Herbal Pharmacology and Toxicology

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In 1981 I was involved in a radio interview on herbal therapy during half-time of the University of Utah vs. BYU football game. Among other statements, I suggested that people should discuss herbal therapy with their physicians before they take herbs or natural products. Shortly after, I received numerous antagonistic letters. Some wrote that they had talked to physicians, and the physicians knew absolutely nothing about these substances. One specific instance concerned the actions of an herb called comfrey. The physician had not heard of comfrey and lost credibility with the patient. Since that time I have felt it important to teach the physician about herbal pharmacology and toxicology.

In 1979 Janice Morin, a BYU graduate student, completed a master's thesis comparing herbal use along the Wasatch Front with parts of Southern California. She reported that up to 50 percent of patients use herbs at least infrequently. Most, however, expressed fear of being misunderstood or of reprisal if their herbal use was discovered. Thus many, if not most, of the subjects in this study did not confide in their physician.

The first drugs used by humanity were herbal drugs, and the first known written record of curative plants was a Sumerian herbal of 2200 B.C. This use may have revolved around the belief that naturally occurring substances possessed properties which affect the physical, emotional, and mental behavior of living organisms. Some of these beliefs may be well founded, yet many were based on superstition and questionable religious practices.

As early as the fifth century B.C., Hippocrates described some 400 herbs that were in common use. Dioscorides, in the first century A.D., wrote an herbal identifying 600 plants to be used as therapeutic agents.

One of the most popular herbals ever written was that of Nicolas Culpepper (1616–1654). In his explanation of healing herbs, he combined astrology and the Doctrine of Signatures. The latter is the notion that nature has indicated the uses of plants by their appearance, shape, color, texture, and habitat.

Each herb had its own particular virtue and legendary lore. Anemones, which according to Greek myth sprang from the blood of Adonis after he was mortallly wounded by a boar, were used to cure colds, gout, and leprosy. Betony, named after Beronice, a woman healed by Christ, was believed to cure almost all ills of the body and of the soul. Blackberry brambles were legendarily used by Christ to drive out the money changers from the temple, and children were at one time passed through a bramble arch as a cure for rickets. Bryony, used by witches in spells, was taken as a purgative and is still considered a potent aphrodisiac. When God caused a deep sleep to fall on Adam so he might remove a rib from which Eve would be created, the Old Testament indicates that this was accomplished by using mandrake. The mandrake root, like its relatives in the Solanaceae family (deadly nightshade, jimson weed, henbane), contains a number of atropine-like alkaloids. The mandrake was used as a sedative, hypnotic, analgesic during surgery, or as an aphrodisiac. Eyebright, which was thought to have been rubbed on Adam's eyes to permit him to see the future mortality of man, is still used by modern herbalists for eye complaints. In popular tradition viper's bugloss was believed to help lumbago and increase milk production in nursing mothers. However, only during the last century have we started to know something about the pharmacology and chemistry of some of these products.

Herbs are, for the most part, pharmacologically active. However, many of the actions are not those attributed by herbalists. In 1973 there were 1.5 billion prescriptions written and refilled in the U.S. Almost 50 percent of those prescriptions contained a natural prod-

Photography by W. Mike Nielson

Lactones—include such compounds as coumarin and tonka beans. Although coumarin is widely distributed in plants, glycosides containing coumarin as such are rare. Cantharides, consisting of the dried insect, may also be classified in this group.

Phenols—the aglycone groups of many of the anturally occurring glycosides are phenolic in character. Arbutin, found in uva ursi, chimaphila, and other ericaceous drugs, yields hydroquinone and glucose upon hydrolysis. Hesperidin, which occurs in various citrus fruits, may be classified as a phenol glycoside. Phloridzin found in the root bark of rosaceous plants and iridin from the iris species are additional examples of phenol glycosides.

Miscellaneous glycosides include gentian, quassia or bitter wood, picrotoxin or cocculin, and saffron or crocus.

Table 2—Tannins

Catechols—when heated these tannins yield catechol and include such agents as hamamelis or witch hazel, krameria or rhatany, chestnut leaves, kino, gambir or catechu, and ceanothus or New Jersey tea.

Pyrogallols—when heated these compounds yield pyrogallol and include such agents as gallotannin in nutgall and ellagintannin in oak bark and pomegranate bark. The dried petals of the rose also yield pyrogallols.

will espouse philosophies vastly different from generally accepted medical concepts. Further problems arise when the physician assumes the patient will do one thing while in many instances they do the opposite. For example, some herbalists believe that diarrhea is an advanced form of constipation. They explain that the colon is impacted and only water can be passed. Their concept of treatment is with stimulant type cathartics. Thus, a fair number of patients develop fluid and electrolyte imbalances.

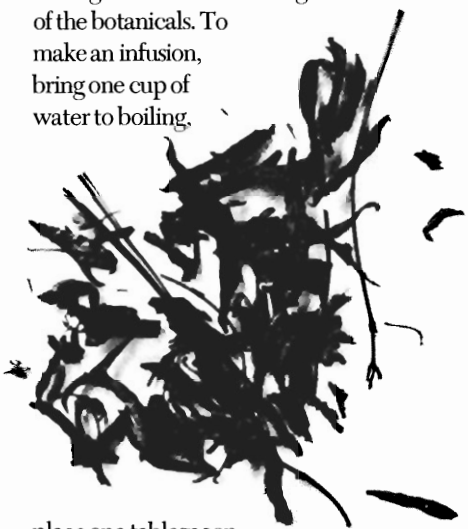
Another example relates to febrile conditions. Some teach that fever is a beneficial physiological compensatory mechanism for burning up body contaminants and toxins. Therefore, their recommended approach is to raise the body temperature to "burn off" greater quantities of toxins.

Herbal Terminology/Definitions

Botanically an herb is any flowering plant whose above-ground stem does not become woody. An herb may be described as either nutritional or medicinal. A nutritional herb is defined as any plant or part of vegetation normally eaten for food. A medicinal herb is defined as any plant or vegetation used beneficially in therapeutic treatment.

For all practical purposes, a natural product is defined as a product that is derived from plant, animal, or microbial sources, primarily through physical processing, sometimes facilitated by simple chemical reactions such as acidification, basification, ion exchange, hydrolysis, salt formation, and microbial fermentation. These chemical reactions do not drastically alter the chemical structure of the natural product to be isolated.

Teas (infusions and decoctions) are generally dilute aqueous extracts containing the water soluble ingredients of the botanicals. To make an infusion, bring one cup of water to boiling, place one tablespoon of leaves and/or blossoms into water, and let it stand for ten minutes.



Decoctions are prepared by placing one tablespoonful of bark and/or roots into one cup of cold water, bringing it to a boil and continue boiling for ten minutes. Because of the dilute and aqueous nature of infusions and decoctions, they are very susceptible to microbial deterioration.

Encapsulation is a process where dried herbs are placed in gelatin capsules.

Plant Constituents

It is difficult, if not impossible, to intelligently discuss herbs and herbal therapy with a patient without some understanding of plant constituents. These constituents make up, for the most part, the active ingredients of the herbs.

Glycosides (Table 1) are compounds that upon hydrolysis yield one or more sugars. The nonsugar component is known as the *aglycone*; the sugar component is called the *glycone*. Glycosides may be classified by the aglycone portion.

Tannins (Table 2) comprise a large group of complex substances found in immature fruits and usually disappear during the ripening process. Almost every family of plants embodies species which contain tannins. They are the source of fruit acids and since they are antiseptic in action, they prevent dam-

Table 3—Volatile Oils

Hydrocarbons occur in practically all volatile oils and consist of unoxygenated terpenes, sesquiterpenes and diterpenes. Major terpenes include limonene (found in citrus oils), caraway oil, coriander, cardamon, fennel, and eucalyptus. Pinene, sabinene, and thujene are commonly occuring diterpenes. Acyclic terpenes are rather rare, but ocimene (ocimum oil) and myricene (myrica oil) are examples.

Alcohols may be classified into acyclic alcohols, terpene alcohols, and sesquiterpene alcohols. Among the more important terpene alcohols are menthol (from peppermint) and borneol (a dicyclic terpene alcohol from Borneo camphor). sesquiterpene alcohols include the santalols (sandalwood oil) and gingerol. Among the important alcohol volatile oils are: peppermint, sage, cardamon, coriander, serpentaria, sandalwood, rose oil, orange flower oil, juniper, and pine oil.

Aldehydes may be divided into acyclic and cyclic. They include benzaldehyde (bitter almond ol), cinnamic aldehyde (cassia oil), vanillin (vanilla, benzoin, tolu and Peru balsams), and cuminic aldehyde (cumin fruit).

Ketones occurring in volatile oils may be divided into (1) monocyclic terpene ketones include menthone (pennyroyal, peppermint), carvone (spearmint, caraway), piperitone (eucalyptus) and pulegone (hedeoma); (2) dicyclic ketones including 2-camphenone (camphor) and thujone (thuja, tansy, wormwood and sage), and (3) nonterpene ketones such as irone (violet, orris root).

Phenols occurring in volatile oils are of two types: those which are present naturally and those which are produced as a result of destructive distillation of various plant products. Eugenool, thymol, and carvacrol are the most important phenols occurring in volatile oils. Eugenol occurs in clove oil, allspice oil, and other oils; thymol and

age by insects and fungi. Tannins precipitate proteins from solution and are able to combine with them, rendering resistance to proteolytic enzymes. When applied to living tissues, this action is known as the "astringent" action. When hydrolyzed, they yield relatively simple polyhydric phenols: gallic acid, photocatechuic acid, and ellagic acid.

The phenolic groups of the tannins are responsible for their astringent and antiseptic action as well as their coloration with iron salts. The classification of tannins is based upon the colors obtained with iron salts.

Lipids are esters of fatty acids. They are divided into fixed oils, fats, and waxes and are differentiated by the type of alcohol attached. Many drugs and herbs contain fixed oils and fats as their principal constituents. Fixed oils and fats differ only as to melting point. Those that are liquid at room temperature are generally known as fixed or fatty oils while those that are solid at room temperature are known as fats.

Volatile Oils (Table 3) are odorous principles found in various plant parts that evaporate when exposed to air at ordinary temperatures. Depending on the plant family, volatile oils may occur in specialized secretory structures such as glandular hairs (Labiatae), modified parenchyma cells (Piperaceae), oil tubes called vittae (Umbelliferae), or in lysigenous or schizogenous passages (Pinaceae, Rutaceae). As a general rule, volatile oils are immiscible with water, but they are sufficiently soluble to impart their odor to water. However, these oils are soluble in ether, alcohol, and most organic solvents.

Resins (Table 4) are amorphous products formed in schizogenous or schizolysigenous ducts and are end products of plant metabolism. Resin-volatile oil mixtures are called oleoresins. Resin-gum mixtures are called gum resins. Resinous mixtures that contain cinnamic or benzoic acid are called balsams.

Alkaloids (Table 5) are pharmacologically active basic, nitrogenous substances that are usually of plant origin. They appear to have a restricted distribution in the plant kingdom but may occur in various parts of the plant. Chemical names of all alkaloids end in "ine." Various schemes have been developed for the classification of alkaloids. One approach is to classify them based on the ring structure or nucleus of the chief alkaloid in the plant drug/herb.

Herb Categories

There does not appear to be any universally accepted categorization of herbs. However, the one selected for this paper may be acceptable to most herbal enthusiasts. The definitions presented are not generally therapeutically valid and are presented for clarification only. It would be impossible within the scope of this paper to discuss many specific herbs. However, seven of the most popular herbs are presented as examples. They are garlic, aloe vera, com-

carvacrol occur in thyme and monarda oils.

Phenolic ethers occur in volatile oils. Some of the more important examples are anethole (from anise and fennel), and safrole (from sassafras, camphor oil, and Japanese star anise). Derivatives of safrole are also found in volatile oils. Some of these include myristicin (from nutmeg and parsley) and apiole (from parsley and East Indian dill).

Oxides are found in several volatile oils. Major substances include eucalyptol (cineol) found in eucalyptus, cajuputol found in cajutpu, and ascaridol a dioxide of cymene found in chenopodium oil.

Esters of a wide variety occur in volatile oils. The most common are the acetates of terpineol, borneol and geraniol. It is a common practice to age perfumes to permit esterification to take place and thus improve the bouquet.

Miscellaneous—various commonly used herbs contain volatile oils. Some of them include yarrow, allium (garlic), angelica root, chamomile, spikenard, sarsaparilla, prickly elder, snakeroot, calendula (marigold), carrot fruit, catnip, and mayweed.

Table 4—Resins

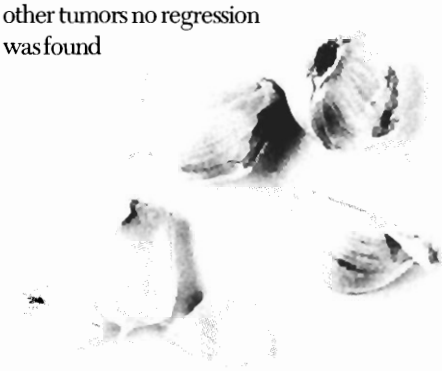
Some of the commonly occurring resins include rosin, podophyllum (mandrake), colocynth (bitter apple), jalap, guaiac, cannabis, black cohosh, wax myrtle, aspidium (bears paw root), capsicum (cayenne), ginger, white pine, myrrh, asafetida, and benzoin.

frey, ginseng, cayenne, goldenseal, and lobelia.

Alteratives (Table 6) are agents to promote a gradual and beneficial change in the body and to restore everything to normalcy. One of the common alteratives that has been used throughout recorded history is garlic. It has many purported uses including antiseptic, antibiotic, and disinfectant action. It is also purported effective in the treatment of cancer and as a cure for hypertension, hypoglycemia, and atherosclerosis.

During World War I garlic juice was used by the British to control the suppuration of wounds. The raw juice was diluted with water and applied on swabs of sterile sphagnum moss. Cavallito used several of the substances found in garlic to test for antibiotic activity, including allicin. He used benzyl penicillin as a standard. By the cylinder-plate method against staph aureus, allicin showed activity equivalent to 15 oxford penicillin units per mg, which is about 1 percent of the activity of benzyl penicillin (Cavallito 1950). However, Stoll reported that the formation of allicin is dependent upon the presence of an enzyme capable of splitting allin. However, this enzyme has not been shown in man. Thus garlic is only active as allicin which would have limited in vitro action and no in vivo action (Stoll 1951).

Garlic was used anciently as a cure for cancer. Hippocrates used it as a treatment for uterine tumors and the Bower manuscript, dating from about 450 A.D. in India, recommended garlic as a cure for abdominal tumors. In Stoll's work with allicin, he described Hans von Euler's work with the growth inhibiting action of allicin on various tumors. He observed that transplanted tumors of Jensen sarcoma in rats regressed or in some cases completely disappeared after injection of 1 to 3 mg of allicin. However, Stoll reported that in other tumors no regression was found



after injection of 20 mg of allicin. In 1957 Weinberger and Pensky noted that compounds with the –SOS– linkage are effective in both enzyme inhibition and bacteriostatic activity. They felt that since allicin contained such a linkage it might also have an inhibitory effect on malignant cells. To test the hypothesis, they inoculated 200 mice with sarcoma 180 ascites tumor. It was found that preincubation of the inoculum with the enzyme or substrate (allicin) resulted in rapid growth of the tumor and death. It would be very difficult to establish any case for any efficacy with garlic or its constituents in the treatment of cancer.

One of the main uses of garlic is to control hypertension. Vinci reports discrepancies in reports as to this action, but perhaps the only plausible reason why garlic would lower some people's blood pressure is that it has weak diuretic action. The action would be transient, however, as blood volume returns to normal with most diuretics.

Probably the one credible action of garlic is as an insect repellent. For the most part, garlic is excreted through the perspiration and saliva and appears to be unpleasant for mosquitos and ticks.

Garlic is not without toxicity. Both Cavallito and Chopra have reported cases where its ingestion has caused irritation and in one case death. They report that the LD_{50} for mice of allicin is 100 mg/Kg intravenously and 120 mg/Kg subcutaneously. Perrin reported that "essence of garlic" is a stimulant on all animals and that .255 cc/Kg is toxic

Table 5—Alkaloids

Pyridine-piperidines are divided into derivatives of piperidine, including piperine from black pepper and methysticin from kava, derivatives of alpha-propylpiperidine, including coniine from conium, derivatives of nicotinic acid, including arecoline from areca and lobelia, and derivatives of both pyridine and pyrrolidine, including nicotine from tobacco.

Tropanes are formed by a condensation by pyrrolidine (5 sided ring containing nitrogen) and piperidine (6 sided ring containing nitrogen). Substances included in this class include the solanaceous alkaloids such as belladonna, byoscyamine (its isomer atropine), scopolamine (also known as hyoscine), hyoscyamus henbane, stramonium (jimson weed), and cocaine.

Quinolines alkaloids are obtained from cinchona: quinine, quinidine, cinchonine and cinchionidine; and anemonine.

Isoquinolines are found in alkaloids such as ipecac, hydrastis (golden seal), sanguinaria (bloodroot), tubocurarine, anhalonium (mescaline), and opium.

Indoles include such products as rauwolfia serpentina, nuxvomice, physostigma, and ergot.

Imidazoles contain a ring structure that forms the principal nucleus in pilocarpine from pilocarpus and in histamine from ergot.

Steroids are characterized by the cyclopenanophenanthrene nucleus. The important substances in this group include ginseng, veratrum viride, hellabore, aconite (monkshood), and larkspur.

Lupinanes have only one representative derived

to rabbits. Chopra quotes cases where extracts produced depressing effect on the heart, slowed the rate, and lessened the contractility of the myocardium.

Anthelmintics (Table 7) are agents to rid the body of worms and parasites.

Astringents (Table 8) are agents to contract organic tissue, thus reducing secretions.

Cathartics (Table 9) are agents to stimulate the evacuation of the bowel. (Sometimes they are called aperients.) An ancient herbal that possesses both of these properties is aloe vera. The medicinal uses are different for each of the two constituents of the plant "spike." However, these constituents are often not distinguished or considered in many herbal articles and literature.

The outer fibrous portion of the leaf provides the cathartic action. This is due to an irritant action upon the mucous membranes of the colon, thus stimulating peristalsis and an explosive stool. It is generally believed that aloe owes its purgative properties to the presence of one or more of three pentosides known as barbaloin (aloin), isobarbaloin, and betabarbaloin. Barbaloin is an anthraquinone glycoside and yields upon hydrolysis, d-arabinose, aloe-emodin and a reduction product, the anthranol aloe-emodin (Gathercoal 1936).

It is not recommended in those conditions in which it is desirable to clean the whole alimentary canal. It is contraindicated in inflammatory conditions of the intestine or in patients with hemorrhoids (Osol 1967).

The internal part of the spike contains a clear mucillaginous material that possesses astringent action. It is used in cosmetics to tighten the skin, particularly on the face. However, the duration of action is only for thirty minutes or less (Nielson 1981). The mucilaginous material is composed of mannuronic and glucuronic units and combines to form a polymer of high molecular weight.

One of the common uses of the aloe vera gel is to treat ulcers. Gastric mucin contains only glucuronic units in its carbohydrate moiety. The glucuronic acids are purported to be natural detoxicants and are released by hydrolytic cleavage of the gel. These components, at least in vitro, have an adherent property to mucous membranes and are purported to serve as a biochemical "bandage" to protect an ulcer from aggravating irritants.

Aloe vera contains high concentrations of tannins which are antiseptic in action. This, in combination with the adherant properties, may be the basis for its use in the treatment of burns. In the 1930s when crude X-ray techniques often resulted in painful and disfiguring keloids and burns, the fresh gel was used to promote healing of the injured tissue. Its astringent properties are also purported to be beneficial in soothing conjunctivitis.

In an evaluation of twenty-seven brands of aloe vera gel conducted by the author, it was found that only one brand actually separated the fibrous portion of the plant from the gelatinous

from scoparius.

Alkaloidal amines contain an aliphatic base with an aromatic nucleus. They include such compounds as tyramine (p-hydro-xyphenylethylamine) from ergot, ephedrine from ephedra, and colchicine from colchicum.

Purines do not occur as such in nature. Xanthine is 2,6-dioxypurine and since the alkaloids of this group are built on the xanthine structure, they are often called the xanthine derivatives. Caffeine is 1,3,7-trimethylxanthine, theophylline is 1,3-dimethylxanthine, and theobromine is 3,7-dimethylxanthine.

Miscellaneous alkaloids include several alkaloid-containing substances, but none are of great importance. Included are senecio, spigelia, passiflora, and corn silk.

Table 6—Alteratives

Plantain: Ribwort (Plantago major)
Clover (Trifolium pratense)
Pokeweed (Phytolacca decandra)
Burdock Root (Arctium lappa)
Chaparral; Creosote Bush (Larra tridentata)
Mountain/Oregon Grape (Bereris aquifolium)
Sassafras (Sassafras officinale)
Sarsaparilla (Smilax officinalis)
Coneflower (Echinacea augustifolia)
*Garlic (Allium sativum)

portion. Thus, adverse reactions may occur. Hypersensitivity has been shown, especially in combination with lanolin. It is contraindicated as an internal agent during the first trimester of pregnancy due to its cathartic action which may be abortifacient, and it possesses possible teratogenic effects. It may also cause severe cramping, diarrhea, nausea, and vomiting (Nielsen 1981).

Diaphoretics (Table 10) are agents to induce perspiration, thus promoting elimination.

Diuretics (Table 11) are agents to stimulate and increase the volume and secretion of urine.

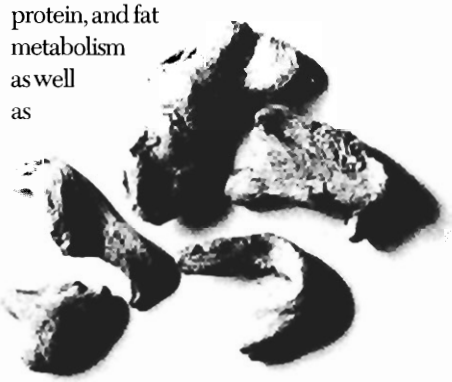
Emmenagogues (Table 12) are agents to promote proper menstruation and solve female complaints. A common herb from this category is ginseng. It was used in Oriental medicine as an adaptogenic or agent to help the patient adapt to stress. Currently the only recognized medical use in the United States is as a demulcent in topical ointments.

The pharmacological properties of ginseng appear to be due to a complex mixture of triterpanoid saponins. However, it also contains a 17-beta-hydroxylated steroid component which is similar to the androgens, estrogens, and progestins. The glycoside component has been differentiated into the panaxosides, the ginsenosides, and the chikusetsusaponins (Claus 1970).

Another study reported that ginseng has direct central stimulant effects and long-term use is associated with development of hypertension. An apparent paradoxical reaction of hypotension and tranquilization is probably due to dammarenetriol glycosides which possess central depressant action (Seigel 1979).

Seigel has proposed a Ginseng Abuse Syndrome which is comprised of hypertension together with nervousness, sleeplessness, skin eruptions, and morn-diarrhea. The syndrome appears to mimic those of corti-costeroid poisoning.

Other reported adverse reactions include interference with carbohydrate, protein, and fat metabolism as well as fluid, electrolyte, and water imbalance. As with all glucocorticoids it has direct action on the heart, kidneys, striated and smooth muscle, and the central nervous system (Stratton 1979).



Expectorants/Demulcents (Table 13) are agents to promote the expulsion of mucous from the respiratory tract. Comfrey is a very commonly used herb in this category. Many of the purported claims have been handed down in folk medicine for centuries, yet they do not have any medicinal basis. One of the more common claims it possesses the ability to knit together fractured bones.

Comfrey contains allantoin which was used in medicine prior to the antibiotic era to combat infections (Hart 1976). It was utilized as a 2 percent topical allantoin application. Due to the low and varible content of allantoin in the leaves of comfrey, it would require anywhere from eight ounces to eight pounds of dried comfrey leaves in a quart of water to formulate a preparation that would possess this pharmacologic action (Hart 1976).

Experimental evidence seems to indicate that the alkaloids present in comfrey may cause damage to the liver and the central nervous system (Hills 1976). Studies done on the pyrrolizidine alkaloids present in comfrey give evidence of an increased incidence of tumors of the liver in rats fed on a diet of 16 percent to 33 percent comfrey leaf or a 0.4 percent to 4 percent diet of comfrey root (Hills 1979). An Australian

Table 7—Anthelmintics

Wormwood (Artemisia absinthium)
Bear's Paw Root (Aspidium filixmas)
Pomegranate (Junies granatum)
Jerusalem Oak (Chenoodium anthelminticum)
Kousso (Brayero anthelmintica)
Bitter Buttons (Tanacatum vulgare)
Pumpkin Seeds (Cucurbita pepa)
Santonica (Artemisia santonicad)
Hyssop (Hyssopus officinalis)

Table 8—Astringents

°Aloe vera
Bayberry (Myrica cerifera)
Red Raspberry (Rubis idaeus)
Mullein (Verbascum thapsus)
White Poplar (Populus tremuloides)
Bistort; Snakeweed (Polygonum bistorta)
Tormentil; Septfoil (Potentilla termentilla)
Witch Hazel (Hamamelis virginiana)

Table 9—Cathartics

Cascara sagrada (Rhamnus purshiana)
Barberry (Berberis vulgaris)
Butternut Bark (Juglans cinerea)
Rhubarb (Rheum officinale)
Licorice (Glycyrrhiza glabra)
Mandrake; May Apple (Podophyllus peltatum)
Wahoo (Euonymus

authority warns against human or animal internal consumption of comfrey due to accumulating evidence of liver damage and carcinoma.

Nervine/Antispasmodics (Table 14) are agents to prevent or ease muscular or CNS convulsions or spasms, to relieve cramps, and to calm and soothe the nerves. A nervine that is considered by many to be the "master herb" is lobelia. One nineteenth century author wrote that, "its virtues are so prized by some that we are almost led to suppose that it is a sovereign remedy for all diseases that flesh and blood are heir to" (Fiedler 1975). It has been used medically as an expectorant. It has also been used parenterally in veterinary medicine as a respiratory stimulant. Currently it serves as a popular smoking deterrent when used orally in small doses.

Lobelia owes its activity to a variety of pyridine alkaloids which have been extensively investigated. These alkaloids are structurally and pharmacologically similar to nicotine. It was formerly believed that the drug produced paralysis of the motor nerve trunks, the peripheral vagi, and probably the respiratory and vasomotor centers as well. However, current knowledge shows that it works by blocking preganglionic cholinergic fibers.

Toxic manifestations start with nausea and vomiting, progress through stupor, tremors, and paralysis and terminate with convulsions, coma, and death. In one study it was reported that as little as 50 mg of dried herb or 1 ml of tincture of lobelia has produced these effects.

Lobelia is one of the constituents of "legal grass" that has been advertised by some "dope magazines." This mixture is advertised for weight loss, which may actually occur, since most individuals do not eat much while nauseated.

The FDA has declared lobelia, along with twenty-six other plants, as "unsafe herbs."

They describe it as "a poisonous plant which contains the alkaloid lobeline, plus a number of other pyridine alkaloids. Overdoses of the plant or extracts of the leaves or fruits produce vomiting, sweating, pain, paralysis, depressed temperatures, rapid but feeble pulse, collapse, coma, and death in the human being" (Weiner 1980).

Stimulants (Table 15) are agents to quicken physiological activity and one of the most commonly used stimulants is cayenne. There are many varieties of the capsicum fruit, yet all are utilized as counterirritants. A counterirritant may be defined as an agent which produces a superficial irritation intended to relieve some other irritation. They are applied topically to cause capillary dilation thus increasing blood flow through surface tension. Capsicum has been used medically for this purpose in OTC products for rheumatism and neuralgias.

The effects of capsaicin (the active constituent in capsicum) have been variously attributed to its phenolic nature and the presence of volatile oils. Its actual action, however, is not clearly understood as most, if not all, studies conducted have been on subjects unaccustomed to capsaicin.

Tyler (1977) says, pharmacologically, capsaicin is an irritant on the skin and mucous membranes, increases the saliva, excites a sensation of warmth in the stomach, promotes appetite and digestion, and stimulates the action of the heart. It is a general stimulant to the nervous system but in repeated doses produces a slight narcotic effect upon the brain.

It has been shown that capsaicin

atropurpureus)
Balm of Gilead (Pupulus balsamifera)
Balmony (Chelone glabra)
Dogbane (Apocynum andros emilfolium)

Table 11—Diuretics

Parsley (Carum petroselium)
Juniper Berry (Juniperus communis)
Gravelroot (Eupatorium purpureum)
Uva Ursi; Bearberry (Arctostaphylos uva-ursi)
Carrot, wild (Daucus carota)
Carrot, garden (Oxheart Chatenay, type)
Clivers (Galium aparine)
Buchu (Barosma betulina)
Burdock Seeds (Arctium lappa)

Table 10—Diaphoretics

Yarrow (Achillea millefolium)
Camomile (Anthemis nobilis)
Pleurisy Root (Asclapias tuberosa)
Boneset (Eupatorium perfoliatum)
Thistle (Carbenia benedicta)
Thyme (Thymus vulgaris)
Hyssop (Hyssopus officinalis)
Sage (Salva officinalis)
Catnip (Nepeta cataris)
Spearmint (Menthaviridis)

Table 12—Emmenagogues

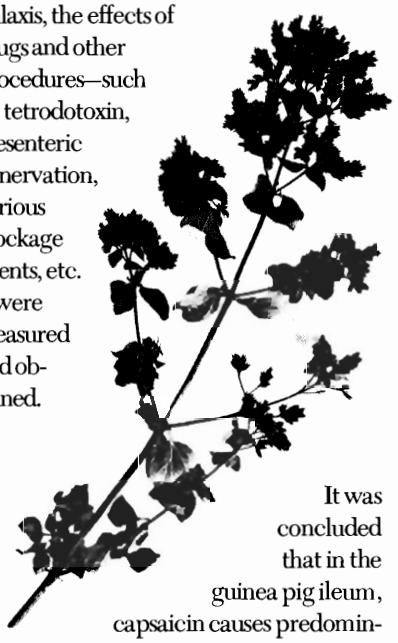
Squaw Vine (Mitchella repens)
Tansy; Bitter Buttons (Tanacetum vulgare)
Pennyroyal (Mentha pelegium)
Thistle
Helonias (Chamalirium lutem)
Cranberry/High (Viburnum opulus)
Colicroot (Aletris farinosa)
Blue Cohosh (Caulophyllum thalictroides)
Rue (Ruta graveoleus)
Motherwort (Leonusus cardiaca)
*Ginseng

exerts a stimulating influence upon gastric secretion of hydrochloric acid (Ketusinh 1966). This increased gastric acidity is believed to be one of the etiologic factors of gastrointestinal disorders (Limlowongse 1979). This increased acidity may also be one possible explanation for the use of capsicum as an aid to digestion. Changes in free acidity after administration of capsicum solution followed an upward trend. In all cases the acidity was still rising at the end of two hours. The mechanism involved, however, remains to be clarified (Ketusinh 1966).

Besides direct stimulatory action in acidic secretion it has been demonstrated that there is increased euglobulin lysis time in healthy persons (familiar with hot foods) after the ingestion of chilies. Euglobulin lysis time was significantly decreased immediately after the test meal with two teaspoons of fresh ground capsicum frutescens. Capsaicin was also reported to increase gastrointestinal motility (Limlowongse 1979). Both of these also being a possible aid in digestion. The observation that intake of capsaicin is followed by an improved digestion and peristalsis is a perplexing one because the mechanism of this phenomenon is still unknown (Bartho 1978).

Bartho and his associate conducted research as to the role of neural elements in the capsaicin effect on the guinea-pig isolated ileum (Bartho 1978). They observed that capsaicin caused contraction of the isolated ileum, and that repeated exposures resulted in a rapid and long-lasting tachphylaxis, the degree being directly related to the concentration applied and contact time.

Following this marked tachyphlaxis, the effects of drugs and other procedures—such as: tetrodotoxin, mesenteric denervation, various blockage agents, etc. —were measured and obtained.



It was concluded that in the guinea pig ileum, capsaicin causes predominantly cholinergic contractions by stimulating terminals of extrinsic, nonparasympathetic nerves. The question arises: how can a cholinergic transmission participate in the effect of capsaicin if the stimulated extrinsic nerves are not parasympathetic (Bartho 1978)?

Bartho (1978) reiterates the classical concept that parasympathetic nerves mediate cholinergic responses while sympathetic nerves, except those which innervate the sweat glands and some vascular beds are responsible for adrenergic effects. If perivascular nerves running to an isolated segment of the mammalian intestine are stimulated, an adrenergic inhibition of the motility of the gut occurs (Bartho 1978). It has been found that treatment with different adrenergic neuron blocking agents or at low frequency of stimulation on untreated preparations is cholinergic, at least in the rabbit and guinea pig. Other studies show possible existence of a cholinergic link in adrenergic transmission process (Bartho 1978).

Tonics (Table 16) are agents to restore and strengthen all systems and organs of the body. Goldenseal, a common tonic, contains three isoquinolone alkaloids, hyrastine, berberine, and canadine. Goldenseal also contains a volatile oil, flourescent compound, gums, fat, starch, and sugar.

Goldenseal has been utilized in eyewashes. Berberine is bacteriocidal and protozoacidal and its mechanism of action is to interact with DNA. Berberine is reported to complex with supercoiled mitochondrial DNA, producing conformational changes and

Table 13—Expectorants/Demulcents

- °Comfrey (Symphytum officinale)
- Mulleiln (Verbascum thapsus)
- Chickweed (Stellaria media)
- Marshmallow (Althea officinalis)
- Slippery Elm (Ulmus fulva)
- Elecampane (Inula helenium)
- Horehound (Marubium vulgare)
- Cherry, wild (Prunus virginiana)
- Licorice (Glycyrrhize glabra)
- Hollyhock (Althea rosea)

Table 14—Nervine/Antispasmodics

- °Lobelia (Lobelia inflata)
- Skullcap (Scutellaria lateriflora)
- Valerian (Valeriana officinalis)
- Mistletoe (Viscum album)
- Wood Betony (Betonica officinalis)
- Hops (Humulus lupulus)
- Black Coshosh (Cimicifuga racemosa)
- Yam, wild; Colicroot (Discorea villosa)

Table 15—Stimulants

- °Cayenne (Capsicum minimum)
- Guarana
- Ginger, Jamaica (Zingiber officinale)
- Virginia Snake Root (Aristolocia serpentaria)
- Peppermint (Mintha peperita)
- Cloves (Cochlearia armoracia)
- Pepper, black (piper nigrum)
- Prickley Ash (Zanthoxylum americanum)

Table 16—Tonics

- Barberry (Berberis vulgaris)
- Calumga (Jateorhiza palmata)
- °Golden Seal (Hydrastis canadensis)
- Peruvian Bark (Cinchona calisaya)
- Poplar, White (Populus tremuloides)
- Thistle
- Myrrh (Commiphora myrrha)
- Balmony (Chelone glabra)
- Gentian (Gentiana lutea)
- Helonias (Chamalirium lutem)

disrupting DNA structure. Since bacteria do not have mitochondria the mechanism of action is different. Canadine is said to operate by hypotensive mechanisms. Toxic symptoms are reported to be the same as strychnine or nux vomica. The symptoms include difficult breathing, suffocation, muscular rigidity, convulsions, and ultimately death. The oral LD_{50} for canadine is 940 mg/Kg.

In spite of the fact that plants have been used for therapeutic purposes for millennia, only a relatively few plants or plant derivatives are currently officially recognized in the United States as effective drugs. This is largely due to the difficulties encountered in plant-drug research and the limitations of scientific methodology employed. Quite often, premature publicity on unconfirmed research data has tainted the reputation of many botanical drugs. Most drug plants have complicated chemical compositions and analytical technology has not been adequate in determining their identities and qualities once extracts are made from them. In addition, adulteration, sophistication, or inconsistencies in potency has made the determination of toxicology and pharmacology difficult. As a result, many natural products have probably been removed from officially recognized status.

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