The pharmacology of herbal products

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Background

There is a vast and rapidly growing body of literature on the pharmacology of conventional drugs. This has been supported not only by the medical universities and state research institutes in many industrialised countries, but by a large number of pharmaceutical companies. In contrast, details of the pharmacological actions of most herbal medicines have yet to be described, although the therapeutic effects of many herbal medicines are reliably documented.

There are several reasons for this. First, the need to determine the mechanism of action has not been a primary concern to complementary healthcare practitioners. The efficacy of individual herbs has been established empirically by extensive clinical experience and observation. As a result, herbal medicines proven to be effective have retained their place in healthcare practice; those that failed to deliver expected treatment outcomes have been discarded. Second, the financial support and research resources, generously provided by government, medical schools and multinational pharmaceutical companies for conventional drug study, are rarely available to herbal practitioners or researchers.

Third, compared to conventional, synthetic, single entity drugs, herbal medicines are vastly more complex. This means that there is often a major disconnect between the actual pharmacological action of herbs and the actual clinical effect brought about. The individual components of herbal medicines and combinations act holistically, often synergistically, so the actual mechanism of action responsible is usually difficult to solate and identify.

Renewed interest in herbal pharmacology

In recent years there has been a major resurgence of interest in herbalism (sometimes called phytotherapy). This interest may be focused either on herbalism itself, or on it as part of complementary medicine. The rise of herbalism reflects a search for a more natural lifestyle, coupled with increasing respect for natural or holistic healing. It is also part of the modern philosophy in which there is an awareness of plants being linked to the rest of the living world in a symbiotic way.

Conventional drugs act by influencing linear body processes; herbal medicines affect highly complex body networks.

This trend has been given impetus by certain misgivings about the negative aspects of conventional, modern, or allopathic drugs, a number of which have recently been withdrawn from the marketplace. There is growing concern,

even suspicion, about the short- and long-term downside to drugs, especially the newer ones, regarding adverse drug reactions, and the real extent to which they occur. Reports of an alarming increase in antibiotic-resistant bacteria, and the potentially fatal outcomes, also contribute. Although the use of conventional drugs in treating acute or life-threatening disorders is generally accepted without question, there is some disquiet about the consequences arising from long-term consumption of drugs used for chronic or recurring disorders.

Compared to the mechanism of action of herbal medicines, conventional drug pharmacology is relatively straightforward. Drugs exert their effects for the most part in only a limited number of ways. They can stimulate, or inhibit, or otherwise interact with specific drug receptors on different body tissues. Or they can reduce the activity of certain enzymes involved in key biochemical or metabolic processes. Or they can affect cell membrane permeability. In contrast, herbs exert their action in a variety of ways. Some we already know about in some detail, and for others we have an inkling of their mode of action. But for perhaps the majority the mechanisms still remain to be identified and characterised.

Differences between conventional and herbal actions

Herbs themselves are made up of many substances, with widely differing actions on the living body. They may have biochemical effects, as with *adaptogens* and *alkaloids*; they may protect from changes to the internal environment, as do the *anti-oxidants*; or they may provide deficient *micro-nutrients* and *minerals*. Other components, such as *saponins* and *polysaccharides*, may act as buffering agents or synergists, although they are not directly active pharmacologically.

The *immune-modulators* have aroused much interest recently. These agents act to alert and regulate the immune system according to the body's needs when threatened by, for example, infection or cancer. This relative newcomer to the herb action scene supports one of the basic tenets of complementary medicine: *help the immune system, and the body will help itself.* Several herbs are known to possess this ability, expressed via the *cytokines*.

Whereas conventional drugs are usually very selective in influencing a specific part of the body's myriad *metabolic pathways*, herbal medicine tends to act to restore harmony to dysfunctional *body systems*. Ultimately, the role of herbal therapy is to restore the body's inner harmony, to strengthen the body's own protective defences, and to augment the natural self-healing mechanisms. The different forms of action of the conventional drugs and the herbal medicines actually reflect the different philosophies; conventional drugs aim primarily at the *disease* with symptom alleviation in mind, whereas herbal medicine focuses mainly on the *person* in order to restore inner harmony.

Herbal medicines are extremely complex when compared to conventional drugs. One herb usually has several different activities, and many herbal medicines combine several herbs.

In the light of renewed interest, there is now growing consensus that herbal medicine (and other forms of complementary medicine) should be subject to the same evidence-based investigations for efficacy and safety as is conventional medicine. The stability, safety and efficacy of herbal medicines are now being increasingly subject to critical scrutiny. One aspect of this examination is to state how important herbal medicines work, and the pharmacological mechanisms involved.

What are herbal medicines?

Herbal medicine, like many natural or traditional therapies, has been around since the dawn of civilisation. Virtually every society or culture has adopted herbal medicine in one guise or another. It may be stand-alone therapy, especially for the minor complaints affecting us all; or it may be part of a more comprehensive complementary healing system, where it is combined with traditional systems like Tibb or Chinese medicine, especially for chronic and recurring disorders.

Something like 60% to 80% of the world's population uses herbal medicine in one form or another.

Until the mid-20th century, complementary medicine in general and herbal medicine in particular took a "back seat", especially in the developed world, and was perceived as the poor cousin of conventional, orthodox or western medicine. Alas, because of the dubious practice of many practitioners – "*quacks*" – who sullied the herbalists' reputation, there had been, understandably, a fierce backlash against complementary medicine, and this accelerated the decline in usage.

Herbal medicines are whole plant and their extracts used in the treatment or prevention of clinical disorders. They may be extracts of a certain part of the plant – flower, leaf, stem, bark, or root – but they are *not* single substances extracted by chemical means – for example, morphine. Neither are they synthetic derivatives of substances extracted from a plant. For instance, the plant substance *salicylic acid* is present in many herbs and fruit; however, the simple chemical derivative *acetyl salicylate* (aka Aspirin) is not a herbal product.

Mechanism of action of herbal medicines

Identifying the pharmaceutical mechanisms of herbal medicines poses numerous challenges not generally faced by conventional drugs. To take one example: herbal medicines are very complex, and they usually contain many active substances which can act in combination. In contrast, conventional drugs are generally single chemical entities, and usually studied in isolation. Another difference is that a single conventional drug may have only one direct action, but the herbal medicine will probably have several, and the one that predominates depends on the dosage employed. What's more, although the herbal medicine may contain a particular active agent, it may not be present in sufficient quantity to elicit a pharmacological action. Yet another difference is that the components of a herbal medicine may act synergistically.

There are many substances present in specific plants or herbs for which the mechanisms of action have been determined. They can be allocated to specific classes of chemicals, with specific functions within the body. The main ones are: the *adaptogens*, the *immune-modulators*, the *alkaloids*, the *anti-oxidants*, the *anti-inflammatory agents*, and the *micro-nutrients*.

Alkaloids

What roles do alkaloids have in plants? The sheer chemical and structural complexity of these substances rules them out being waste medicines, as once thought. A great deal of metabolic energy is consumed in their biosynthesis. It now appears that many alkaloids are essential elements of plants' defence mechanisms. In their natural state, plants need protection from a variety of predators, from micro-organisms like fungi, bacteria and viruses, to parasites, insects and grazing animals. In addition, some alkaloids may be part of as yet undiscovered communication systems within plants; interestingly, a number of neurotransmitters in humans (*serotonin*, *dopamine*

More than 12,000 different alkaloids have been discovered, from over 300 plant families.

and *histamine*, for example) are structurally similar to certain plant alkaloids. Finally, alkaloids appear to be involved in the growth processes in specific parts of the plant, such as root tips, leaves and fluid transport systems.

Medical applications. Many plants have been used medicinally for ages, purely on their alkaloid content, and these are still used in many facets of complementary medicine. Beginning a hundred years or so ago, several alkaloids were isolated from identified plants, purified. and on the basis of observed clinical benefit, incorporated into the *material medica* of conventional medicine. A number of these are shown in the table below:

Plant	Alkaloid	Pharmacological action	Clinical application
Belladonna	*Atropine; scopolamine*	Anti-cholinergic agents	Parkinson's disease Gut spasms; eye surgery
Periwinkle	*Vinblastine; vincristine*	Anti-tumour agents	Anti-cancer therapy
Poppy flower	*Codeine*	Anti-tussive agent	Cough suppressant
Rauwolfia	*Reserpine*	Anti-hypertensive agent	Lowers high blood pressure
Crocus	*Colchicine*	Anti-inflammatory agent	Relieves gout flare-ups Anti-cancer activity

Many alkaloid extracts have been used clinically for decades, and for a wide range of disorders or clinical procedures. The table below lists a selection of these; their source and their known mechanisms of action.

Alkaloid	Source	Pharmacological action	Desired activity
Atropine	Deadly nightshade *(Atropa belladonna)*	*Cholinergic receptor antagonist; anti-muscarinic agent*	Low heart rate and heart block; pupil dilation in eye surgery; antidote for some poisons
Reserpine	Indian snakeroot *(Rauwolfia serpentina)*	*Vesicular monoamine transporter inhibitor*	Anti-psychotic; anti-hypertensive
Ephedrine	Ephedra (*Ephedra sinica)*	*Sympathomimetic amine*	Stimulant; decongestant; appetite suppressant
Theophylline	Tea bush *(Camellia sinensis)*	*Adenosine receptor agonist; phosphodiesterase inhibitor*	Bronchodilator in asthma; heart stimulant; nervous system stimulant
Vinblastine **Vincristine**	Madagascar periwinkle *(Catharanthus roseus)*	*Mitotic inhibitor; cytotoxic agent*	Anti-cancer agent
Caffeine	Coffee bush *(Coffea canephora)*	*Adenosine receptor agonist; phosphodiesterase inhibitor; glycine receptor antagonist*	Nerve stimulant; exercise recovery; hair growth stimulant
Paclitaxel	Pacific yew *(Taxus brevifolia)*	*Mitotic inhibitor*	Anti-cancer; Kaposi's sarcoma
Noscapine	Poppy *(Papaver Somniferum)*	*Sigma receptor agonist*	Cough suppressant; (poss.) anti-cancer activity
Colchicine	Autumn crocus *(Colchicum autumnale)*	*Mitotic inhibitor*	Anti-gout, anti-inflammatory agent; (poss.) anti-cancer activity
Morphine	Poppy *(Papaver Somniferum)*	*Opioid receptor antagonist*	Relief from moderate-severe pain

Many herbs in the natural state contain one or more alkaloids. As alkaloids are quite capable of provoking adverse drug reactions, the use of herbal medicines in high concentrations (which can occur in liquid formulations), can cause side effects such as diarrhoea, vomiting or headache in sensitive individuals.

If a herbal medicine contains an alkaloid which has been identified, whenever it is administered to a patient for a particular disorder, it will stimulate its dedicated receptors. For example, the anti-tussive agent noscapine will provide relief from a troublesome cough whether it is given in a conventional cough and cold drug formulation, or whether it is part of a herbal medicine. (This applies only if the given dose is equivalent in both conventional and herbal forms). However, the herbal medicine will contain several other pharmacologically active components which may modify the action of the alkaloid – change in duration of effect, or reduction in the intensity of side effects, for example.

Adaptogens

An *adaptogen* refers to any plant-derived substance which increases a person's resistance to stress, trauma, anxiety and fatigue. From the patient's point of view, the term describes herbs which are *tonics* and act by restoring harmony to the body. It includes multi-herb restoratives in Tibb Medicine, *qi tonics* in Chinese herbal medicine, *prana* in Ayurvedic Medicine, and *vital energy* in Western herbalism. There are no equivalent drugs in conventional medicine, although synthetic vitamins and supplements are often used to boost metabolism in both healthy and sick people, and those who are pregnant, nursing or convalescing.

The benefit of tonics is most evident in people showing signs and symptoms of disturbed homeostasis.

A separate group of herbal products with adaptogenic action, the *immune-modulators (see later),* is able to stimulate the immune system when dealing with infection and cancer. At the same time, they modulate the immune processes that promote inflammation following a wound or other injury.

Mechanism of action. The active ingredient in the herbs, once absorbed into the body, penetrates the cell membrane. Some adaptogens are capable of moving, and then attaching, to the DNA of the nucleus. This interaction leads to modified secretion of hormones, and the transfer of messages by the nervous system. In addition, secretion of hormones from the endocrine system is also regulated.

Adaptogen-rich plants like licorice and ginseng have a long history of use as tonics in traditional healing.

Adaptogens differ from other medicinal herbs in that they help maintain optimum homeostasis in the body. They act as metabolic checks and balances. This is achieved by influencing both the immune system and the endocrine system. Adaptogens speed up or slow down a number of bodily functions, depending on the person's needs at the time.

> ***Adaptogens in practice.*** *A good example of an adaptogen is hawthorn berries. These can help normalise a person's blood pressure: if too high, the adaptogen will reduce it; if too low, the adaptogen will raise it. Another example concerns the use of valerian for treating an anxious patient. One herbal component will elicit a sedative action, whereas another will have a slight stimulatory effect. The net result is a dynamic, well-controlled anxiety reducing effect, responsive to changing situations, without unwelcome adverse reactions.*

Desired actions. The major effect of an adaptogen on the body is to help it cope with metabolic stress, so restricting any disturbance to internal homeostasis. The beneficial effects of the adaptogens, confirmed empirically over the years, are many and varied. They:

- Act as *anti-oxidants*, so limiting the impact of free radicals and oxidative species upon the body's metabolic processes

- Enhance the body's *immune competence* and resistance, so protecting against the deleterious effects of pathogens
- Support the liver's *metabolic activity*, so helping to oppose toxic influences from the diet or the environment
- Improve *blood sugar* metabolism, so decreasing fatigue, and provide energy at critical times
- Accelerate *recovery* from convalescence, surgery and trauma
- Help to improve a person's *focus and concentration*, decrease anxiety, and correct disturbed sleeping patterns

In addition, they:

- Improve voluntary *muscle tone*
- Reduce *craving* for alcohol or sugar
- Slow down the *ageing* process

Adaptogen types. Apart from a few exceptions, the chemical nature of the adaptogens has not been fully worked out. We do know that several are composed of *polysaccharides,* whilst others are *phytosterols,* which are plant sterols derived from sitosterol, the plant's version of cholesterol.

Perhaps the best documented adaptogen is the class of *saponins*, a complex *mevalonate*-derived group of phyto-chemicals. These have traditionally been used as a general mental and physical tonic, providing a wide range of medicinal benefits. The saponins are included in the group adaptogens because they seem to protect and restore homeostasis in the body, especially when under unremitting stress. *Ginseng* is a widely used member of this group.

One saponin present in one species of ginseng, *ginsenoside*, has been used traditionally and more recently in the clinic for improving cognitive function, treating insomnia, and alleviating anxiety. The pharmacological profile of ginseng is complex, and difficult to comprehend. Many ginsenosides have been isolated, with sometimes opposing pharmacological effects. However, it seems that the underlying mechanism of action of the ginsenosides has much in common with that of steroid hormones.

Mevalonate is the basic component of many key substances in plants; e.g. saponins, phytosterols, flavonoids and

These saponins appear to possess marked anti-tumour and anti-mutagenic activity. Several individual ginsenosides suppress tumour cell growth, induce cell differentiation, regulate apoptosis and inhibit metastases (the formation of colonising groups of cancer cells). Their mechanism of action apparently involves binding to the cholesterol molecules embedded in cancer cell membranes, so inhibiting their viability and frustrating cellular growth.

Saponins may also exert their action by means of a built-in anti-oxidant effect, although this is controversial at present. This mechanism of action is invoked to explain the anti-cancer and cardio-protective effects. In this connection, saponins also seem capable of promoting programmed cell suicide/death, or *apoptosis*, in cancer cells of patients with leukaemia.

The herb *Tribulus*, or *Bull's Head*, is widely used as a sexual tonic. One component, the saponin *protodioscin,* apparently exerts its pharmacological action (in animals) by boosting the secretion of luteinising hormone from the anterior pituitary, leading to increasing levels of circulating testosterone and related male sex hormones. This in turn leads to increased skeletal muscle mass.

Different saponins derived from the *Baby's Breath* plant appear capable of decreasing the effect of immunotoxins. This property is put to good use in the treatment of patients with cancers such as leukaemia and lymphoma.

Immune-modulators

The adaptogens overlap to some extent with the *immune-modulators*. These are herbal medicines that alter some activities of the immune system via the dynamic regulation of the body's informational molecules – *cytokines, hormones, neurotransmitters*, and other peptides. In fact, many of the effects of herbal medicines, particularly the adaptogens, are expressed by one or more groups of the cytokines.

Empirical and scientific evidence confirm that whole plants, not just isolated constituents, have immune modulating activity.

Cytokines (*literally* cell movers) are signalling molecules that help maintain communication between organ systems, providing molecular cues for conserving physiological stability; that is, homeostasis. The onset and progress of many disorders, from cardiovascular disease to muscle wasting, are influenced by cytokines. They are involved in the body's antiviral or anti-cancer activity, and are crucial to inflammatory response, cell growth, repair and death.

The cytokines are small protein (*peptide*) or glycoprotein molecules released from a number of different cells in both the immune and nervous systems. They carry regulating and mobilising signals between different cells within the body. There is a large, diverse group of these regulators, which differ in structure and function. Particular groups are the *interferons*, the *chemokines*, the *tumour necrosis factors*, and the *interleukins*.

Cytokines help in the removal of foreign bodies from the body – viruses, bacteria, fungi and even cellular debris. They instruct effector cells like the *neutrophils, macrophages* and *monocytes* to divide and mount an attack on these foreign bodies, and digest the resulting remnants. Most of the time they are effective in keeping the body's tissues free from the effects of microbe invasion, but sometimes certain organisms can provoke a '*cytokine storm'*, which can have grave clinical consequences. The secretion of cytokines becomes excessive for some reason. This leads to massive reactions in the body's organs and tissues, followed by collapse of internal metabolic processes, and sometimes death. The response to the infection is out of all proportion to the risk posed, so the cells which should be protecting the body actually cause it possibly serious harm.

Cytokines regulate major sections of the immune response to infections and cancer.

A number of herbal medicines have an effect on the secretion of cytokines. *Garlic* is one example. It possesses the ability to modulate cytokine activity, and increase the number of *natural killer cells.* It has shown an effect, albeit in an *in vitro* human model, on a number of cytokines, including interleukins -1, -6 and -8, and also TNF. Interleukin-1 is a pro-inflammatory cytokine implicated in hyperglycaemia due to pancreatic beta-cell destruction. Garlic has also been shown in animal models to stimulate secretion of interleukin-10, which is an antagonist of pro-inflammatory cytokines. These preliminary results provide some biochemical basis for the use of garlic in such diverse fields as diabetes, inflammatory bowel disease and Alzheimer's disease.

Severe reaction and even fatalities from virus diseases such as influenza and SARS often result from a cytokine storm.

A selection of herbal medicines where cytokine secretion seems to be involved is shown in the table below.

Herbal medicine	Active agent	Pharmacological action	Disorders responding
St John's wort	*Hypericin*	Antiviral and anti-bacterial activity Modulation of brain monoamine neurotransmitters (serotonin; nor-adrenaline)	Infection and inflammation Anti-depressant effect
Green tea	*Catechin*	Anti-oxidant activity Enhances lymphocyte response	Viral infections Cancer chemoprevention
Turmeric	*Curcumin*	Secretion from T cells, B cells, neutrophils, macrophages, and natural killer cells is modulated	Alzheimer's disease Osteoarthritis Cancer chemoprevention
Cat's claw	*Oxindole* alkaloids	White blood cell activity enhanced Production of cytokine TNF-alpha decreased	Influenza Microbial infections Inflammatory disorders

Nitric oxide synthesis modulators

Nitric oxide (NO) is a highly reactive free radical that is involved in muscle and immune system activity. It is a key player in several biochemical processes, and is involved in a number of diseases, especially of the heart and blood circulation. Chemically it is a simple gaseous compound, originally called the *endothelial-derived relaxing factor*.

The presence of NO in many parts of the body suggests that NO plays an important role in health and disease.

It arises in the body from the reaction of oxygen and the amino acid *arginine*, which is catalysed by the enzyme *nitric oxide synthase*. NO is also produced from *nitrate*, which is present in food, or from the breakdown of *nitroglycerine,* which is used in treating angina pectoris. The site of synthesis is mainly the cells lining the blood vessels, or *endothelium*. Some NO is also produced in nerve cells, or *neurons*, where it serves as a neurotransmitter. In other tissues it can appear as a result of cytokine activity. As it is broken down in seconds in the body, it is synthesised at the required site of action, according to local need.

Several plant-derived substances are known to influence the synthesis of NO in

Role in the body. NO diffuses freely across cell membranes, and acts to relax smooth muscle in blood vessels. This leads to *vasodilatation;* that is, an increase in blood flow to surrounding tissues. Nitric oxide is therefore crucial to the cardiovascular system, because it assists the flow of blood through the heart and circulatory system. It also helps to remove dangerous blood clots, lowers high blood pressure and inhibits plaque build-up in the arteries. A constant level of NO formation is important in protecting organs such as the liver from poor blood circulation, so reducing the risk of ischaemic damage.

Reduced availability of NO in blood vessels encourages the onset and progression of cardiovascular diseases.

Generally, nitric oxide modulates homeostasis in blood vessels. It inhibits several adverse processes in the body that may turn into diseases. The contraction of vascular smooth muscle is restrained; the unregulated growth and development of blood vessels is prevented; platelet clumping is prevented; and the attachment of white blood cells to the inner endothelial lining of blood vessels is inhibited.

NO is also involved in inflammation, one of the body's main defence mechanisms for dealing with infection and damage.

NO in diseases. If the production of NO is not tightly regulated, toxic damage to certain tissues can occur. At normal levels, NO dilates the blood vessels and so maintains satisfactory blood circulation. At low levels, blood circulation becomes sluggish, and this can give rise to certain disorders, such

Certain diseases can arise from either too much or too little NO produced in the body.

as thrombosis, angina pectoris and hypertension. Conversely, at abnormally high levels it causes circulatory shock, and may even induce tissue death. A number of disorders are known to be linked to wide swings in blood flow, such as arthritis and ulcerative colitis, juvenile diabetes, multiple sclerosis and a number of cancers.

The emergency vasodilators amyl nitrite and nitroglycerin are used in the treatment of angina pectoris. They are converted to nitric oxide in the body. *Sildenafil* ('Viagra') stimulates erections primarily by enhancing signaling through the nitric oxide pathway in the penile blood vessels.

Diet and nitric oxide. A number of everyday dietary components are known to activate or modulate the enzyme nitric oxide synthase. These include cocoa (active agent *epicatechin*), black and green tea (*flavonoids*), pomegranates (*polyphenols*), olive oil (*oleic acid* and *polyphenols*), soy (*genistein*), and red wine (*resveratrol*). The high level of NO synthase activators present in vegetables and fruit, such as flavonoids, catechins, tannins and other polyphenolic compounds is believed to contribute to their proven beneficial health effects. Vitamin C is thought to increase nitric oxide synthesis, so foods rich in this vitamin should have a beneficial effect on the blood circulation.

People with hypertension, diabetes or atherosclerosis often show impaired nitric oxide synthesis, release or use.

Herbs and nitric oxide. Several herbs increase nitric oxide production, and these are often used to treat cardiovascular disorders. A major response is the activation of *macrophages*. These scavenger cells, located in various tissues, identify, engulf and digest invading microbes. Other herbs act as vasodilators by increasing NO in vascular tissue. For example, the saponins from ginseng (*ginsenosides*) are known to relax blood vessels. This probably contributes to the fatigue-relieving and blood pressure-lowering effects of ginseng. In addition, herbal products from ginkgo and hawthorn have been shown to affect endothelial NO production.

Safed musli, a traditional tonic, improves reproductive function (in animals) by stimulating NO synthesis.

Anti-inflammatory activity

Inflammation is a complex biological process that helps to restore homeostasis to the body after it has been disturbed by physical damage, chemical irritants, pathogenic micro-organisms or damaged tissues. It is a major protective system, and works closely with the immune system in initiating the healing process. It is modulated by interacting with both the endocrine and nervous systems.

Conventional drug treatment involves the use of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. The former group acts by counteracting two enzymes; *cycloxygenase* (which results in pain relief) and *prostaglandin synthetase* (which is largely responsible for the signs and symptoms of inflammation). Corticosteroids work by attaching to steroid receptors in the cell's cytoplasm, then stimulating the nucleic acids.

Extensive NSAID use can lead to erosion of the stomach lining. This may develop into serious, even life-threatening, stomach ulcers and perforations.

As inflammation is part of the normal healing process, there is no real clinical advantage in completely suppressing this beneficial phenomenon long-term. The total shut down of a healing process is often the outcome of conventional NSAIDs and exogenous corticosteroids, with the aim of suppressing symptoms of inflammation. What the person suffering from a persistent or severe inflammatory reaction needs is gentle control and regulation of the process. Several herbs are able to provide this, without the adverse drug reactions that usually accompany conventional anti-inflammatory agents.

Ginger, hyssop, arnica and *turmeric* are known to contain an inflammatory agent *helenalin*, a lactone adaptogen. Another anti-inflammatory agent, salicylic acid, is present in many herbs, including willow bark. Cannabinoids, although not generally available for consumption, have been used effectively to treat inflammation.

Anti-oxidants

These operate by opposing and neutralising free radical damage within the body. Free radicals, or *oxidative species*, are normally produced in the body as a routine part of the immune system's total defensive mechanism against invasion by micro-organisms. They also appear as a by-medicine of the normal energy-generating processes located in the cells' mitochondria. However, if they reach abnormally high levels they can initiate serious biochemical and structural damage. Free radicals are also produced in response to a poor or unsuitable diet, or from an imprudent lifestyle, or by many environmental toxins.

Examples of free radicals are oxygen and hydroxyl radicals, superoxide, and hydrogen

Free radicals can also be formed from the body's internal metabolism of foreign substances, including drugs. Paracetamol, for example, is metabolised in the body at high doses, *inter alia*, to a type of free radical. This is the agent that causes severe liver damage following overdose, or when used excessively by alcoholics and others with poor liver function. The quinoline-based antibiotics and the anti-cancer agent etoposide are also known to generate free radicals.

Free radicals, if unchecked, can inflict serious damage on many structures within the cell.

The general effect of free radicals is to disturb the body's inner homeostasis and metabolic harmony. They degrade the DNA in the nucleus, structural proteins, especially collagen and enzymes, and phospholipids in cell membranes. In addition, the mitochondria, the energy producing structures in cells, may be badly affected. Although not usually fatal, free radicals can lead to certain diseases and to premature aging. The table below summarises the situation.

Formation	Effect	Result
Natural – immune system response to infection. Formed by white blood cells.	Destruction of pathogens (bacteria, viruses, fungi) and tumour cells.	*Beneficial:* Pathogens eliminated.
Lifestyle – diet, toxins, cigarette smoke, drugs, dyes, colorants and other foreign substances.	Degrade proteins, especially enzymes. Attack phospholipids. Impair the cell's nuclear DNA. Damage to mitochondria.	*Damage:* Premature aging, especially of the skin. Development of cancers. Deterioration in metabolic processes.
Environment – occupational radiation, sun-beds, air pollution, insecticides, UV light, cigarette smoking.	Progressive DNA damage. Failure of cell reproduction.	*Damage:* Change in behaviour, cancer formation. Reproductive problems.

The body's immune system has a number of *anti-oxidants* for dealing with free radicals. Enzymes like catalase, superoxide dismutase and peroxidise can mop up the free radicals as they appear, before they can cause serious damage. However, circumstances can arise where free radical production overwhelms these, or the mechanisms are worn down by the aging process, constant exposure, or unrelenting physical or emotional stress.

The main natural anti-oxidants arise from several sources. Metallic elements such as zinc, manganese, selenium and copper are effective anti-oxidants, and these are usually present in herbal medicines to greater or lesser extent. Certain vitamins possess anti-oxidant properties, especially vitamin A, C and E. Beta-carotene could also be included in this category. All vegetables and fruits contain one or more anti-oxidants, present in varying amounts.

Anti-oxidants seem to work best when combined. Together, they operate synergistically as a

Micro-nutrients

Micro-nutrients, or *trace elements,* refer *to* the *micro-minerals*, vitamins, essential fatty acids and amino acids. Their role in the body is not to provide energy as such, but to assist existing enzyme systems operate more efficiently. Micro-minerals include the metallic elements iron, chromium, zinc, copper, cobalt, manganese and molybdenum.

The mechanism of action of many micro-nutrients is to act as co-factors for certain enzymes. Zinc, for example, is a co-factor for several enzymes, including *alcohol dehydrogenase, phosphodiesterase* and *aminopetidase.* Iron is not only an important co-factor for several enzymes involved in energy production in the mitochondria, but is also an essential component of non-enzyme proteins like *hemoglobin* and *cytochrome*.

Apart from their enzyme support activity, micronutrients protect against damaging environmental toxins, especially over the longer term. If an essential nutrient is missing from the diet, or in short supply, or lacking the potency necessary to maintain natural balance within the body, then the body systems become distressed. This has a "knock-on" effect on other organs, so that the body as a whole becomes unbalanced. This can happen when a person is malnourished or deficient in a certain nutrient.

Herbal medicines contain a host of nutritional factors – minerals (such as potassium), vitamins (especially the water-soluble B complex), and trace elements (molybdenum, zinc and cobalt, for example), which contribute to resolving chronic deficiency disorders in the patient. Deficiencies may be minor in terms of symptoms, but they may have a disproportionate impact on the person's well-being. The range of micronutrients expands if several herbs are included in the medicine.

Vitamins are often present in particular herbal medicines, albeit at relatively low levels. Vitamin C, found in several products, assists in the absorption of dietary iron, so reducing the risk of iron-deficiency anaemia. Conversely, the herbal product's components may assist in the absorption of specific vitamins provided by the diet, or from vitamin supplements. Two flavonoid glycosides, *rutin* and *hesperidin*, present in some herbal products, help in the absorption of Vitamin C from the digestive tract.

Conclusion

There is now considerable scientific evidence that a large number of herbal medicines exert their effect on different body systems, and this supports and confirms the extensive empirical testimony gained over the years. This increasing body of evidence reinforces the case for including herbal medicines in the mainstream therapy of a number of chronic disorders, either alone, or as part of a programme of integrative medicine.

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