition, such as a detached placenta, that puts you or your baby at risk. Planned C-sections that occur before a baby's lungs have fully matured also can increase the risk of RDS. Your doctor can do tests before delivery that show whether it's likely that your baby's lungs are fully developed. These tests assess the age of the lungs.

What Are the Signs and Symptoms of Respiratory Distress Syndrome?

Signs and symptoms of respiratory distress syndrome (RDS) usually occur at birth or within the first few hours that follow.

Rapid, shallow breathing

Sharp pulling in of the chest below and between the ribs with each breath

Grunting sounds

Flaring of the nostrils

The infant also may have pauses in breathing that last for a few seconds. This condition is called apnoea (AP-ne-ah).

Respiratory Distress Syndrome Complications

Depending on the severity of an infant's RDS, he or she may develop other medical problems.

Lung Complications

Lung complications may include a collapsed lung (atelectasis), leakage of air from the lung into the chest cavity (pneumothorax), and bleeding in the lung (haemorrhage).

Some of the life-saving treatments used for RDS may cause bronchopulmonary dysplasia, another breathing disorder.

Blood and Blood Vessel Complications

Infants who have RDS may develop sepsis, an infection of the bloodstream. This infection can be life threatening.

Lack of oxygen may prevent a fetal blood vessel called the ductus arteriosus from closing after birth as it should. This condition is called patent ductus arteriosus, or PDA.

The ductus arteriosus connects a lung artery to a heart artery. If it remains open, it can strain the heart and increase blood pressure.

Other Complications

Complications of RDS also may include blindness and other eye problems and a bowel disease called necrotizing enterocolitis (EN-ter-o-ko-LI-tis). Infants who have severe RDS can develop kidney failure.

Some infants who have RDS develop bleeding in the brain. This bleeding can delay mental development. It also can cause mental retardation or cerebral palsy.

How Is Respiratory Distress Syndrome Diagnosed?

Respiratory distress syndrome (RDS) is common in premature infants. Thus, doctors usually recognize and begin treating the disorder as soon as babies are born.

Doctors also do several tests to rule out other conditions that could be causing an infant's breathing problems. The tests also can confirm that the doctors have diagnosed the condition correctly.

The tests include:

Chest x ray. A chest x ray creates a picture of the structures inside the chest, such as the heart and lungs. This test can show whether your infant has signs of RDS. A chest x ray also can detect problems, such as a collapsed lung, that may require Blood tests. Blood tests are used to see whether an infant has enough oxygen in his or her blood. Blood tests also can help find out whether an infection is causing the infant's breathing problems.

Echocardiography (echo). This test uses sound waves to create a moving picture of the heart. Echo is used to rule out heart defects as the cause of an infant's breathing problems.

Surfactant dysfunction

What is surfactant dysfunction?

Surfactant dysfunction is a lung disorder that causes breathing problems. This condition results from abnormalities in the composition or function of surfactant, a mixture of certain fats (called phospholipids) and proteins that lines the lung tissue and makes breathing easy. Without normal surfactant, the tissue surrounding the air sacs in the lungs (the alveoli) sticks together (because of a force called surface tension) after exhalation, causing the alveoli to collapse. As a result, filling the The signs and symptoms of surfactant dysfunction can vary in severity. The most severe form of this condition causes respiratory distress syndrome in newborns. Affected babies have extreme difficulty breathing and are unable to get enough oxygen. The lack of oxygen can damage the baby's brain and other organs. This syndrome leads to respiratory failure, and Less severe forms of surfactant dysfunction cause gradual onset of breathing problems in children or adults. Signs and symptoms of these milder forms are abnormally rapid breathing (tachypnea); low concentrations of oxygen in the blood (hypoxemia); and an inability to grow or gain weight at the expected rate (failure to thrive).

There are several types of surfactant dysfunction, which are identified by the genetic cause of the condition. One type, called SP-B deficiency, causes respiratory distress syndrome in newborns. Other types, known as SP-C dysfunction and ABCA3 deficiency, have signs and symptoms that range from mild to severe.

How common is surfactant dysfunction?

One type of surfactant dysfunction, SP-B deficiency, is estimated to occur in 1 in 1 million newborns worldwide. The prevalence of surfactant dysfunction due to other causes is unknown.

What genes are related to surfactant dysfunction?

Surfactant dysfunction is caused by mutations in one of several genes, including SFTPB, SFTPC, and ABCA3. Each of these genes is involved in the production of surfactant. The production and release of surfactant is a complex process. The phospholipids and proteins that make up surfactant are packaged in cellular structures known as lamellar bodies. These structures are also important for some processing of surfactant proteins, which is necessary for the proteins to mature and become functional. Surfactant is released from the lung cells and spreads across the tissue that surrounds alveoli. This The SFTPB and SFTPC genes provide instructions for making surfactant protein-B (SP-B) and surfactant protein-C (SP-C), respectively, two of the four proteins in surfactant. These two proteins help spread the surfactant across the surface of the lung tissue, aiding in the surface tension-lowering property of surfactant. In addition, SP-B plays a role in the formation Mutations in the SFTPB gene cause a type of surfactant dysfunction sometimes referred to as SP-B deficiency. These mutations lead to a reduction in or absence of mature SP-B. In addition, SFTPB gene mutations cause abnormal processing of SP-C, resulting in a lack of mature SP-C and a build-up of unprocessed forms of SP-C. These changes lead to abnormal surfactant composition and decreased surfactant function. The loss of functional surfactant raises surface tension in the alveoli, causing severe breathing problems. The combination of SP-B and SP-C dysfunction may explain why the signs Mutations in the SFTPC gene are involved in a type of surfactant dysfunction sometimes called SP-C dysfunction. These mutations result in a reduction or absence of mature SP-C and the build-up of abnormal forms of SP-C. It is unclear which of these outcomes causes the signs and symptoms of SP-C dysfunction. Lack of mature SP-C can lead to abnormal composition of surfactant and decreased surfactant function. Alternatively, research suggests that abnormally processed SP-C proteins form the wrong three-dimensional shape and accumulate inside the lung cells. These misfolded proteins may The ABCA3 gene provides instructions for making a protein that is found in the membrane that surrounds lamellar bodies. The ABCA3 protein transports phospholipids into lamellar bodies where they form surfactant. The ABCA3 protein also appears to be involved in the formation of lamellar bodies.

ABCA3 gene mutations, which cause a type of surfactant dysfunction sometimes referred to as ABCA3 deficiency, lead to reduction or absence of the protein's function. Without ABCA3 protein function, the transport of surfactant phospholipids is decreased. In addition, lamellar body formation is impaired, which causes abnormal processing of SP-B and SP-C. ABCA3 gene mutations result in abnormal surfactant composition and function. It has been suggested that mutations that eliminate ABCA3 protein function cause severe forms of surfactant dysfunction, and mutations that leave some residual

Read more about the ABCA3, SFTPB, and SFTPC genes.
See a list of genes associated with surfactant dysfunction.

How do people inherit surfactant dysfunction?

Surfactant dysfunction can have different inheritance patterns depending on its genetic cause.

When caused by mutations in the SFTPB or ABCA3 gene, this condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. When caused by mutations in the SFTPC gene, this condition has an autosomal dominant inheritance pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In about half of cases caused by changes in the SFTPC gene, an affected person inherits the mutation from one affected parent. The remainder result from new mutations in the gene and occur in people with no history of the disorder in their family.

The resources on this site should not be used as a substitute for professional medical care or advice. Users seeking information about a personal genetic disease, syndrome, or condition should consult with a qualified healthcare

SURFACTANT DEFICIENCY DISORDER

<http://www.mypacs.net/cases/SURFACTANT-DEFICIENCY-DISORDER-163859.html>

Contributed by: Faculty and residents Children's Hospital, Radiologist, Children's Health System, Birmingham, Alabama.,

Patient: 1 day old male

History:

premature infant with respiratory distress

Findings:

diffuse granular opacities with low lung volumes
rapid clearing following treatment with improved expansion

Diagnosis:

Surfactant Deficiency Disorder (HMD, RDS)

Discussion:

Surfactant deficiency is an expression of biochemical immaturity that leads to alveolar collapse and hypoxia. The term RDS (respiratory distress syndrome) has been used to describe the clinical expression of surfactant deficiency: alveolar instability and collapse, decreased functional residual capacity, uneven air expansion, increased capillary permeability, alveolar oedema, and focal pulmonary haemorrhage. However, the term respiratory distress syndrome is non-specific and imprecise. HMD (hyaline membrane disease) has also been used to describe the histologic counterpart to RDS. However, these membranes are the result and not the cause of the disease so again the name is limited. Surfactant deficiency
Approximately 50% of neonates born between 26-28 weeks and 20-30% of neonates born at 30-31 weeks of gestation develop lung disease due to surfactant deficiency. The disease is more severe and more common in males, and occurs more
Within 24-48 hours of exogenous surfactant administration, rapid uniform clearing of granular opacities is often seen. Maldistribution results in heterogeneous clearing.

<http://www.amazon.com/Herbs-Botanicals-Teas-Dave-Oomah/dp/1566768519>

Herbs, Botanicals and Teas presents the latest scientific and technical information on the chemical, pharmacological, epidemiological and clinical aspects of major herbal and tea products. Written by leading researchers contributing to the field, this is the first reference to provide in-depth coverage of garlic, ginseng, Echinacea, ginger, fenugreek, St. John's Wort, Ginko Biloba, goldenseal, saw palmetto, valerian, evening primrose, licorice, bilberries and blueberries and black and green teas. Also included are chapters on international regulations and quality assurance and quality control for the

www.emptyteabags.net/

the nature and physiological effects of biologically active plant metabolites

Shipping Weight: 1.5 pounds (View shipping rates and policies)

<http://www.wlbcenter.org/publications.htm>

The journal DIVERSITY was published between 1982 and the year 2000. It was an important vehicle for the dissemination of news and information pertaining to the maintenance of genetic diversity within the breeding stocks of various crop plants. Now the William L. Brown Centre is making available all back issues of DIVERSITY via the internet. The Wm. L. Brown Centre intends to use the Diversity website to publish a series of occasional papers that will be of interest to the plant genetics resources community. The internet is an excellent vehicle for electronic publication of translations of important work, thus making it available to a very broad audience. When the situation demands it, hard copies will be printed. Each publication will be identified as an "Occasional Contribution from Diversity." Several manuscripts have been proposed for publication in this series. One title under consideration is a translation of a monograph currently available only in Spanish entitled Bioprospecting and Access to Genetic Resources. The proceedings of the NSF-sponsored workshop on Priorities in Ethnobiology organized by Ian Salick and her colleagues would also be suitable for

279

Empty page

280

Functional Medicine

Functional Medicine

281

Empty page

282

Empty page

283

Anthroposophic medicine

Anthroposophic medicine

284

148 Anthroposophic medicine

285

Anthroposophic medicine

Anthroposophical medicine

Anthroposophical medicine

http://en.wikipedia.org/wiki/Anthroposophical_medicine

Anthroposophical medicine is a complementary medicine that combines elements of conventional medicine with homoeopathy and naturopathy. It is based on the spiritual philosophy of anthroposophy, which regards human wellness and illness as biographical events connected to the body, mind and spirit of the individual. It often incorporates physical and artistic therapies, and biographical counselling. Anthroposophical medicine was founded in the 1920s by Rudolf

According to its practitioners, anthroposophical medicine uses a holistic approach ("salutogenesis") that focuses on factors that support human health by strengthening the patient's physiology and individuality, rather than just addressing factors that cause disease. The self-determination, autonomy and dignity of patients is a central theme. Practitioners believe the therapies enhance a patient's capacities to heal. *Conventional medical treatments*, including surgery and medications, are employed as necessary, [when?] and anthroposophical physicians must have a conventional medical education, including a degree from an established and certified medical school, as well as post-graduate study. There are currently

Scientists, mainstream medical doctors, and other sceptics regard anthroposophical medicine as unscientific, pseudoscientific, "a system of medicine that extends medical science into the realm of the spiritual", and quackery due to its incorporation of objectively unverifiable ideas such as patients' "karmic destiny".

Anthroposophical medicine seeks to extend, not replace, mainstream Western medicine. *Its practitioners do not regard it as an "alternative", but as an extension, to conventional science-based medicine:*

Anthroposophical medicine is based on Steiner's concept that spiritual awareness is the foundation of individual health and of the health of society. Steiner believed that many of the oldest systems of healing, such as traditional Chinese medicine, Ayurvedic medicine, and Tibetan medicine, were based on a spiritual perception of the world that modern science has lost. Steiner wanted medicine to get back in touch with spirituality, and at the same time keep and use wisely the gains that science and technology have made. Thus, conventional medicine needed to be extended beyond physical science to include —"Anthroposophical medicine", AltMD ,

Based upon the anthroposophical view of the human being, the approach considers the patient's:

Physical constitution;

Life or etheric body, sometimes considered to be analogous to chi or prana;

The physio-psychological organization (also called the astral body), understood as the bearer of both the emotional or psychological state (affect), and of consciousness;

The 'ego', source of the self-reflection and free will that co-form the patient's biography.

Each of these is considered to have an influence on a patient's health.

In particular, anthroposophic medicine raises the question of a chronic or acute illness' significance in the biography of the patient: in what ways does the illness express, or appear as a result of, what is happening in the patient's life; and in what way does it open up or close down life paths? The events of an illness are considered to constitute decisive decision points in the patient's life: through overcoming an illness a patient may open up biographical doors and/or develop aspects of his or her being that he or she might not otherwise have achieved. The medical goal is then not necessarily to restore the previous condition of the patient, which led to the illness, but rather to achieve a new and healthier condition. Biographical Practitioners believe that spending time with a patient is important to discern the most important factors about the patient, and that aspects of patients' well being are not helped by the rush; many doctors, both anthroposophic and conventional, are critical of the stresses on the medical system today that lead to rushing patients through.

Anthroposophical doctors try to minimize the use of antibiotics, antipyretics, pharmaceutical drugs, and vaccinations. In particular, some children treated by anthroposophic doctors are vaccinated only against tetanus and polio, while for others vaccinations may be given later than recommended by health authorities. Steiner believed that vaccination "interferes with karmic development and the cycles of reincarnation". When this was put into practice, it caused a pertussis outbreak in a To find remedies to treat a particular illness, anthroposophical medicine considers the nature of the source of the substances used. The character of a mineral, plant or animal is considered to have been formed by the substances that are most active within it. Thus this character may also reveal what the substance will accomplish when given to treat another organism. This is related to Hahnemann's Doctrine of signatures. Willow, for example, has an unusual character: "... plants that grow near water are usually heavy, with big, dark green leaves that wilt and break easily. An exception is... the white willow, a tree that always grows near water and loves light. However, unlike other "watery" plants, the willow has fine, almost dry leaves and looks very light... Its branches are unbelievably tough. They are elastic and cannot be broken. They bend easily and form "joints" rather than break. These few signatures can give us the clue to what salix can

There is no scientific evidence that the shape of plants has ever caused a new medical property to be discovered. The intent of the medical approach is to consider both the effective substances and the character (not just shape) of the mineral, plant The American Heart Association describes the normal heart as a "strong, muscular pump a little larger than a fist [that] pumps blood continuously through the circulatory system"; for example, Steiner believed that the heart was not a pump, but a regulator of flow. that in the circulatory system blood is "propelled with its own biological momentum, as can be

Mistletoe treatment for cancer

In 2005, a Swiss government study identified 178 clinical studies of anthroposophical medicine. For many treatments used in anthroposophical medicine, however, proofs of efficacy have not been made through strictly controlled medical testing. The use of mistletoe extracts in the treatment of cancer was first proposed by Rudolf Steiner and developed by anthroposophical researchers; it is now probably the best-known anthroposophic therapy. Various forms of the extract are available in Central Europe, where the treatment regimens of up to two-thirds of all oncology patients includes mistletoe. The extracts are generally no longer used to reduce or inhibit tumor growth, but to improve the patients' quality of life and to reduce tumor-induced symptoms and the side-effects of chemotherapy and radiotherapy; a wide array of clinical studies support the efficacy of the treatment regimen for the latter purposes. There are also phytotherapeutic preparations using In the United States, mistletoe "holds interest as a potential anticancer agent because extracts derived from it have been shown to kill cancer cells in vitro" but no forms of the extract have been approved by the FDA for any indications. Mistletoe extracts may not be distributed in or imported into the US except for the purpose of clinical research.

Although preclinical (animal) studies suggested a potential role for mistletoe extracts in cancer therapies, no such effects have been convincingly reported. Evidence for the efficacy of mistletoe as an anticancer drug from human studies is weak. double blinded studies have tended not to support this effect. Though numerous cohort studies and case series have reported tumor remission and regression, the cohort and case studies have been criticized as biased due to their small size and lack of double-blinding. The National Cancer Institute (US) suggests that many studies done on human beings have major weaknesses that raise doubts about the reliability of their findings: in some studies without such weaknesses no

The institutes's position on mistletoe is: "Extracts of mistletoe have been shown to kill cancer cells in the laboratory and to boost the immune system (the complex group of organs and cells that defends the body against infection or disease). For this reason, mistletoe has been classified as a type of biological response modifier (a substance that stimulates the body's response to infection and disease). Extracts of mistletoe have also been shown in the laboratory to prevent the growth of new blood vessels needed for tumors to grow....At this time, there is not enough evidence to recommend the use of mistletoe as a treatment for cancer except in carefully designed clinical trials. These trials will give more information about

Anthroposophical medicine ...

http://en.wikipedia.org/wiki/Anthroposophical_medicine

Anthroposophical medicine

Alternative medical systems

Acupuncture · Anthroposophic medicine · Herbalism · Homeopathy · Naturopathy · Orthopathy · Chiropractic

Traditional medicine

Chinese · Mongolian · Tibetan · Unani · Siddha · Ayurveda

NCCAM classifications

Whole medical systems · Mind-body interventions · Biologically based therapies · Manipulative therapy · Energy

Anthroposophical medicine is a complementary medicine that combines elements of conventional medicine with homeopathy and naturopathy. It is based on the spiritual philosophy of anthroposophy, which regards human wellness and illness as biographical events connected to the body, mind and spirit of the individual. It often incorporates physical and artistic therapies, and biographical counselling. Anthroposophical medicine was founded in the 1920s by Rudolf Steiner in

According to its practitioners, anthroposophical medicine uses a holistic approach ("salutogenesis") that focuses on factors that support human health by strengthening the patient's physiology and individuality, rather than just addressing factors that cause disease. The self-determination, autonomy and dignity of patients is a central theme. Practitioners believe the therapies enhance a patient's capacities to heal. Conventional medical treatments, including surgery and medications, are employed as necessary,^[when?] and anthroposophical physicians must have a conventional medical education, including a degree from an established and certified medical school as well as post-graduate study. There are currently

Part of a series on Anthroposophy

General Anthroposophy · Rudolf Steiner

Anthroposophical Society · Goetheanum

Anthroposophically inspired work

Waldorf education

Biodynamic agriculture

Anthroposophical medicine

Camphill Movement · Eurythmy

Philosophy

Philosophy of Freedom

Sociology

Social threefolding

Scientists, mainstream medical doctors, and other sceptics regard anthroposophical medicine as unscientific, pseudoscientific, "a system of medicine that extends medical science into the realm of the spiritual", and quackery due to its incorporation of objectively unverifiable ideas such as patients' "karmic destiny".

Anthroposophical medicine seeks to extend, not replace, mainstream Western medicine. Its practitioners do not regard it as an "alternative", but *as an extension, to conventional science-based medicine*:

Anthroposophical medicine is based on Steiner's concept that spiritual awareness is the foundation of individual health and of the health of society. Steiner believed that many of the oldest systems of healing, such as traditional Chinese medicine, Ayurvedic medicine, and Tibetan medicine, were based on a spiritual perception of the world that modern science has lost. Steiner wanted medicine to get back in touch with spirituality, and at the same time keep and use wisely the gains that science and technology have made. Thus, conventional medicine needed to be extended beyond physical science to include —"Anthroposophical medicine", AltMD ,

Based upon the anthroposophical view of the human being, the approach considers the patient's:

Physical constitution;

Life or etheric body, sometimes considered to be analogous to chi or prana;

The physio-psychological organization (also called the astral body), understood as the bearer of both the emotional or psychological state (affect), and of consciousness;

The 'ego', source of the self-reflection and free will that co-form the patient's biography.

Each of these is considered to have an influence on a patient's health.

In particular, anthroposophic medicine raises the question of a chronic or acute illness' significance in the biography of the patient: in what ways does the illness express, or appear as a result of, what is happening in the patient's life; and in what way does it open up or close down life paths? The events of an illness are considered to constitute decisive decision points in the patient's life: through overcoming an illness a patient may open up biographical doors and/or develop aspects of his or her being that he or she might not otherwise have achieved. The medical goal is then not necessarily to restore the previous condition of the patient, which led to the illness, but rather to achieve a new and healthier condition. Biographical Practitioners believe that spending time with a patient is important to discern the most important factors about the patient, and that aspects of patients' well being are not helped by the rush; many doctors, both anthroposophic and conventional, are critical of the stresses on the medical system today that lead to rushing patients through. Anthroposophical doctors try to minimize the use of antibiotics, antipyretics, pharmaceutical drugs, and vaccinations. In particular, some children treated by anthroposophic doctors are vaccinated only against tetanus and polio, while for others vaccinations may be given later than recommended by health authorities. Steiner believed that vaccination "interferes with karmic development and the cycles of reincarnation". When this was put into practice, it caused a pertussis outbreak in a To find remedies to treat a particular illness, anthroposophical medicine considers the nature of the source of the substances used. The character of a mineral, plant or animal is considered to have been formed by the substances that are most active within it. Thus this character may also reveal what the substance will accomplish when given to treat another organism. This is related to Hahnemann's Doctrine of signatures. *Willow, for example, has an unusual character:* "... plants that grow near water are usually heavy, with big, dark green leaves that wilt and break easily. An exception is... the white willow, a tree that always grows near water and loves light. However, unlike other "watery" plants, the willow has fine, almost dry leaves and looks very light... Its branches are unbelievably tough. They are elastic and cannot be broken. They bend easily and form "joints" rather than break. These few signatures can give us the clue to what salix can do. There is no scientific evidence that the shape of plants has ever caused a new medical property to be discovered. The intent of the medical approach is to consider both the effective substances and the character (not just shape) of the mineral, plant or animal. The American Heart Association describes the normal heart as a "strong, muscular pump a little larger than a fist [that] pumps blood continuously through the circulatory system"; for example, Steiner believed that the heart was not a pump, but a regulator of flow, that in the circulatory system blood is "propelled with its own biological momentum, as can be

Mistletoe treatment for cancer

In 2005, a Swiss government study identified 178 clinical studies of anthroposophical medicine. For many treatments used in anthroposophical medicine, however, proofs of efficacy have not been made through strictly controlled medical testing. The use of mistletoe extracts in the treatment of cancer was first proposed by Rudolf Steiner and developed by anthroposophical researchers; it is now probably the best-known anthroposophic therapy. Various forms of the extract are available in Central Europe, where the treatment regimens of up to two-thirds of all oncology patients includes mistletoe. The extracts are generally no longer used to reduce or inhibit tumor growth, but to improve the patients' quality of life and to reduce tumor-induced symptoms and the side-effects of chemotherapy and radiotherapy; a wide array of clinical studies support the efficacy of the treatment regimen for the latter purposes. There are also phytotherapeutic preparations using mistletoe. In the United States, mistletoe "holds interest as a potential anticancer agent because extracts derived from it have been shown to kill cancer cells in vitro" but no forms of the extract have been approved by the FDA for any indications. Mistletoe extracts may not be distributed in or imported into the US except for the purpose of clinical research. Although preclinical (animal) studies suggested a potential role for mistletoe extracts in cancer therapies, no such effects have been convincingly reported. Evidence for the efficacy of mistletoe as an anticancer drug from human studies is weak. double blinded studies have tended not to support this effect. Though numerous cohort studies and case series have reported tumor remission and regression, the cohort and case studies have been criticized as biased due to their small size and lack of double-blinding. The National Cancer Institute (US) suggests that many studies done on human beings have major weaknesses that raise doubts about the reliability of their findings: in some studies without such weaknesses no

The institutes's position on mistletoe is:

"Extracts of mistletoe have been shown to kill cancer cells in the laboratory and to boost the immune system (the complex group of organs and cells that defends the body against infection or disease). For this reason, mistletoe has been classified as a type of biological response modifier (a substance that stimulates the body's response to infection and disease). Extracts of mistletoe have also been shown in the laboratory to prevent the growth of new blood vessels needed for tumors to grow....At this time, there is not enough evidence to recommend the use of mistletoe as a treatment for cancer except in carefully designed clinical trials. These trials will give more information about whether mistletoe can be useful in treating

One review concluded:

"Although there is laboratory evidence of biological activity that may be beneficial to cancer patients, the evidence of clinical benefit from human studies remains weak and inconclusive. Because of the absence of serious side effects and the limited evidence that mistletoe products may offer some therapeutic advantages, further research is warranted."

According to the American Cancer Society, "A number of laboratory experiments suggest mistletoe may have the potential to treat cancer, but these results have not yet been reflected in clinical trials. Available evidence from well-designed clinical trials that have studied mistletoe did not support claims that mistletoe could improve length or quality of life. Review of evidence from carefully conducted controlled human clinical studies indicates that mistletoe does not have any significant anti-tumor activity. Most of the studies that have found positive results from mistletoe extract in the treatment or prevention of cancer are not considered scientifically dependable....Researchers are working to identify the most important components, which are thought to be the lectins (proteins). Laboratory experiments also hint that mistletoe. Approximately 30 types of mistletoe extracts are used clinically; the most commonly used is known as Iscador. Mistletoe extracts are used to treat cancer patients in Holland, and in Great Britain. The treatment has been approved as palliative. In the United States it is approved for clinical trial only.

Though no serious side effects are normally found from mistletoe treatments, in one case a patient allergic to mistletoe. Minor side-effects of injections reported include redness, pain or, in a few cases, subcutaneous inflammation.

791 History - Anthroposophical medicine

History - Anthroposophical medicine

http://en.wikipedia.org/wiki/Anthroposophical_medicine

Ita Wegman, co-founder of the medical approach, before 1900 in Berlin.

The first steps towards an anthroposophical approach to medicine were made before 1920, when homoeopathic physicians and pharmacists began working with Rudolf Steiner, who recommended new medicinal substances as well as specific methods for preparing these. In 1921, Dr Ita Wegman opened the first anthroposophic medical clinic, now known as the Ita Wegman Clinic, in Arlesheim, Switzerland. Wegman was soon joined by a number of other doctors. They began to train

At Wegman's request, Steiner regularly visited the clinic and suggested treatment regimes for particular patients. Between 1921 and 1925, he also gave several series of lectures on medicine. In 1925, Wegman and Steiner wrote the first book on the anthroposophic approach to medicine, *Fundamentals of Therapy*.

The clinic expanded and soon opened a branch in Ascona. Wegman lectured widely, visiting Holland and England particularly frequently, and an increasing number of doctors began to include the anthroposophic approach in their practices. A cancer clinic, the Lukas Clinic, opened in Arlesheim in 1963.

Modern history and prevalence of practice

There are about 28 anthroposophic hospitals, departments of hospitals, rehabilitation centers and sanatoria located in Germany, Switzerland, Sweden, the Netherlands, Great Britain, Italy, the USA and Brazil, as well as over 140 outpatient clinics worldwide. Four of the German and Swiss anthroposophic hospitals are state-sponsored; three are academic teaching hospitals under the aegis of nearby universities. Three European universities (Bern, Hamburg and Witten/Herdecke) have professorships in anthroposophic medicine and other universities offer courses on the field. Anthroposophic medicine is recognized in Germany as a "Special Therapy System", along with homoeopathy and herbal medicine, under the Medicines Act and has its own committee at the Federal Institute for Drugs and Medical Devices. Anthroposophical Medical Associations estimates that there are currently approximately 2,000 Anthroposophical doctors worldwide. Based on the number of prescriptions it has been estimated that anthroposophic medicinal products are

We believe that SASIM incorporates the next wave in medicine. SASIM actively campaigns for the maintenance and protection of a broad scope of practice, so that the principles of Integrative Medicine are not excluded by increasing

<http://www.integrativemedicine.co.za/benefits-of-membership-of-sasim.html>

Benefits of membership

To become part of the increasing energy that is Integrative Medicine in South Africa.

To belong to a body, which promotes the principles of Integrative Medicine.

To belong to a body, which protects the professional interests of its members.

To network with colleagues with similar interests and practices.

To advertise your practice on the SASIM website, for more efficient patient referrals.

To receive a regular newsletter with up to date developments, both political and medical, and advance notices of local and
<http://www.integrativemedicine.co.za/sasim-constitution.html>

SASIM Constitution

1. NAME

The Society is an official interest group of the South African Medical Association (SAMA), "an Association incorporated under Section 21 of the Companies Act, 1973, registered No. 05/00136/08", and its name shall be THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE. hereafter known as SASIM.

2. OBJECTIVES OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE

- 2.1 To promote the science, art, philosophy and practice of integrative medicine.
- 2.2 To define clearly the relationship between promoting health and treating disease.
- 2.3 To establish a philosophical foundation for the practice of integrative medicine.
- 2.4 To promote the study and practice of integrative medicine by establishing an Educational Programme.
- 2.5 To keep a register of the practitioners completing such a study and to apply for registration with the HPCSA.
- 2.6 To protect the professional and legal interests of practitioners registered with the society.
- 2.7 To maintain professional standards for such practitioners.
- 2.8.1 To define and establish relationships amongst practitioners of integrative medicine and their colleagues in hospitals, academic centres of learning, private and government institutions, other medical professionals and interested bodies.
- 2.9 To maintain dialogue with practitioners and other health practitioners who are not members of SAMA.
- 2.10 To manage all matters related and beneficial to the achievement of the above mentioned goals, collectively or

3. MEMBERSHIP OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE

Any person who is registered with the Health Professions Council of South Africa (HPCSA) is eligible for membership, provided he / she has a special interest in the subject of integrative medicine.

3.1 FULL MEMBERSHIP

3.1.1 Any medical practitioner who is registered as such with the HPCSA and who is a full member of SAMA, shall be entitled to apply for full membership of the Society. Membership of SASIM shall at all times consist of at least 85% of full

3.2 AFFILIATED MEMBERSHIP

3.2.1 Any medical practitioner who is registered with the HPCSA but not a member of SAMA shall be entitled to apply for affiliated membership. These members will enjoy all the benefits of the Society but shall not be allowed to participate or vote on matters concerning SAMA or have the right to be elected to any office of SAMA.

3.3 ASSOCIATED MEMBERS

3.3.1 Associated membership may be granted to persons who are not medical practitioners, but who are registered in terms of the Health Professions Act, the Nursing Act, the Veterinary Act or the Pharmacy Act and who are eligible for

3.3.2 Associated members shall not have voting rights in matters affecting SASIM as a whole, and their participation in the activities of SASIM shall be limited to professional and technical matters.

3.3.3 Candidates for associated membership shall be approved by majority vote of the SASIM Executive Committee.

3.4 HONORARY MEMBERSHIP

Honorary Membership, as defined in the Articles of Association of SAMA, may be granted to:

3.4.1 a member of SASIM who has given exceptional service to the organisation

3.4.2 a non-member who, in the opinion of the members of SASIM, has by his\her actions served integrative medicine in

3.4.3 Honorary Members shall be entitled to such privileges as may from time to time be determined by the Executive

3.5 UNATTACHED MEMBERSHIP

Unattached Membership may be granted to foreign medical practitioners registered with or licensed by foreign Medical

3.6 LIFE MEMBERSHIP

Members who have been Full or Unattached Members of SASIM for at least 15 years in the aggregate, shall automatically become Life Members, provided that the Executive Committee of SASIM may, if circumstances justify it, according to its discretion grant Life Membership to a Member who does not meet the said requirement.

3.7 ELECTION

Candidates for all categories of membership shall be elected by majority votes by the Executive Committee, after having been duly proposed and seconded in writing by any two full members.

3.8 TERMINATION OF MEMBERSHIP

Every member shall remain a member until his / her membership is terminated either by his/ her resignation in writing addressed to the Honorary Secretary/Treasurer or by a decision of the Executive Committee, after due process, or by failing to pay the annual subscription fee. The amount of the subscription shall be determined by the executive committee.

3.9 SUSPENSION

The activities of SASIM shall be suspended if at any time its membership shall be less than eleven full members of SAMA.

4. CONTROL OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE

4.1 The general control and direction of the policy and the affairs of SASIM shall be vested in the Executive Committee of

4.2 In exercising control over SASIM, the Executive Committee shall at all times abide by the Articles of Association of

4.3 The SASIM Executive Committee shall consist of a Chairperson, a Vice-chairperson, and Honorary

4.4 The Executive Committee shall hold office for a period of two years. The election of the members of the Executive Committee shall be by popular vote at the annual general meeting of SASIM.

4.5 The Honorary Secretary / Treasurer may call for postal nominations for the new Executive Committee. Notice of the election and a request for nominations will be despatched at least 30 days before the Annual General Meeting. Each nomination must be referred to the Honorary Secretary/Treasurer and must be signed by the proposer, the seconder and the candidate. The closing time for the nominations will be 48 hours before the first day of the Annual General Meeting.

4.6 A list of the office-bearers, together with a complete list of the members of SASIM, shall be furnished annually to the Chief Executive of SAMA within thirty days of the election of such office-bearers.

4.7 The Honorary Secretary/Treasurer shall keep records of all the meetings of SASIM and of its Executive Committee and shall conduct all correspondence concerning the affairs of SASIM. He/she shall receive all monies due to SASIM and shall make all disbursements authorized by the Executive Committee.

5. MEETINGS OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE

5.1 The Annual General Meeting of SASIM shall be held on a date determined by the Executive Committee.

5.2 Extraordinary General Meetings of SASIM may be held from time to time, and shall be called by the Executive Committee or on the written request of eleven (11) full members of SASIM.

5.3 Voting by proxy, according to the Articles of SAMA, shall be allowed at all general meetings.

6. ACTION OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE

6.1 SASIM may take such action as may be deemed necessary in all matters affecting the legitimate interests of its members, provided that SAMA as such be not involved in or pledged to any actions, and that any action contemplated by

6.2 Should SASIM refer a matter affecting the interests of its members to the National Council or the Board of Directors of SAMA for action, it shall take no further independent action unless requested to do so by the National Council or the

7. ORGANISATION

7.1 It shall be competent for SASIM to allow the formation of sub-groups of the Society within the framework of one or more of the branches or divisions of SAMA or in such other manner as may be desirable. Such sub-groups may be allowed powers or independent action in local matters provided that such action is not in conflict with the general policy and the

7.2 Such sub-groups shall elect a Chairperson, an Honorary Secretary/Treasurer, and an Executive Committee consisting of 3 members annually at the annual general meeting of the sub-group which shall be held 1 (one) month prior to the

7.3 Reports of local action taken shall be submitted by the Honorary Secretary/Treasurer of the sub-group to the Honorary Secretary/Treasurer of SASIM.

7.4 Each sub-group shall have a minimum membership of four full members.

8. SUBSCRIPTIONS OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE.

An annual subscription shall be payable by members of SASIM, with exception of Life Members, to procure funds for the execution of the work of SASIM. The Executive Committee shall determine the subscription fee.

9. ANNUAL REPORTS OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE.

The Honorary Secretary/Treasurer shall submit an Annual Report and an Annual Financial Statement respectively at the Annual General Meeting of SASIM. A copy of each shall thereafter be sent to the Chief Executive of SAMA within thirty

10. AMENDMENTS TO THE CONSTITUTION OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE

Amendments to the Constitution shall be effected only if passed by a two-thirds majority of those paid up voting members in person or by proxy at an Annual General Meeting or extraordinary meeting of SASIM. The National Council or the Board of Directors of SAMA shall approve any amendment to the constitution of SASIM before becoming operative.

11. DISSOLUTION OF THE SOUTH AFRICAN SOCIETY OF INTEGRATIVE MEDICINE

In the event of the dissolution of SASIM, any remaining assets, after all debts had been settled and all obligations discharged, shall not be paid or given to, or divided among the members of SASIM, but shall be given or transferred to a specialty or special interest group of SAMA engaged in activities similar to those for which SASIM was established. Members attending the final general meeting of SASIM or of its Executive Committee will designate such group. The

289

Empty page

290

What is Integrative Medicine

What is Integrative Medicine

<http://www.integrativemedicine.co.za/what-is-integrative-medicine.html>

DEFINITIONS

"Integrative Medicine recognises the holistic and unique nature of human-beings, which encompasses physio-energetic information systems. It investigates the multi-factoral causes of dis-ease. In this approach the practitioner and the sick individual form a team working towards an integrated protocol of management best suited for that person. The priority is to support health using the least invasive and most natural approach; this does not exclude symptomatic treatment of disease, where appropriate."

SASIM mission statement, April 2006

"Integrated or Integrative Medicine is practising medicine in a way that selectively incorporates elements of Complementary and Alternative medicine into comprehensive treatment plans alongside solidly orthodox methods of British Medical Journal 2001;322:119-120

Integrative Medicine:

Is based on a partnership of patient and practitioner, within which conventional and alternative modalities may be used to stimulate the body's healing response;

Shifts the orientation of medicine from one of disease to one of healing;

Engages the mind, spirit, and community as well as the body;

Neither rejects conventional medicine nor uncritically accepts alternative practices;

Is committed to good science that is driven by inquiry and open to new paradigms;

Is grounded in the philosophy that prevention is a primary responsibility of medicine and that healing is possible even

Works to activate innate, natural healing mechanisms

Uses natural, less invasive interventions before costly, invasive ones whenever possible; and

Asks that practitioners seek to model health and healing and commit to the process of self-exploration.

As the philosophy develops and become more sophisticated a newer medicine will emerge which will naturally integrate many aspects of traditional medicine, newer developments in physics and quantum theory and recent advances in

COMPARISON BETWEEN ARO-HEALING REVISED COMPLEMENTARY THERAPY (ARC) AND

New terminology of Aro-healing Revised Complementary Therapy (ARC) includes the following:

- 1 Art of medicine
- 2 Systems
- 3 Webs
- 4 Non-linear dynamics
- 5 Informational systems
- 6 Patterns
- 7 Probability dynamics
- 8 Relationships
- 9 Complexity
- 10 Meaning and medicine
- 11 Order and chaos
- 12 Intuition and experience

THE 3 PILLARS OF ARO-HEALING REVISED COMPLEMENTARY THERAPY (ARC):

Aro-healing Revised Complementary Therapy (ARC) is not Alternative Medicine or Complementary Medicine. It is really an expansion of the limited conventional medicine as practised today. Conventional medicine has become focused on 'the disease' to the exclusion of the person and the dysfunction within the system. This would be equivalent to fixing the part that is broken in a motor car without doing a tune-up or speaking to the driver.

First pillar:

Lifestyle Management

Deficiencies in the following aspects of lifestyle comprise the underlying causes of ill-health:

- 1 Healthy food choices
- 2 Appropriate and sufficient exercise
- 3 Appropriate weight-to-height ratio [*Body Mass Index*]
- 4 Ability to process and remove toxins from the body
- 5 Stress management
- 6 Psycho-spiritual balance

Second pillar:

Management of the Underlying Dysfunctions

The dysfunction is not quite the disease yet. Dysfunction precedes the disease just as the motor car getting out of tune. The dysfunction takes on many forms such as insulin resistance, nutrient deficiencies, under- or over-functioning of glands, sympathetic or parasympathetic imbalance, stomach acid too high or too low, immune system imbalance, hormonal dysregulation, pH abnormalities, metabolic disturbances of many kinds, etc.

Integrative Medical doctors will detect and diagnose the dysfunctions and will correct these problems before they manifest as breakdown/disease. Natural products that work well with [rather than against] the body's own systems, are usually employed to correct the imbalances. *Aro-healing Revised Complementary Therapy (ARC) therapists will*

Third pillar:

Treatment of Disease

This is often not necessary, as correcting the body's deficiencies and dysfunctions, allows the body's own innate healing processes to deal with the 'disease'. Herbal or homoeopathic medicines may be needed at this point to complete the healing. Integrative Medical doctors are also able to use drugs and surgery, to relieve symptoms when appropriate, *but Aro-healing Revised Complementary Therapy (ARC) therapists* When these are required the body still needs the Information provided by Dr B Brom www.creatinghealth.co.za

Empty page

Anthroposophically Integrated Medicine

Anthroposophically Integrated Medicine

<http://www.integrativemedicine.co.za/anthroposophically-integrated-medicine.html>

Anthroposophically Integrated Medicine is a holistic system of medicine developed by Rudolf Steiner as an extension of conventional bio-medicine. It evolved out of Anthroposophy - a system of knowledge of the whole human being - formulated by Rudolf Steiner in the first quarter of the twentieth century. It is founded on the understanding of the human being as a living Body, Soul and Spirit, and on a spiritual-scientific description of these three aspects in health and illness. Health is seen in the healthy interaction of these members: ill-health in the disturbance of their equilibrium: and healing is

Anthroposophically Integrated Medicine describes the correspondences and specific relationships that exist between the human being, the starry universe and the surrounding world of nature. Understanding the nature of the specific substances and forces within the mineral, plant and animal kingdoms enables these to be harnessed pharmaceutically and used rationally and individually in therapy. Understanding the nature of Soul and Spirit and their connection to the Body provides for the exploration of the psycho-spiritual dimensions in illness and healing. Illness can thereby be treated at a

Transformation and self-empowerment is actively supported as part of the healing process. Anthroposophically Integrated Medicine forms a broad medical framework into which other therapeutic systems such as homoeopathy, naturopathy and

Other therapies used in this integrated medical system to assist the healing process include therapies evolved out of

psychophonetic counseling

art therapy

therapeutic eurythmy

nutritional therapy

rhythmical massage

hydrotherapy

as well as other therapies derived from health disciplines such as:

Homoeopathy

naturopathy

phytotherapy [herbal medicine]

acupuncture

Chiropractic

craniosacral therapy

aromatherapy and others.

Isador mistletoe therapy is a cancer therapy developed out of anthroposophically integrated medicine.

Information provided by Dr R Goldberg www.drraoulgoldberg.com and www.syringahealth.co.za

Empty page

Empty page

What is SASIM

What is SASIM

<http://www.integrativemedicine.co.za/what-is-sasim.html>

The South African Society of Integrated Medicine [SASIM] is an association of medical practitioners in South Africa, who practise, or have an interest in Integrative Medicine.

OBJECTIVES & GOALS OF SASIM

To promote the science, art, philosophy and practice of Integrative Medicine.

To define clearly the relationship between promoting health and treating disease.

To protect the professional and legal interests of practitioners registered with the society.

To maintain professional standards for such practitioners.

To define and establish relationships amongst practitioners of Integrative Medicine and their colleagues in hospitals, academic centres of learning, private and government institutions, other medical professionals and interested bodies.

To maintain dialogue with practitioners and other health practitioners who are not members of SASIM.

To establish a philosophical foundation for the practice of Integrative Medicine.

To promote the study and practice of Integrative Medicine by establishing an Educational Programme. This has been achieved at the University of Stellenbosch since 2010.

To keep a register of the practitioners completing such a study and to apply for registration with the HPCSA.

To manage all matters related and beneficial to the achievement of the above mentioned goals, collectively or partially.

SASIM has different goals to its predecessor SACMA [SA Complementary Medical Association], whose members were subjected to dual registration with the Allied Health Professions Council [AHPCSA]. SASIM is concerned that increasing definition of scopes of practice may leave its members in a "no man's land".

Conventional medicine must change as the demands by the public for Integrated Medicine increase, and the grey areas between conventional medicine and complementary medicine become blurred. Medical doctors are responding to the demands of patients by including integrative approaches in practice.

296

Empty page

297

Empty page

298

Allopathy

Allopathy

299

What is Allopathy

What is Allopathy

<http://www.wisegeek.com/what-is-allopathy.htm>

The term "allopathy" is used by some alternative medical practitioners to describe people who practice conventional or "Western" medicine. Because this word was essentially developed as an epithet to insult traditional medical practitioners, it is rare to see regular doctors calling themselves allopaths. Some doctors also reject the use of the term because they feel Samuel Hahemann, the founder of homoeopathy, coined the term "allopathy." It is derived from Greek roots, and roughly translates as "opposite suffering." He used the word to describe the often harsh and sometimes pointless treatments employed by conventional medical practitioners in the 19th century. Many practitioners relied on a theory of "humors" which dated back to the Ancient Greeks, and they believed that medical conditions were characterized by an excess or deficit of a particular humor. Blood letting, cupping, and a variety of other techniques were used to restore the balance of Hahemann also wanted to clearly distinguish homoeopathy from the more traditional practice of medicine. He argued that allopathy involved treating the symptoms of the disease, rather than the underlying cause of the condition. The goal of allopathic treatment was to produce effects which would counter the symptoms, but not necessarily to get to the root of the problem. Homoeopathy, on the other hand, was treatment tailored to the individual patient, with a focus on the whole. While the practice of conventional medicine might have once deserved the label of allopathy, many physicians believe that this is not the case any more. Osteopathic doctors, for example, practice a whole-body approach to medicine, and their credentials are almost identical to those of regular medical doctors. Many doctors also recognize the importance of looking at the whole body when assessing patient health and needs, and modern medical treatment is focused on general wellness.

The pejorative implications of this term are sometimes lost on the people who use it. Some alternative practitioners refer to allopathy in scathing tones when talking with clients, to emphasize the value of the treatments they offer. Other practitioners of alternative medicine avoid the term, however, recognizing that there are many approaches to medicine, and some even work hand in hand with conventional practitioners. A chiropractor, for example, might work with a spine

Chest Pain After ER Discharge Should Be Checked Out

Rob Williams on Changing Your Perception with Psych-K

Alternative Options to Soothe a Sore Throat

What Is the Difference Between Allopathic and Osteopathic Medicine?

What Does an Allopathic Physician Do?

How Do I Become an Allopathic Physician?

What Are the Uses of Sepia in Homoeopathy?

What Are the Uses of Lycopodium in Homoeopathy?

What Is Allopathic Medicine?

What Is Reconstructive Therapy?

There are so many variables that go in to something like this that I have a hard time making a blanket statement saying that any doctor who practices conventional medicine is only there to treat the symptoms.

I have had several wonderful medical doctors who have treated myself and many family members with great results. These were very qualified physicians who did care about the whole person and did their best to determine what the causes of the

I also know several very good doctors who practice alternative medicine. There have been many people who have achieved great results with homoeopathy that they were unable to get with conventional medicine.

I think it is important for anyone to do their research on the physicians they are seeing. There are many options available and if one doctor is not meeting your needs, it is not hard to find one that will work with you.

Sometimes there can be quite a bit of negative feelings between those doctors who practice conventional medicine and those who use alternative medicine. I think it takes some work and research to find the doctors who you feel are best

Every month I go to an osteopathic doctor for manipulation treatments that are similar to what a chiropractor would do. She is a licensed doctor of osteopathy and can write prescriptions if needed. She has really helped me with my headaches

She is also a great resource for me as she has connections with many physicians in our city. Some of them are medical doctors and some of them are osteopathic doctors. I feel very comfortable with the approach she takes towards treating her patients. She is very thorough and really tries to focus on what is causing the underlying problem.

When I think of all the advances that have been made in modern medicine I am amazed. We have so many treatment options that were not available several years ago.

I am thankful for conventional Western medicine as I think it has been very helpful for many people. I also like to approach things from a natural perspective and have been interested in homoeopathy.

There have been some good strides made towards the acceptance of alternative medicine options, but most insurance plans will not cover their services.

I see nothing wrong with using a balance of both and still focusing on the treatment of the patient as a whole, and not just

Maybe your doctor just wasn't very good. I've definitely noticed a shift in the last few years in my regular doctor, and I

I feel like my doctor really takes the time to ask about what's going on with me and actually get to the cause of the problem. This is the exact strategy recommended by homoeopathic practitioners!

Maybe it varies by doctor, but I'm more than pleased with my "allopathic" doctor.

I think this term still describes conventional medicine just fine. As much as I hear about wellness and prevention, every time I visit the doctor it's always the same. They spend about five minutes with me, treat whatever symptom I have, and

I think this is a really poor approach to medicine. I've definitely had serious problems overlooked before by doctors that

When I was younger I had a really bad fungal infection in my stomach and it took a really long time for any doctor to diagnose me. The first few doctors visits the doctor spent a few minutes with me, prescribed antacids, and that was it.

In the end I suffered two months before I got a proper diagnosis! I really think if the doctor had taken her time and focused on the whole picture, I would have been diagnosed much sooner.

300

Empty page

301

empty

200

201

202

203

what qualifies as a whole food," says Tara Gidus,
other terms. Whole foods might be organic, or

all of the vitamins, minerals, and other nutrients
It's the difference between an apple and apple

where in the country. Most dietitians feel that
protect you from disease.

community nutrition specialist in the department of

204

riguation).

have its structure solved by X-ray crystallography.
ecule (red).

. Proteins perform a vast array of functions within
cles from one location to another. Proteins differ
d which usually results in folding of the protein

mino groups of adjacent amino acid residues. The
the genetic code specifies 20 standard amino
rtly after or even during synthesis, the residues in
, folding, stability, activity, and ultimately, the
factors. Proteins can also work together to achieve

nd participate in

sm. Proteins also have structural or mechanical
maintains cell shape. Other proteins are important
imals cannot synthesize all the amino acids they
in into free amino acids that are then used in

tion, electrophoresis, and chromatography; the
study protein structure and function include

acent amino acid

All proteinogenic amino acids possess common features. They are bonded to a central carbon atom (the alpha carbon). Only proline differs from the others in that it is a secondary amine. The side chains of the standard amino acids are attached to the alpha carbon. The effect of all of the amino acid side chains in a polypeptide chain are linked by peptide bonds. Once linked, the amino acids are known as the main chain or protein backbone.

so that the alpha carbons are roughly coplanar. The polypeptide with a free carboxyl group is known as the C-terminus. The terms protein, polypeptide, and peptide are a little ambiguous. Polypeptide is generally reserved for long chains, whereas peptide is generally reserved for short chains.

and usually lies near 20–30 residues. Polypeptide can be defined as a chain of amino acids.

sequence that is specified by the nucleotide sequence. Each nucleotide combination designates an amino acid, and the number of possible codons is 64; hence, there is a redundancy. The mRNA is first transcribed into pre-messenger RNA (pre-mRNA) and then processed (spliced) using various forms of Post-transcriptional modification. In prokaryotes, the mRNA may either be used as soon as it is synthesized or it may be stored in the cell nucleus and then translocate it across the nuclear envelope. In eukaryotes, the mRNA can reach up to 20 kb in length.

some and is read three nucleotides at a time by the ribosome. The ribosome is moving along the mRNA depending on the codon it recognizes. The enzyme

ribosome.

which is normally reported in units of daltons
is long and 53 kDa in mass. The largest known
of almost 27,000 amino acids.

o synthesis techniques such as chemical ligation to
chains, such as attachment of fluorescent probes to
mercial applications. Chemical synthesis is
ative tertiary structure. Most chemical synthesis

the conformation. Although many proteins can fold
fold into their native states. Biochemists often refer

alpha helix, beta sheet and turns. Because

another. Tertiary structure is generally stabilized by
disulfide bonds, and even posttranslational
controls the basic function of the protein.

s in this context, which function as a single protein

structures while they perform their functions. In the
, and transitions between them are called
or the physical region of the protein that
collision with other molecules.

antibody), haemoglobin, insulin (a hormone),

, fibrous proteins, and membrane proteins. Almost
component of connective tissue, or keratin, the
molecules to pass through the cell membrane.

their own dehydration, are called dehydrons.

to determine how the protein performs its function. Common
methods produce information at atomic resolution.
The number of conformations is estimated, and the final possible conformations
are determined by a statistical method for measuring the overall protein
structure. A unique method for determining internal beta sheet/ helical
content is available for large protein complexes, including assembled viruses;
three-dimensional crystals of membrane proteins. Solved
structures of thousands of proteins can be obtained in the

that can be easily subjected to the conditions
relatively easy to crystallize in preparation for X-
ray crystallography. Structural genomics initiatives have attempted to
use high-throughput screening methods to provide a means of

With the exception of certain types of RNA, most
proteomes are known from the Escherichia coli cell, whereas other
proteomes from other bacterial cell or cell type is known as its proteome.

of the two of its substrates, ATP and glucose.

specifically and tightly. The region of the protein
on its surface. This binding ability is mediated by the
amino acids' side chains. Protein binding can be
extremely strong (dissociation constant $<10^{-15}$ M) but
a single methyl group on a binding partner can
be discriminated against the very similar side chain

of the same molecule, they can oligomerize to form
dimers. Protein-protein interactions also regulate
many biological processes. Protein-protein interactions
control many closely related reactions with a common
mechanism. Induction of conformational changes in proteins allows
them to bind substrates and products. These interactions
often depend heavily on the availability of different
amino acids. The interaction between specific proteins is a key to understand

enzymes are specific and accelerate only one or a few chemical
reactions, such as DNA replication, DNA repair, and
protein modification. About 4,000 reactions are known
to be catalyzed by enzymes. Enzymes increase the rate of a reaction
by increasing the rate over the uncatalyzed reaction in

amino acids, it is usually only a small fraction of the
amino acids that are directly involved in catalysis. The region of the

enzymes.

cellular proteins that transmit a signal from the
The main function is to bind a signaling molecule and
remain within the cell, which may have enzymatic

ances in the body, and target them for destruction.
s plasma cells. Whereas enzymes are limited in
An antibody's binding affinity to its target is

multicellular organism. These proteins must have a
at low concentrations in the target tissues. The
tissues in all vertebrates and has close homologs in
usually play a role in biological recognition

small molecules and ions. The membrane alone has a
that allow such molecules to enter and exit the cell.
often discriminate for only one of the two ions.

is proteins; for example, collagen and elastin are
; nails, feathers, hooves, and some animal shells.
mers, but polymerize to form long, stiff fibers that

generating mechanical forces. These proteins are
usually. They also generate the forces exerted by

in vitro and in vivo. In vitro studies of purified proteins studies explore the chemical mechanism of action on proteins' activities within cells or even within

with cell lysis, in which a cell's membrane is being ultra-centrifugation, which fractionates the cell and nucleic acids. Precipitation by a method known as immunoprecipitation or proteins of interest based on properties such as size, charge, or hydrophobicity. Purification by gel electrophoresis if the desired protein's pI is known, or by enzyme assays if the protein has enzymatic activity.

proteins. To simplify this process, genetic engineering techniques have been developed. Here, a "tag" consisting of a specific amino acid sequence is fused to the protein of interest. The tagged protein is then passed over a chromatography column where the tag binds to a specific resin, while the rest of the protein passes unimpeded. A number of different tags

are used for this purpose. Many intracellular proteins are synthesized in the cytoplasm and then move to specific organelles or cellular structures. The use of a tag to identify a protein or chimera consisting of the natural protein of interest and a tag allows for the protein to be easily and efficiently visualized using microscopy,

such as the ER, the Golgi, lysosomes or vacuoles, and other organelles. When combined with known markers, it becomes much easier to perform fluorescence colocalization and demonstration of location.

of interest that are conjugated to enzymes yielding
another applicable technique is cofractionation in
a compartment of known density and the protein of

of interest, along with classical
an antibody to the protein of interest that is
as well as the protein of interest.

ence and hence its structure, cellular localization,
modified tRNAs, and may allow the rational design

large-scale data sets defines the field of proteomics,
which allows the separation of a large number of
of (often after in-gel digestion), protein micro-arrays,
which allows the systematic exploration of
a systematic attempt to determine the structures of

researchers to efficiently identify homologous
manipulations such as restriction enzyme maps,
can be constructed and evolutionary hypotheses
the field of bioinformatics seeks to assemble,
finding and cladistics.

feasible models for proteins whose structures have
lies on the existence of a "template" structure with
structures to model most of those that remain.
It has been suggested that sequence alignment is the
structure prediction methods have served to inform the
central problem is the prediction of intermolecular

molecular dynamics and Monte Carlo, which
the folding of small alpha-helical protein domains
that combine standard molecular dynamics with

obtain some of the amino acids from the diet. The
realize certain amino acids are not present in animals
If amino acids are present in the environment,
synthetic pathways.

break down into amino acids through digestion, which
digested amino acids are used for protein
protein as a fuel is particularly important under
amino acids are also an important dietary source of

proteins, distinguished by the molecules' ability to
from egg whites, blood serum albumin, fibrin, and

by Berzelius in 1838. Mulder carried out elemental analysis of urea. [64] He came to the erroneous conclusion that urea was proposed by Mulder's associate Berzelius or "standing in front". Mulder went on to determine the molecular weight of urea as 131 Da.

maintaining the structure of the body, because it was not known until 1926, when James B. Sumner showed that urease was a protein.

In the early 1950s, studies focused on proteins that could be used as a source of amino acids. In the 1950s, the Armour Hot Dog Company discovered that pepsin was a major target for biochemical research.

An idea first put forth by William Astbury in 1933. The first understanding of protein folding and structure was proposed by Linus Pauling and Robert Corey in 1951.

The discovery of insulin, thus conclusively demonstrating that insulin is a protein. Pauling received the Nobel Prize for this achievement in 1958.

Pauling, in 1958. The first atomic-resolution structure of a protein was determined in 1962, earning Pauling the Nobel Prize in Chemistry for these structures of proteins. In more recent times, X-ray crystallography and cryo-EM are two methods approaching atomic resolution.

muscles? Or is it the last high-protein diet craze of us eat more protein than we need. Protein is in fact essential for life.

is when we eat more protein than we need.

replaced. The protein in the foods we eat is digested

who is healthy and eating a varied diet to not get

join together to make all types of protein. Some of
le these.

high quality proteins. Animal-based foods; for

two or more incomplete protein sources that together

found in greater amounts in dry beans. Similarly, dry
foods can provide adequate amounts of all the

amino acids together. Now studies show that your body can

amino acids come from protein. Below are the

other foods that add smaller amounts of protein to

well as other nutrients.

alized plan just for you.

ou eat more protein than you need, your overall

rotein (LDL) cholesterol, a risk factor for heart

nt in kidney function.

As an example, if you refer to MyPlate Daily Food
oup. Some pre-cut slices of meat and poultry, such

our diet.

their protein needs. With some planning, a

ary Reference Intakes for Energy, Carbohydrate,

bout food plans. There are five groups consisting building blocks for a healthy diet using a familiar

Examples

The vegetables you eat may be fresh, frozen, canned or dried and may be eaten whole, cut-up, or mashed. You should eat a variety of dark green, red and orange vegetables, as well as beans and peas (which are also considered part of the protein group). Examples include broccoli, carrots, collard greens, split peas, green beans, black-eyed peas, kale, lima beans, potatoes, spinach, squash, sweet potatoes, tomatoes and kidney beans. Any vegetable or 100% vegetable juice counts in this group.

The fruits you eat may be fresh, canned, frozen or dried and may be eaten whole, cut-up, or pureed. Examples include apples, apricots, bananas, dates, grapes, oranges, grapefruit, mangoes, melons, peaches, pineapples, raisins, strawberries, tangerines, and 100% fruit juice.

There are two types of grains – whole grains and refined grains. At least half of the grains you eat should be whole grains, such as whole-wheat bread, whole-grain cereals and crackers, oatmeal, bulgur, and brown rice. Refined grains include white bread, white rice, enriched pasta, flour tortillas, and most noodles.

Most of your choices should be fat-free or low-fat milk and milk products, but all milks and calcium-containing milk products count in this category. Examples include milk, cheeses, and yoghurt as well as lactose-free and lactose reduced products and soy beverages. Foods that are made from milk but have little or no calcium are not included, such as butter, cream, sour cream, and cream cheese.

Choose a variety of lean meats and poultry, seafood, beans and peas, eggs, processed soy products, unsalted nuts, and seeds. Make sure to eat at least 8 ounces of seafood each week.

te good health. A healthy eating plan can also help

ount of foods to meet your calorie needs.

living cell. In the form of skin, hair, callus, cartilage,
1. In the form of enzymes, hormones, antibodies,
lipoproteins, they effect the transport of oxygen

sly ill if they do not eat enough suitable protein, the
e, and we warm and protect our bodies with

um, is regarded as the most powerful poison
e toxins produced by tetanus and diphtheria micro-
s, and ricin, the toxic protein found in castor beans.

a rigid solid, and the enzyme pepsin water soluble
compared with carbohydrates and lipids, the
'5 to 85% carbon. Carbohydrates are roughly 50%
are composed of 15 to 25% nitrogen and about an
aving molecular weights less than 10,000.

tified as α -aminocarboxylic acids. More
e amino acids having green colored names are
ents is protein, but it is important to recognize that
but the proportion of essential amino acids in
tructures of proteins and peptides, each amino acid

h the exception of glycine, they are all chiral. The
right, and this was defined as the L-configuration
ther, and in proline R is a three-carbon chain that
chiral amino acids, with the exception of cysteine,

have hydroxyl functional groups, and the first two
ctions in their side-chains; histidine and tryptophan
nd glutamic acid, and the last two compounds in

g of mono-functional analogs. The formulas are in
; in the table are roughly the same size, and all
three compounds are soluble in organic solvents
mine has a pKa of 10. The simple amino acid
on times weaker as an acid than ordinary carboxylic

o group. The resulting ammonium carboxylate

strength of a 1°-ammonium ion. To the right above
with the display. Examples of a few specific amino
carboxyl group is more basic than the alpha-
boxylate, resulting in a coiled conformation.

molecular species present in an aqueous solution
aqueous solutions at different pH's, we make use
function (HA). When the pH of the solution equals

amine functions are protonated, so the alanine
ate base, so the alanine molecule has a net
c point (pI), the negatively and positively charged
g from a fully protonated state, the pKa's of the
titration curves show the neutralization of these

arlottesville. (Click this name)

es in an electric field, using the technique of
a cross-linked gelatin-like substance. A small
applied at the ends of the strip, as shown in the
they are inserted, unless acted upon by the
ferred medium. To see the result of this experiment,
rless.

field. Arginine is a basic amino acid. Both base
; positive charge, and they move toward the
es move toward the anode in the electric field.

at the electrophoresis of these compounds at a pH
oring differences in molecular size and shape, the
le positive charge.

oxyl group ($pK_{a1} = 1.8$ to 2.4), and the other for
asidity of 2° -amines.

he right. A third pK_a , representing the acidity or
1 very different from those noted above for the
rations of arginine and aspartic acid shown below.
hese species are written to the right of the titration
proton from arginine reflects the exceptionally

cules on average have no net charge. In other
; alanine, the pI is an average of the pK_a 's of the
mentally determined value. If additional acidic or
determining similarity we define two classes of
are positively charged in their protonated state
rboxyl function ($pK_a = 3.9$), so $pI = (2.1 + 3.9)/2$
unction ($pK_a = 9.0$), so the calculated $pI = (12.5 +$

ne genetic code. Many other naturally occurring
e, are simply functionalized derivatives of a
ne and homocysteine are higher homologs of their
ic acid,
nzyme A is a pyrophosphorylated derivative of a

ide ornithine, which is a component of the

opriate value. Esterification of the carboxylic acid
nctions are converted to their ammonium salts and
uct is a stable ammonium salt. The amino ester

d as an acid catalyst. Once the carboxyl function is

so that free amine nucleophiles are present in the
acylation reactions. The following two reactions
ilicity of nitrogen in acylation reactions, since
n the Hinsberg test. The second reaction employs
ith which the t-butylcarbonyl (t-BOC) group can be
zwitterionic character, and may be converted to a

a unique reaction with the triketohydrindene
to derivative, which provides as a useful color test
acids in paper chromatography. As shown in the
set of paper (the baseline). The bottom edge of the
ample spots, the compounds in each sample are
r. Some compounds move rapidly up the paper,
solvent front from the baseline is defined as the
e compounds have respective Rf values of 0.54,

and the heterocyclic rings in tryptophan and
Iso oxidized by iodine. Quantitative measurement
d arginine are onium cations at pH less than 8, and

to acid under the name cystine. Disulfide bonds of
er by two disulfide links. Our hair consists of a
ent waving", disulfide bonds are first broken and
sulfoxide.

preparing alpha-aminocarboxylic acids. The
roach gave mediocre results when used to prepare
nitrogen atom in the product. Nevertheless, more

and a single clean substitution reaction of 1°- and
omomalic esters, as shown in the upper equation
by the two ester groups, this intermediate may be
ollowed by acidification and thermal

rsor), cyanide (the carboxyl precursor), and an
med in this way can then be hydrolyzed to an

acid products. If pure L or D enantiomers are
It formation with a pure chiral acid or base. This is
cles, from optical rotation signs, shown in

st converted to a benzamide derivative to remove
ly pure amine, such as brucine (a relative of
nce the amino acid moiety is racemic and the base
green shaded box). Diastereomers may be separated
urther treatment, in this illustration it is the (+):(-)
covered resolving agent (the optically active

mple, an aminoacylase enzyme from pig kidneys
amides shown in the green shaded box above is
ereas the D-enantiomer will remain largely
iomers, based on very different rates of reaction, is

206

with a side-chain specific to each amino acid. The

group.

What are found within proteins convey a vast array of functions determined by the sequence of the bases in the gene. Proteins not only catalyze all (or most) of the chemical reactions, they also encode the necessary information to determine how a protein is synthesized and stability has been a critically important area of research. Much progress is being made every day.

The primary structure and properties of a protein are a composite of the properties of the amino acids.

Of the 10 essential amino acids, those that we cannot synthesize are called essential. Unlike fat and starch, the human body does not store amino acids.

Proline, serine and tyrosine. Tyrosine is produced from phenylalanine. Arginine (required for the young, but not for adults) is produced from glutamine. Plants, of course, must synthesize all of the amino acids.

Proteins are the building blocks of biological molecules. Otherwise, it is difficult to understand the structure and function of a protein.

the "organic amides" ($n = 1$, $E = C$, $x = 1$), but many sulfonamides ($E = S$, $x = 2$). The term amide refers

to a class of these "anionic amides," see Metal

Amide is generally represented as $RC(O)NH_2$.

Amides are also commonly derived from secondary hydroxyl group has been replaced by an amine or

the carbonyl carbon. Consequently the nitrogen

is occupied by delocalized electrons. One

from acetic acid is named acetamide

It is derived from a primary or secondary amine, the N,N-dimethylacetamide (CH_3CONMe_2 , where $Me =$ methyl). Secondary or tertiary amides. Functional groups

Amide / æmad/[contradictory] for the anion. Others

The acid of an amide has a pKa around -0.5.
Due to the electron-withdrawing nature of the carbonyl group, amides are weaker bases than carboxylic acids, esters, aldehydes, and ketones. Structure A for 62% and by B for 28%. Resonance

due to the presence of a C=O dipole and, to a lesser extent a N-C dipole, amides function as H-bond donors as well. Thus, they are more soluble in water and the N-H hydrogen atoms can form H-bonds with hydrocarbons.

Exercise 15. Conversely, under extremely acidic

conditions, amides are more soluble in water than carboxylic acids since these compounds can both form H-bonds with water and are more soluble in water.

Amides are a common non-basic functional group. They are characterized by a strong, intense ν CO band near 1650 cm⁻¹ in IR. The presence of a hydrogen bond between directly adjacent atoms characteristically defines a secondary amide.

Amides are rigid, and resist hydrolysis. Nylons are polyamides. Amide linkages constitute a major component of proteins. Low molecular weight amides, such as urea, are used in fertilizers. Plant N-alkylamides have a wide range of

properties, including a favorable equilibrium to the right:

Amide formation reaction, which involves conversion of the acid

romatic amide.

ruthenium-based catalyst was reported to be

lehydrogenation of the alcohol to the aldehyde
miaminal to the imine is not observed.

l forming a tetrahedral intermediate. Thiols,
e under physiological conditions than esters.
hot alkali, as well as in strong acidic conditions.
nonia. Amides are also versatile precursors to

l and water and are absorbed by plants. Animals
develop normally.

rb the amount of calcium (a mineral) it needs to
lies inability to absorb the mineral calcium.) The
e, iron, selenium, and zinc are called trace
iced diet with a variety of foods. You can usually

erals, as well as herbs, botanicals and other

ealth.

chronic diseases. Eating fruits and vegetables of
: chart of Nutrition Information for Fruits and

calorie needs for your age, sex, and activity level.

vegetables and their role in your weight management
snack ideas that are 100 calories or less. With

fruit and vegetable consumption recommendations,

fruit and vegetable (F&V) consumption and policy and
the policy and environmental indicators measure a
communities. The report can be used to inform

provides potential actions that government and
along with resources for taking action.

better for you than others. Trans fats, saturated fats

assumption as low as possible.

oseMyPlate.gov has personalized plans that will

210

ing.

ded sugars.

add extra calories but not many nutrients to your

r and added sugars).

hydrates that take longer to break down into

ch carbohydrate choices from the vegetable, fruit,

also more likely to get other nutrients that you might

ong the best sources of dietary fibre, but currently
n of beans peas other vegetable, fruits and whole

nds more often. Over time, you'll gradually be

guide is to make at least ½ of your grain choices be

bananas may come to your mind first, you can add
tion of your grocery store.

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

d (sometimes called the kernel). These parts of the

in must still have about the same proportions of

called a "refined" grain.

ing and added back. These are called enriched

d (sometimes called the kernel). These parts of the

in must still have about the same proportions of

called a "refined" grain.

ing and added back. These are called enriched

d (sometimes called the kernel). These parts of the

in must still have about the same proportions of

called a "refined" grain.

ing and added back. These are called enriched

ving microwave popcorn, look for a lower-fat

has a tender and chewy texture.

nd to other seasonings.

ous.

bohydrates also include sugars added during food
turally-occurring sugars.

of that sugar is in the food.

arly as far as kids are concerned. Be sure to also

211

212

213

214

215

medical practitioners and medicines. However that
solutions include homoeopathic treatment and

esses may be avoided or corrected. For instance

ility of body healing.

cold virus or the flu. These alternative healing

pointment costs. It's also possible to experience
side effects.

techniques offer a rapid recovery time as well. In
ing therapy and be on the road to recovery.

t always have to get accomplished with a certain
zation of yoga or meditation to remain healthy. If

t balance.

so long as a proper balance is achieved.

ves, there is character. The foods you ate were
ease.

lical practitioners in the United States.

medical practitioners and medicines. However that
olutions include homoeopathic treatment and

esses may be avoided or corrected. For instance

ility of body healing.

old virus or the flu. These alternative healing

techniques offer a rapid recovery time as well. In
ing therapy and be on the road to recovery.

t always have to get accomplished with a certain
zation of yoga or meditation to remain healthy. If

t balance.

so long as a proper balance is achieved.

ves, there is character. The foods you ate were
ease.

ients

216

217

enzymatic action of glucosamine synthetase plays a
role in mucous secretions of the digestive,
1 Sulfate allows cells in tissues to adhere to one

and rheumatoid arthritis should focus on both

osteoarthritis pain, rehabilitating cartilage,

the capacity to make enough glucosamine, so the
causing pain, deformed joints, limited joint

Glucosamine has shown to be very effective at:

al or vitamin company put out a glucosamine
practor's office.

ie product. These are:

001, the very large majority of companies simply
known that liquids are absorbed faster and more
you will not have any relief whatsoever no matter

