CHAPTER 2

2. PLANTS IN MEDICINE

2.1 APPROACHES TO PLANT-DERIVED DRUG DEVELOPMENT

2.1.1 Brief history

Fossils of plants date back as early as 3.2 billion years ago. These plants provided the foundation upon which animal life and later, human life were based on. They provide bodybuilding food and calories as well as vitamins essential for metabolic regulation. Plants also yield active principles employed as medicines [Shultes, 1992].

Finding healing powers in plants is an ancient idea. Hundreds, if not thousands, of indigenous plants have been used by people on all continents as poultices and infusions dating back to prehistory. There is evidence of Neanderthals, living 60 000 years ago in present-day Iraq, using hollyhock (*Alcea rosea* L.), which is still in ethnomedicinal use around the world today [Cowan, 1999]. The Bible offers descriptions of at least 30 healing plants of which frankincense (*Boswellia sacra* L.) and myrrh (*Commiphora myrrha* L.) were employed as mouthwashes due to their reported antiseptic properties.

The fall of ancient civilisations resulted in the destruction or loss of much of the documentation of plant pharmaceuticals but many cultures continued in the excavation of the older works as well as building upon them. Native Americans were reported to have used 1625 species of plants as food while 2564 found use as drugs, while the Europeans started turning towards botanicals when treatment in the 1800s became dangerous and ineffective [Cowan, 1999]. Today some 1500 species of medicinal and aromatic plants are widely used in Albania, Bulgaria, Croatia, France, Germany, Hungary, Spain, Turkey and the United Kingdom [Hoareau, 1999].

2.1.2 Secondary plant compounds

So why have plants been so widely used in the treatment of disease? And how would plant chemicals kill human and animal pathogens and influence immune systems, hormonal balances, organs and cells of the body?

Living organisms, whether they are plants, animals or microbes, are all made up of basically the same chemical components. Comparative biochemistry has shown that minor or major modifications of chemical processes have been evolved by different organisms to suit their particular requirements [Goodwin and Mercer, 1983]. Chemical compounds have been extensively used in plant systematics and two major categories of systematically useful chemical compounds can be recognised: secondary metabolites, which perform non-essential functions in the plant, and the information containing proteins, DNA and RNA.

Most secondary compounds function in defence against predators and pathogens, as allelopathic agents or attractants in pollination and seed dispersion. The major categories are discussed briefly below.

2.1.2.1 Terpenoids

Terpenoids are a large and structurally diverse group of secondary compounds that are important in numerous biotic interactions. They are widely distributed and many have primary physiological functions, either forming part of membrane-bound steroids, carotenoid pigments, side-chain of chlorophyll and the hormones giberellic acid and abcisic acid. Volatile monoterpenoids are the major components of essential oils and often function as floral odour glands [Goodwin and Mercer, 1983]. More information regarding these compounds is discussed in chapter 3.

2.1.2.2 Alkaloids

Cinchona alkaloids present in the bark of *Cinchona* spp. have quinine as their main constituent, known since 1630 for its antimalarial properties. All alkaloids contain nitrogen, which frequently forms part of a heterocyclic ring and make them basic in nature. Widespread distribution in all parts of plants has stimulated searches for a function of these compounds in the general metabolism of plants. These compounds offer protection against predators, act as growth regulators, maintain ionic balance, act as a nitrogen reserve and possibly serve as nitrogen excretion products [Goodwin and Mercer, 1983].

2.1.2.3 Flavonoids

These represent a widespread group of water-soluble phenolic derivatives, many of which are brightly coloured. At least nine classes of flavonoids are recognised and are of great interest in phytochemistry. They probably function in defence against herbivores and in regulation of auxin transport. Attraction of insects and birds also play an important role in seed dispersal and pollination [Goodwin and Mercer, 1983].

2.1.2.4 Others

Stilbenes and tannins are both synthesised via the same pathway resulting in isoflavones and other phenolic metabolites [Figure 8.1]. These compounds are used by plants as growth inhibitors and antimicrobial compounds [Goodwin and Mercer, 1983].

2.1.3 The birth of pharmacology

Natural products have been used to elucidate physiological processes and even define them, hence the naming of ‘nicotinic’ and ‘muscarinic’ receptors and even more recently ‘endorphins’ from ‘endogenous morphines’. Natural products are the basis of many standard drugs used in modern medicine and are so widely used that even some members of the medical profession are not aware of their plant origin. Some of the newer pharmacological tools such as colforsin (an adenyl cyclase stimulator), ginkgolide B (a specific platelet activating factor (PAF) antagonist) and phorbol esters that activate proteinkinase C, are at the forefront of biochemical research and are obtainable only from plant sources [Williamson, 1996].

Although medicinal plants may not always lead to the discovery of novel compounds which may be employed in the treatment or cure of disease, plants may give valuable insight into the pathology of diseased conditions or the disturbed human mind. Hallucinogenic plants have been thought to transport the mind to realms of ethereal wonder and some were even considered to be gods. It is only recently, the past twenty years, that modern westernised societies have realised the significance of these plants in shaping the history of primitive and even advanced cultures. Some of these plants contain chemicals capable of inducing visual, auditory, tactile, olfactory and gustatory hallucinations or causing artificial psychoses and the question is whether a thorough understanding of the chemical composition of these drugs may lead to discovery of new drugs for the treatment of psychiatric conditions. As a result of the complexity of the human brain and central nervous system, psychiatry has not developed as rapidly as other fields of medicine, mainly due to the lack of adequate tools, therefore these drugs may provide the necessary pharmacological tools for the discovery of more appropriate and effective drugs [Shultes, 1992].

Although the first chemical substance to be isolated from plants was benzoic acid in 1560, the search for useful drugs of known structure did not begin until 1804 when morphine was separated from *Papaver somniferum* L. (Opium). Since then many drugs from higher plants have been discovered but less than 100 of defined structure are in common use today. Less than half of these are accepted as useful drugs in industrialized countries [Farnsworth, 1984].

Table 2.1: Plant-derived drugs widely employed in Western medicine (Adapted from Farnsworth, 1984]

Acetyldigoxin	Ephedrine*	Pseudoephedrine*
Aescin	Hyoscyamine	Quinidine
Ajmalicine	Khellin	Quinine
Allantoin*	Lanatoside C	Rescinnamine
Atropine	Leurocristine	Reserpine
Bromelain	α-Lobeline	Scillarens A & B
Caffeine*	Morphine	Scopolamine
Codeine	Narcotine	Sennosides A & B
Colchicine	Ouabain	Sparteine
Danthron*	Papain	Strychnine
Deserpidine	Papaverine*	Tetrahydrocannabinol
Digitoxin	Physostigmine	Theobromine*
Digoxin	Picrotoxin	Theophylline*
L-Dopa*	Pilocarpine	Tubocurarine
Emetine	Protoveratrines A & B	Vincaleukoblastine
		Xanthotoxin

* Produced industrially by synthesis

Less than 10 of these well-established drugs are produced commercially by synthesis although laboratory synthesis has been described for most of them [Farnsworth, 1984].

In 1875 a folk healer told the English physician William Withering that the leaves of *Digitalis purpurea* L. were useful for treating dropsy, a swelling of the body caused by inadequate pumping action of the heart. In an effort to standardise the dosage, he began to administer water infusions of leaves and later ground leaf powder.

Since then more than 30 cardiac glycosides have been isolated from *D. purpurea*. Withering's success in translating folk knowledge into new pharmaceuticals is not unique. Of all plant-derived drugs listed in Samuelsson [1992], at least 50 were derived from ethnobotanical leads [Table 2.2). Farnsworth [1990] estimated that there are at least 88 ethnobotanically derived drugs [Cox, 1994].

Plants seem to have served as models in drug development for 3 reasons. Firstly at least 25% of all prescriptions contain active principles extracted from higher plants, which has persisted for at least the last 25 years [Farnsworth & Morris 1976, Farnsworth 1982b] and as many as two-thirds of people in developing countries rely on plants as sources of drugs [Farnsworth, 1984]. Secondly, biologically active substances derived from plants may have poor pharmacological or toxicological profiles for use in humans per se. They can, however serve as templates for synthetic modification and structure-function studies with anticipation of useful drugs in man will result. Thirdly, many secondary, highly active, plant constituents are found to be useful in studying biological systems and disease processes.

2.1.4 Current developments

The rationale for studying plants as traditional medicines is that 80% of 5200 million people live in less developed countries. The WHO estimates that 80% of these people rely almost exclusively on traditional medicine for their primary health care needs. Since medicinal plants are the 'backbone" of traditional medicine, this means that more than 3300 million people utilize medicinal plants on a regular basis. [Farnsworth, 1994].

It cannot be denied that higher plants have yielded many useful drugs to alleviate the medical problems facing the World's population. In 1985, Farnsworth identified 119 secondary metabolites isolated from higher plants that were being used globally as drugs [Table 2.2][Farnsworth, 1990]. About 75% of these drugs have the same or related uses as the plant from which they were discovered. These 119 useful

drugs are still obtained commercially for the most part by extraction from only about 90 species of plants. With more than 250 000 species of higher plants more useful drugs remain to be discovered.

There is a great demand and potential for medicinal plant research as shown by the growing market in medicinal herbs. They are high in value, low in shipping volume, popular with the public interested in natural products and strong competitors for synthetic drugs developed at high costs.

In 1980 the consumer paid about $ 8.0 billion for prescription drugs in which the active principles were derived from plants [Farnsworth & Morris, 1976, Farnsworth 1982b]. Dollar values from 1994 also provide strong support: $6.5 billion in Europe, $2.1 billion in Japan, $2.3 billion in the rest of Asia and $1.5 billion in North America. It is estimated that medicinal plants are therefore a $12 billion market and expected to increase for another 10 or 20 years [http://www.bizjournals]. In spite of this, not a single pharmaceutical manufacturer in the United States had a serious research program designed to discover new drugs from the plant kingdom at that stage [Farnsworth, 1984].

In developed countries, the cost of taking a drug from the discovery stage to the market place can exceed $50 million and span a period of several years. The industry is therefore reluctant to invest in the development of any drug when its investment cannot be recovered.
Failure of many programs to produce useful drugs after several years of intensive effort and millions of dollars, signals to many that plants are an uninteresting source of useful drugs [Farnsworth, 1984].

In spite of the widespread usage of plants and plant products, there is often no evidence to support their use. No clear rationale is proposed for most product use over the traditional beliefs and superstition and therefore a scientific explanation is warranted.

Table 2.2: Fifty drugs discovered by ethnobotanical leads [Farnsworth, 1990]

Drug	Medical use	Plant Source
Ajmaline	Heart arrhythmia	Rauvolfia spp.
Aspirin	Analgesic, anti-inflammatory	Filipendula ulmaria
Atropine	Pupil dilator	Atropa belladonna
Benzoin	Oral disinfectant	Styrax tonkinensis
Caffeine	Stimulant	Camellia sinensis
Camphor	Rheumatic pain	Cinnamomum camphora
Cascara	Purgative	Rhamnus purshiana
Cocaine	Ophthalmic anaesthetic	Erythoxylum coca
Codeine	Analgesic, antitussive	Papaver somniferum
Colchicine	Gout	Colchicium autumnale
Demecoline	Leukaemia, lymphomata	C. autumnale
Deserpidine	Antihypertensive	Rauvolfia canescens
Dicoumarol	Antithrombotic	Melilotus officinalis
Digoxin	Atrial fibrillation	Digitalis purpurea
Digitoxin	Atrial fibrillation	D. purpurea
Emetine	Amoebic dysentery	Psychotria ipecacuanha
Ephedrine	Bronchodilator	Ephedra sinica
Eugenol	Toothache	Syzygium aromaticum
Gallotanins	Haemorrhoid suppository	Hamamelis virginia
Hyoscamine	Anticholinergic	Hyoscyamus niger
Ipecac	Emetic	Psychotria ipecacuanha
Ipratropium	Bronchodilator	H. niger
Morphine	Analgesic	Papaver somniferum
Noscapine	Antitussive	P. somniferum
Papain	Attenuator of mucous	Carica papaya
Papaverine	Antispasmodic	Papaver somniferum
Physostigmine	Glaucoma	Physostigma venenosum
Picrotoxin	Barbiturate antidote	Anamirta cocculus
Pilocarpine	Glaucoma	Pilocarpus jaborandi
Podophyllotoxin	Condyloma acuminatum	Podophyllum peltatum
Proscillaridin	Cardiac malfunction	Drimia maritima
Protoveratrine	Antihypertensive	Veratrum album
Pseudoephedrine	Rhinitis	E. sinica
Psoralen	Vitiligo	Psoralea corylifolia
Quinine	Malaria prophylaxis	Cinchona pubescens
Quinidine	Cardiac arrhythmia	C. pubescens
Rescinnamine	Antihypertensive	R. serpentia
Reserpine	Antihypertensive	R. serpentia
Sennosides A,B	Laxative	Cassia angustifolia
Scopolamine	Motion sickness	Datura stramonium
Sigma sterol	Steroidal precursor	Physostigma venenosum
Strophanthin	Congestive heart failure	Strophanthus gratus
Tubocurarine	Muscle relaxant	Chondrodendron tomentosum
Teniposide	Bladder neoplasms	Podophyllum peltatum
Tetrahydrocannibinol	Antiemetic	Cannabis sativa
Theophylline	Diuretic, antiasthmatic	Camellia sinensis
Toxiferine	Relaxant in surgery	Strychnos guianensis
Vinblastine	Hodgkin’s disease	Catharanthus roseus
Vincristine	Paediatric leukaemia	C. roseus
Xanthotoxin	Vitiligo	Ammi majus

Table 2.3: Number of records of worldwide medicinal plant uses according to NAPRALERT

Induce menstruation	4110	Epilepsy	299
Induce abortion	2630	Genitourinary problems	298
Reduce inflammation	1879	Kills fish	294
Prevent post-partum bleeding	1547	Insecticide	289
Bacterial diseases	1521	Vermifuge	265
Induce diuresis	1327	High blood pressure	264
Reduce fever	1299	Induce vomiting	260
Impotence	1275	Induce perspiration	255
Pain relief	1255	Snake and spider bites	250
Contraception	1249	Cardiotonic	224
Laxative / cathartic	1032	Flatulence	214
Diarrhoea	922	Produces hallucinations	213
Antihelmitinic	867	Tuberculosis	178
Antispasmodics	856	Prevents vomiting	146
General tonics	749	Treponema infections	145
Jaundice / liver disease	733	Haemorrhoids	145
Stimulate lactation	629	Fungal infections	142
Suppress cough	621	Emollient	118
Dysmenorrhoea	620	Narcotic	115
Sedative	606	Stomach ulcers	110
Accelerates wound healing	576	Increases bile flow	107
Malaria	565	Schistosomiasis	101
Cancer	552	Flu symptoms	98
Digestive aids	540	Tapeworm	91
Diabetes	514	Stimulates hair growth	84
Expectorant	473	Bitters (appetite stimulant)	80
Fertility promotion	432	Dissolves kidney stones	79
Food products	414	Anticoagulant	78
Asthma	410	Haematinics	71
Astringent	380	Burn wounds	70
Haemostatic	323	Caustic	67
Central nervous system stimulant	321	Prevents miscarriage	63
Viral infections	315	Insect repellent	62

2.2 PLANTS AS A SOURCE OF ANTIBIOTICS

Plants have developed an arsenal of weapons to survive attacks by microbial invasion. These include both physical barriers as well as chemical ones, i.e. the presence or accumulation of antimicrobial metabolites. These are either preformed in the plant (prohibitins) or induced after infection, the so-called phytoalexins. Since phytoalexins can also be induced by abiotic factors such as UV irradiation, they have been defined as ‘antibiotics formed in plants via a metabolic sequence induced either biotically or in response to chemical or environmental factors’.

When an infection or damage to a plant takes place, a number of processes are activated and some of the compounds produced become activated immediately whereas phytoalexins take two to three days to produce. Sometimes it is difficult to determine whether the compounds are phytoalexins or prohibitins and moreover, the same compound may be a preformed antimicrobial substance in one species and a phytoalexin in another [Grayer and Harborne, 1994]. The chemical class in which these substances can be found varies greatly as can be seen in Table 2.4, which makes the isolation thereof even more intriguing.

Since the advent of antibiotics in the 1950s, the use of plant derivatives as antimicrobials has been virtually non-existent but that pace is rapidly on the increase as we begin to realise the need for new and effective treatments. The worldwide spending on finding new anti-infective agents is expected to increase 60% from 1993 and plant sources are especially being investigated. A summary of useful antimicrobial phytochemicals is given in Table 2.4 [Cowan, 1999].

Table 2.4: Plants containing antimicrobial activity [Adapted from Cowan, 1999]

Common name	Scientific name	Compound	Class	Activity[d]	R.T[b]
Alfalfa	Medicago sativa	?		Gram-positive	2.3
Allspice	Pimenta dioica	Eugenol	Essential oil	General	2.5
Aloe	Aloe barbadensis, Aloe vera	Latex	Complex mixture	*Corynebacterium*, *Salmonella*, *Streptococcus*, *S. aureus*	2.7
Apple	Malus sylvestris	Phloretin	Flavonoid derivative	General	3.0
Ashwagandha	Withania somniferum	Withafarin A	Lactone	Bacteria, fungi	0.0
Aveloz	Euphorbia tirucalli	?		*S. aureus*	0.0
Bael tree	Aegle marmelos	Essential oil	Terpenoid	Fungi	
Balsam pear	Mormordica charantia	?		General	1.0
Barberry	Berberis vulgaris	Beriberine	Alkaloid	Bacteria, protozoa	2.0
Basil	Ocimum basilicum	Essential oils	Terpenoids	Salmonella, bacteria	2.5
Bay	Laurus nobilis	Essential oils	Terpenoids	Bacteria, fungi	0.7
Betel pepper	Piper betel	Catechols, eugenol	Essential oils	General	1.0
Black pepper	Piper nigrum	Alkaloid	Alkaloid	Fungi, Lactobacillus, Micrococcus, *E. coli*, *E. faecalis*	1.0
Blueberry	Vaccinium spp.	Fructose	Monosaccharide	*E. coli*	
Brazilian pepper	Schinus terebinthifolius	Terebinthone	Terpenoids	General	1.0
Buchu	Barosma setulina	Essential oil	Terpenoid	General	2.0
Burdock	Articum lappa		Polyacetylene, tannins, terpenoids	Bacteria, fungi, viruses	2.3
Buttercup	Ranunculus bulbosus	Protoanemonin	Lactone	General	2.0
Caraway	Carum carvi		Coumarins	Bacteria, fungi, viruses	
Cascara sagrada	Rhamnus purshiana	Tannins	Polyphenols Anthraquinone	Bacteria, fungi, viruses	1.0
Cashew	Anacardium pulsatilla	Salicylic acids	Polyphenols	*P. acnes*, bacteria, fungi	
Castor bean	Ricinus communis	?		General	0.0
Ceylon cinnamon	Cinnamomum verum	Essential oils, others	Terpenoids, tannins	General	2.0 2.3
Chamomile	Matricaria chamomilla	Anthemic acid	Phenolic acid	*M. tuberculosis*, *S. typhimurium*, *S. aureus*, helminths	
Chapparal	Larrea tridentata	Nordihydroguaiarti acid	Coumarins Lignan	Viruses Skin bacteria	2.0
Chili peppers	Capsicum annuum	Capsaicin	Terpenoid	Bacteria	2.0
Clove	Syzygium aromaticum	Eugenol	Terpenoid	General	1.7
Coca	Erythroxylum coca	Cocaine	Alkaloid	Gram-negative and positive cocci	0.5
Cockle	Agrostemma githago	?		General	1.0
Coltsfoot	Tussilago farfarva	?		General	2.0
Coriander, cilantro	Coriandrum sativum	?		Bacteria, fungi	
Cranberry	Vaccinium spp.	Fructose Other	Monosaccharide	Bacteria	
Dandelion	Taraxacum officinale	?		*C. albicans*, *S. cerevisiae*	2.7
Dill	Anethum graveolens	Essential oil	Terpenoid	Bacteria	3.0
Echinacea	Echinaceae angustifolia	?		General	
Eucalyptus	Eucalyptus globulus	Tannin -	Polyphenol Terpenoid	Bacteria, viruses	1.5
Fava bean	Vicia faba	Fabatin	Thionin	Bacteria	
Gamboge	Garcinia hanburyi		Resin	General	0.5
Garlic	Allium sativum	Allicin, ajoene	Sulfoxide Sulphated terpenoids	General	
Ginseng	Panax notoginseng		Saponins	*E. coli*, *Sporothrix schenckii*, *Staphylococcus*, *Trichophyton*	2.7
Glory lily	Gloriosa superba	Colchicine	Alkaloid	General	0.0
Goldenseal	Hydrastis candensis	Berberine, hydrastine	Alkaloids	Bacteria, *Giardia duodenale*, trypanosomes Plasmodia	2.0
Gotu kola	Centella asiatica	Asiatocoside	Terpenoid	*M. leprae*	1.7
Grapefruit peel	Citrus paradisa		Terpenoid	Fungi	
Green tea	Camellia sinensis	Catechin	Flavonoid	General, *Shigella*, *Vibrio*, *S. mutans*, viruses	2.0
Harmel, rue	Peganum harmala	?		Bacteria, fungi	1.0
Hemp	Cannabis sativa	β-Resercyclic acid	Organic acid	Bacteria and viruses	1.0
Henna	Lawsonia inermis	Gallic acid	Phenolic	*S. aureus*	1.5
Hops	Humulus lupulus	Lupulone, humulone	Phenolic acids (Hemi)terpenoids	General	2.3
Horseradish	Armoracia rusticana	-	Terpenoids	General	
Hyssop	Hyssopus officinalis	-	Terpenoids	Viruses	
(Japanese) herb	Rabdosia trichocarpa	Trichorabdal A	Terpene	*Helicobacter pylori*	
Lantana	Lantana camara	?		General	1.0
-	Lawsonia	Lawsone	Quinone	*M. tuberculosis*	-
Lavender-cotton	Santolina chamaecyparissus	?		Gram positive bacteria, Candida	1.0

Legume	Millettia thonningii	Alpinumisoflavone	Flavone	Schistosoma	
Lemon balm	Melissa officinalis	Tannins	Polyphenols	Viruses	
Lemon verbena	Aloysia triphylla	Essential oil	Terpenoid	Ascaris	1.5
			?	E.*coli*, *M. tuberculosis*, *S. aureus*	
Licorice	Glycyrrhiza glabra	Glabrol	Phenolic alcohol	*S. aureus*, *M. tuberculosis*	2.0
Lucky nut (yellow)	Thevetia peruviana	?		Plasmodium	0.0
Mace, nutmeg	Myristica fragrans	?		General	1.5
Marigold	Calendula officinalis	?		Bacteria	2.7
Mesquite	Prosopis juliflora	?		General	1.5
Mountain tobacco	Arnica montana	Helanins	Lactones	General	2.0
Oak	Quercus rubra	Tannins	Polyphenols		
		Quercetin (available commercially)	Flavonoid		
Olive oil	Olea europaea	Hexanal	Aldehyde	General	
Onion	Allium cepa	Allicin	Sulfoxide	Bacteria, Candida	
Orange peel	Citrus sinensis	?	Terpenoid	Fungi	
Oregon grape	Mahonia aquifolia	Berberine	Alkaloid	Plasmodium, Trypanosomes, general	2.0
Pao d'arco	Tabebuia	Sesquiterpenes	Terpenoids	Fungi	1.0
Papaya	Carica papaya	Latex	Mix of terpenoids, organic acids, alkaloids	General	3.0
Pasque-flower	Anemone pulsatilla	Anemonins	Lactone	Bacteria	0.5
Peppermint	Mentha piperita	Menthol	Terpenoid	General	
Periwinkle	Vinca minor	Reserpine	Alkaloid	General	1.5
Peyote	Lophophora williamsii	Mescaline	Alkaloid	General	1.5
Poinsettia	Euphorbia pulcherrima	?		General	0.0
Poppy	Papaver somniferum	Opium	Alkaloids and others	General	0.5
Potato	Solanum tuberosum	?		Bacteria, fungi	2.0
Prostrate knotweed	Polygonum aviculare	?		General	2.0
Purple prairie clover	Petalostemum	Petalostemumol	Flavonol	Bacteria, fungi	
Quinine	Cinchona sp.	Quinine	Alkaloid	*Plasmodium* spp.	2.0
Rauvolfia	Rauvolfia serpentina	Reserpine	Alkaloid	General	1.0
Rosemary	Rosmarinus officinalis	Essential oil	Terpenoid	General	2.3
Sainfoin	Onobrychis viciifolia	Tannins	Polyphenols	Ruminal bacteria	
Sassafras	Sassafras albidum	?		Helminths	2.0
Savory	Satureja montana	Carvacrol	Terpenoid	General	2.0
Senna	Cassia angustifolia	Rhein	Anthraquinone	*S. aureus*	2.0
Smooth hyrangea, seven barks	Hydrangea arborescens	?		General	2.3
Snakeplant	Rivea corymbosa	?		General	1.0
St. John's wort	Hypericum perforatum	Hypericin, others	Anthraquinone	General	1.7
Sweet flag,calamus	Acorus calamus	?		Enteric bacteria	0.7
Tansy	Tanacetum vulgare	Esssential oils	Terpenoid	Helminths, bacteria	2.0
Tarragon	Artemisia dracunculus	Caffeic acids, tannins	Terpenoid Polyphenols	Viruses, helminths	2.5
Thyme	Thymus vulgaris	Caffeic acid	Terpenoid	Viruses, bacteria, fungi	2.5
		Thymol	Phenolic alcohol		
		Tannins	Polyphenols		
		-	Flavones		
Tree bard	Podocarpus nagi	Totarol	Flavonol	*P. acnes*, other Gram-positive Bacteria	
		Nagilactone	Lactone	Fungi	
Tua-Tua	Jatropha gossyphiifolia	?		General	0.0
Tumeric	Curcuma longa	Curcumin	Terpenoids	Bacteria, protozoa	
		Turmeric oil			
Valerian	Valeriana officinalis	Essential oil	Terpenoid	General	2.7
Willow	Salix alba	Salicin	Phenolic glucoside		
		Tannins	Polyphenols		
		Essential oil	Terpenoid		
Wintergreen	Gaultheria procumbens	Tannins	Polyphenols	General	1.0
Woodruff	Galium odoratum	-	Coumarin	General, viruses	3.0
Yarrow	Achillea millefolium	?		Viruses, helminths	2.3
Yellow dock	Rumex crispus	?		*E. coli*, *Salmonella*, *Staphylococcus*	1.0

[b] Relative toxicity: 0, very safe; 3, very toxic

[d] "General" denotes activity against multiple types of microorganisms (e.g. bacteria, fungi and protozoa) and "bacteria" denotes activity against Gram-positive and Gram-negative bacteria.

Literally thousands of phytochemicals with inhibitory effects on microorganisms have been found to be active *in vitro*. One may argue that these compounds have not been tested *in vivo* and therefore activity cannot be claimed but one must take into consideration that many, if not all, of these plants have been used for centuries by various cultures in the treatment of disease. Another argument could possibly be that at very high concentrations, any compound is likely to inhibit the growth of microorganisms. Firstly if this is the case, the high concentrations required would no doubt have serious side-effects on the patient unfortunate enough to contract an illness and secondly, these compounds are compared with those of standard antibiotics already available on the market. This means that the concentrations used must compare favourably to those that have already passed the test.

Asiaticoside, an antimicrobial compound isolated from *Centella asiatica* (used traditionally in skin diseases and leprosy), has been studied in normal as well as delayed-type wound healing. The results indicated significant wound healing in both models [Shukla, 1999]. Another compound, cryptolepine, isolated from *Cryptolepis sanguinolenta* and active against *Campylobacter* species, has been used traditionally in Guinea Bissau in the treatment of hepatitis and in Ghana for the treatment of urinary and upper respiratory tract infections and malaria [Paulo, 1994]. The debate continues…

Preliminary screening tests performed by Noristan scientists on a number of plants species resulted in the finding that *Combretum erythrophyllum* had antimicrobial activity but due to changes in company policy no further work was performed. A comprehensive study into this family and specie was therefore initiated to determine whether there was activity and whether these compounds could be isolated. This is discussed in further detail in chapter 3.