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Medicinal and Aromatic Plants - Australia

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Biography of Dr Ian Cock

Dr Ian Cock obtained his PhD for studies in reproductive biology/immunology into “Early Pregnancy Factor (EPF)” and very early pregnancy detection from Griffith University, Brisbane, Australia in 1994. Following his PhD studies, Dr Cock undertook postdoctoral studies into cytochrome’s P450 and multiple drug interactions in the Department of Biochemistry and in the Department of Physiology and Pharmacology, both at the University of Queensland. He returned to Griffith University as an academic staff member in 1998 and has taught and developed a number of courses across three campuses of Griffith University since this time. His teaching broadly encompasses biochemistry, biological chemistry, cell biology, immunology, plant biology and biotechnology. Specific areas of expertise and interest include metabolism and its regulation, phytochemistry and natural product discovery,

redox biochemistry and redox control systems, protein structure/function, enzymology, biomolecular isolation and characterisation techniques, and drug bioassays.

Dr Cock currently also leads a research team in the Department of Biomedical and Biophysical Sciences at Griffith University. The Griffith University research team is involved in bioactivity and phytochemical studies into a variety of plant species of both Australian and international origin. The current research interests of this team involve bioactivity, structural and mechanistic studies into the medicinal potential of *Aloe vera*, South Asian and South American tropical fruits, as well as Australia plants including *Scaevola spinescens*, *Pittosporum phylliraeoides, Terminalia ferdinandiana* (Kakadu plum), Australian Acacias, Syzygiums, Petalostigmas and *Xanthorrhoea johnsonii* (grass trees). This range of projects has resulted in numerous scientific publications in a variety of peer reviewed journals. Dr Cock is also a member of the editorial boards of four scientific journals, including being the chief and foundation editor of the journal Pharmacognosy Communications.

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Biomolecular and Physical Sciences, Griffith University, Australia.

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This volume is dedicated to my father, Ted Cock, who passed away during the preparation of this manuscript. He will be missed.

Summary

Plants contain a myriad of natural compounds which exhibit important bioactive properties. These compounds may provide alternatives to current medications and afford a significant avenue for new drug discovery. As a result of geographic isolation, Australia is home to a large variety of unique and distinct flora not found elsewhere in the world. Due to the harsh conditions seen in many parts of Australia, plants have developed unique survival methods and phytochemicals specific to the environmental conditions they inhabit and may hold the key to the treatment of many diseases and medical conditions. Herbal medicines have played an important role in the health, culture and traditions of Australian Aboriginal people prior to the arrival of Europeans. Much of our understanding of the medicinal potential of Australian native plants is from accounts of Aboriginal ethnopharmacology. However, traditional Aboriginal knowledge of plants as therapeutics is disappearing as the Aboriginal culture merges into main stream society and the passing of oral traditions between each generation diminishes. Given the diverse nature of the flora present and the diminishing traditional knowledge, Australian plants remain relatively unstudied and it is surprising more research has not been done.

Much of our understanding of Australian medicinal plants is fragmented. With the exception of Lassak and McCarthy's book "Australian Medicinal Plants" and various early colonial texts (such as the 1889 work "The Useful Plants of Australia" by Maiden) which describe Aboriginal and early colonial ethnopharmacologies, most information is scattered throughout various scientific journals and government reports. Whilst readily available to scientific researchers in this field, much of this information is difficult to obtain for interested lay persons. Furthermore, the Lassak and McCarthy and the Maiden texts deal almost exclusively with our understanding of Australian ethnopharmacology and little understanding of phytochemistry and bioactivity mechanisms is

provided. This volume builds on these ethnopharmacological reports and summarises the current knowledge of Australian medicinal and aromatic plants. The ethnoparmacologies of various groups, from Aborigines, to early colonial settlers, to later migrant ethnopharmacologies are explored and tabulated as quick reference sources. Knowledge of Australian medicinal plants phytochemistry and mechanisms of action are also summarised, particularly where relating to the aromatic Australian plants (eg. Eucalypts, Melaleukas, Leptospermums etc). This volume also provides an introduction to current scientific studies into Australian medicinal plants (with specific examples) and some of the techniques used in the hopes of stimulating interest and further studies in this field.

Keywords: Australian plants, medicinal plants, aromatic plants, ethnopharmacology, phytochemical, pharmacological screening.

Medicinal and Aromatic Plants - Australia

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Medicinal and Aromatic Plants - Australia

1.1. Natural Plant Medicines Worldwide - A Historical Perspective

Plants have a long history of being used for a wide variety of purposes including food, clothing, shelter, tools, weapons and as therapeutic agents. Before the advances of modern medicine, civilizations confronted with illness and disease discovered a wealth of useful therapeutic agents from within the plant and fungi kingdoms. Knowledge of these medicinal preparations and of their toxic potential was passed down through generations by oral tradition and sometimes recorded in herbal literature. The earliest records outlining mans usage of plant medications are more than 6000 years old. Sumerian clay tablets (4000 BC) detail 1000 medicinal plants and plant remedies (Afzal and Armstrong, 2002; Levetin and McMahon, 2003). The Pun-tsao, a Chinese record of thousands of herbal cures dates to 2500 BC. The Hippocratic Corpus (a collection of medical texts of herbal remedies) by Greek physician Hippocrates was recorded in the late fifth century BC and the Roman writings De Materia Medica by Dioscorides, document more than 600 plant species with medicinal value (Levetin and McMahon, 2003). These records have more value than merely as an anthropologic or archaeological. They provide an understanding of ancient plant medicinal preparations, some of which are currently still in use.

Many developing cultures (particularly Asian and African) have assimilated herbal medicine into their primary modality of health care (Farnsworth et al., 1985) and herbal medications remain an

important component of their medicinal systems. By documenting and practicing traditional medicine these cultures have accumulated comprehensive ethnobotanical data and improved their skills over time. Today, Ayuvedic medicine is still commonly practiced within India with an estimated 85% of Indians still using crude plant formulations for the treatment of various diseases and ailments (Kamboj, 2000).

Even allopathic/Western medicine practiced in developed countries owes much to our understanding of plant based remedies. Table 1 lists some commonly used allopathic drugs derived from plants. The listed drugs have widespread medicinal uses including as analgesics, central nervous system stimulants/depressants, antimalarial drugs, antiseptics, anti-tumour and anti-cancer agents, cardiac drugs, cholesterol lowering agents, anti-diabetic agents, as well as psychoactives. This is merely a sampling of current plant derived pharmaceuticals and serves only to illustrate the importance of herbal derived medicines and semi-synthetic drugs derived from purified phytochemicals to allopathic medicine. Indeed, it has been estimated that approximately 25% of all prescription drugs currently in use are originally derived from plants (Hostettmann and Hamburger, 1993; Newman et al., 2000; Walsh, 2003). Furthermore, approximately 75% of new anticancer drugs marketed between 1981 and 2006 are derived from plant compounds (Newman et al., 2000).

Table 1: Plant derived drugs commonly used in allopathic medicine.

Acetyldigoxin	Colchicine	Khellin	Rotenone
Adoniside	Convallotoxin	Lanatosides A, B, C	Rotundine
Aescin	Curcumin	Lobeline	Salicin
Aesculetin	Cynarin	Lovostatin	Santonin

Agrimophol	Danthron	Morphine	Scillarin A
Ajmalicine	Deserpidine	Neoandrographolide	Scopolamine
Allantoin	Deslanoside	Noscapine	Sennosides A & B
Allyl isothiocyanate	Digitalin	Ouabain	Silymarin
Andrographolide	Digitoxin	Papain	Stevioside
Anisodamine	Digoxin	Phyllodulcin	Strychnine
Anisodine	Emetine	Physostigmine	Teniposide
Arecoline	Ephedrine	Picrotoxin	Tetrahydropalmatine
Asiaticoside	Etoposide	Pilocarpine	Theobromine
Atropine	Gitalin	Podophyllotoxin	Theophylline
Berberine	Glaucaroubin	Protoveratrines A & B	Trichosanthin
Bergenin	Glycyrrhizin	Pseudoephedrine	Tubocurarine
Bromelain	Gossypol	Quinine	Valepotriates
Caffeine	Hemsleyadin	Quisqualic Acid	Vincamine
(+)-Catechin	Hydrastine	Rescinnamine	Xanthotoxin
Chymopapain	Hyoscamine	Reserpine	Yohimbine
Cocaine	Kainic Acid	Rhomitoxin	Yuanhuacine
Codeine	Kawain	Rorifone	Yuanhuadine

As a result of geographic isolation, Australia is home to a large variety of unique and distinct flora not found elsewhere in the world. Due to the harsh conditions seen in many parts of Australia, plants have developed unique survival methods specific to the environmental conditions they inhabit. Australian Aborigines had developed a good understanding of the botany in their local areas and have used a variety of plant medicines to help maintain their health for approximately 40, 000 years (Barr et al., 1993; Lassak and McCarthy, 2006). However, traditional Australian Aboriginal

knowledge of plants as therapeutics is disappearing as the Aboriginal culture merges into main stream society and the passing of oral traditions between each generation diminishes (Lassak and McCarthy, 2006). Given the diverse nature of the flora present and the diminishing traditional knowledge, Australian native plants remain relatively unstudied and it is surprising more research is not being undertaken. There is a very real need to document the traditional usage of Australian native and indigenous plants before this knowledge is permanently lost.

This volume aims to document and summarise the current understanding of Australian aromatic and medicinal plants and to stimulate further research in this field. Before undertaking a description of the usage of Australian native plants, it is necessary to understand the classes of phytochemicals present in plants and the divergent evolution that has resulted in Australia's high degree of endemic species. Many of these species live in extremely harsh environments, making them candidates for scientific examination.

1.2. Phytochemicals of Therapeutic Significance

Plants have evolved to synthesise an extremely diverse range of chemical compounds known as secondary metabolites. These secondary metabolites have no apparent role in primary plant growth or development processes, are often unique to plants from a single species and increase during times of high stress such as drought, fire and bacterial infection (Taiz and Zeiger, 2006). Many of these compounds exhibit anti-microbial, anti-oxidant, cytotoxic and other medicinally useful properties (Taiz and Zeiger, 2006). These activities can be attributed to the presence of a variety of phytochemical constituents, which can be divided into three main chemically distinct groups: terpenes, phenolics and nitrogen containing compounds (alkaloids).

The nomenclature and classification of secondary metabolites can be confusing. In many instances, properties common to the three major classes overlap (eg. a phenolic compound may contain nitrogen, making it both a phenolic compound and an alkaloid). Proanthocyanidins are examples of tannins (phenolic compounds) which contain nitrogen and are found in Australian *Acacia* species. Similarly, terpenes present within the essential oils from a variety of Australian plant species (eg. Eucalyptus and Melaleuca species) may be considered both terpenes and phenolics as they structure their five carbon atoms into phenolic rings.

1.2.1. Terpenes

Terpenes or terpenoids are formed by the union of five carbon elements (isoprene units) (Figure 1) to form more complex biomolecules.

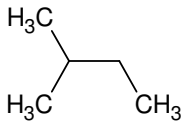


Figure 1: The structure of isoprene, the basic unit of terpenes and terpenoids.

The union of two isoprene units forms a monoterpene. Examples of well known monoterpenes include limonene (lemon oil) (Figure 2a) and menthol (peppermint oil) (Figure 2b) which provide defence against potential predators and are sometimes used as food flavouring agents (Taiz and

Zeiger, 2006). Monoterpenes can undergo further modification to form sesquiterpenes (15 carbon units), diterpenes (20 carbon units) and polyterpenes (many carbon units).

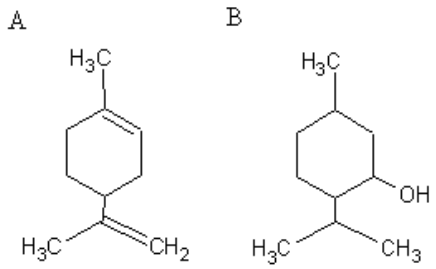


Figure 2: The chemical structure of (a) limonene and (b) menthol.

Terpenes are toxins which act as feeding deterrents to many plant feeding insects and mammals and are relatively insoluble in water (Taiz and Zeiger, 2006). Pyrethroids for example, are a class of terpenes which exhibit toxicity as well as insecticidal and anti-microbial activities. They occur in the leaves and flowers of Chrysanthemum species (Taiz and Zeiger, 2006). They are often used as a component of insecticides due to their low persistence in the environment and negligible toxicity to mammals (Taiz and Zeiger, 2006). Recent research has shown that some terpenes are only produced and emitted from the plant after insect feeding has begun (Taiz and Zeiger, 2006). These substances may have no effect on the insects that stimulated their production, but increase resistance to future attack, or they may attract predatory and parasitic insects which in turn kill the plant feeding insects (Taiz and Zeiger, 2006).

Many Australian plants contain mixtures of terpenes known as essential oils. In particular, the essential oils of members of the family Myrtaceae (Eucalypts, Melaleucas, Leptospermums and Callistemons) are known to be particularly rich in terpenes. These plants, their medicinal uses and

their phytochemistry will be described separately in more detail in later sections of this volume. The terpene containing essential oils of these plants add a characteristic odour and flavour to plant foliage and some therefore may be used as food flavouring agents. Some essential oils possess a broad spectrum of anti-microbial activities and may be used to fight against pathogens (Deininger, 1984; Manohar et al., 2000).

1.2.2. Phenolic Compounds:

Phenolic compounds are secondary metabolites that contain a phenol group (Figure 3).

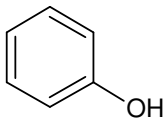


Figure 3: A phenolic ring, the primary building block of a phenolic compound.

Phenolic compounds include a variety of different sub-classes including tannins, flavones, isoflavones, flavonols, anthocyanins, coumarins, chalcones and phytoelaxins (Figure 4). In plants, phenolic compounds act as a defence mechanism against herbivores and pathogens, attract pollinators, absorb UV radiation, minimise oxidative stress and reduce the growth of nearby competing plants (allelopathy) (Taiz and Zeiger, 2006).

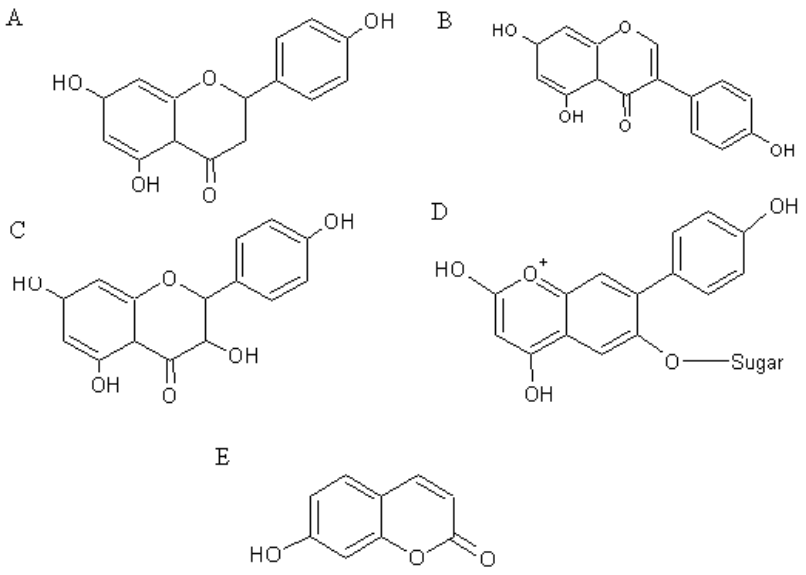


Figure 4: Structure of (a) Flavones, (b) Isoflavones/Isoflavonoids, (c) Flavonols, (d) Anthocyanins, and (e) Coumarins.

The function of phenolic compounds varies greatly. Flavones and flavonols (Figure 4a and 4c) are present in the leaves of all green plants and protect them from UV damage by absorbing light in the shorter wavelengths (Taiz and Zeiger, 2006). Anthocyanins (Figure 4d) are pH dependent coloured flavonoids which attract pollinators (Taiz and Zeiger, 2006) whilst isoflavones/isoflavonoids (Figure 4b) exhibit strong antimicrobial activity (Taiz and Zeiger, 2006). Isoflavones and isoflavonoids have also been identified for use in the treatment of a wide range of health conditions such as menopause, cardiovascular disease, cancer and osteoporosis (Yen et al., 2008).

Tannins may act as general toxins that reduce growth and survival of many herbivores when added to their diet (Taiz and Zeiger, 2006). Tannins inhibit the growth of many fungi, yeast, bacteria and viruses and have also been suggested as anti-carcinogens (Scalbert, 1991). Tannic acid and propyl gallate inhibit food borne, aquatic and off-flavour-producing micro-organisms (Scalbert, 1991). In

contrast, foods containing tannins (eg. tea tannins) are regularly consumed by humans and have been shown to promote health rather than hinder it (de Mejia et al., 2009).

Phytoalexins are antibiotics produced by plants when under stress. They exhibit strong antimicrobial activity and are generally undetectable before initial infection. They are synthesized very rapidly after microbial attack and accumulate around the site of infection (Taiz and Zeiger, 2006). Phytoalexins from different plant families can be produced as different secondary metabolites eg. Capsidiol (from pepper and tobacco; Figure 5a) is a sesquiterpene whilst resveratrol (from grape skin; Figure 5b) is an isoflavonoid. Because of its structural resemblance to estrogen, resveratrol exhibits agonistic and antagonistic activities towards the estrogen receptor and it has been suggested that resveratrol could reduce localized estrogen production in breast cancer cells (Wang et al., 2006). Resveratrol also displays chemo-preventive activity by inhibiting, delaying or reducing carcinogenesis (Signorelli and Ghidoni, 2005).

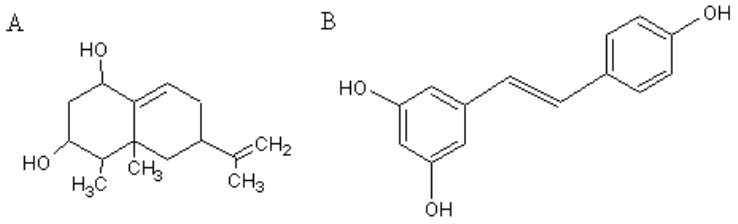


Figure 5: Chemical structures of (a) Capsidiol and (b) Resveratrol.

The interaction of several flavonoids with ATP-binding cassette (ABC) transporters such as P-glycoprotein (Di Pietro et al., 2002), multi drug resistance associated protein 1 (Leslie et al., 2001), and Breast Cancer Resistance Protein (BCRP) (Zhang et al., 2004) (which are believed to limit the

intracellular accumulation of cytotoxic agents in cancer cells when over expressed) have been reported. These same flavonoids have been shown to modulate breast cancer resistance protein BCRP on a transcriptional level in Caco-2 and MCF-7 cells (Ebert et al., 2007). The flavonoid, acacetin-7-o-b-D-galactopyranoside from *Chrysanthemum morifolium* was found to be active towards HIV by inhibiting HIV replication (Hu et al., 1994).

Many Australian plants are known to contain high levels of phenolic compounds. These plants, their medicinal uses, and their phytochemistry will be described in more detail in later sections of this volume.

1.2.2.1. Phenolic Compounds as Antioxidants

An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules by removing free radical intermediates or inhibiting other oxidation reactions by becoming oxidized themselves. Free radicals or Reactive Oxygen Species (ROS) are highly reactive compounds that damage cells and are created by both the external environment (eg. smoking, UV radiation and stress) and the internal environment (eg. purine metabolism or adrenaline synthesis) (Herna´ndez et al., 2008).

In order to minimize oxidative stress-related trauma, ROS homeostasis in plants is tightly regulated. It has been suggested that phenolic compounds such as flavonoids, coumarins, phenolic acids, tannins, and phenolic diterpenes act as antioxidants through two mechanisms (Herna´ndez et al.,

2008): by protecting plants from oxidative stress by scavenging free radicals such as ROS, and by preventing the formation of ROS by chelating metals (Felton, 1992).

Through these mechanisms, antioxidants protect cells against oxidative stress related damage, thereby maintaining the redox homeostasis of biological fluids and preventing disease (Rice-Evans et al., 1996; Rice-Evans, 2001; Miniati, 2007; Hsu and Yen, 2008). Antioxidants have been found to play an important role in the reduction of atherosclerosis, inflammatory injury, cancer (Hertog et al., 1996; Lambert et al., 2005), cardiovascular disease (Geleijnse et al., 2002) and neurological degenerative disorders such as Alzheimer's and Parkinson's disease (Youdim et al., 2002). They are also linked with anti-diabetic bioactivities (Matsui et al., 2002) and have been associated with the reduction of obesity (Tsuda et al., 2003). In addition, flavonoids are inhibitory to a variety of human pathogens including bacteria, fungus and viruses (Bylka et al., 2002). Studies have shown that many dietary phenolic constituents derived from plants are more effective antioxidants in vitro than standards used for determining antioxidant activity such as vitamin C or vitamin E (Wu et al., 2008). Several Australian plants have been identified as having particularly high levels of phenolic antioxidants (Netzel et al, 2007; Netzel et al, 2006). These are described in more detail in section 2.1.4.

1.2.2. Nitrogen Containing Compounds (Alkaloids)

Nitrogen containing compounds (alkaloids) are secondary metabolites which are biosynthesized from common amino acids. The basic structure of a phenolic alkaloid is shown in Figure 6. Alkaloids are of considerable interest due to their unique properties and include many subclasses such as cyanogenic glycosides.

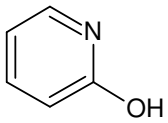


Figure 6: The basic structure of a phenolic alkaloid.

Morphine (Figure 7a), the first medically useful alkaloid identified, was isolated from *Papaver somniferum* (opium poppy) in 1805 (Fessenden and Fessenden, 1982). Other major alkaloids include cocaine (Figure 7b), nicotine (Figure 7c) and caffeine (Figure 7d).

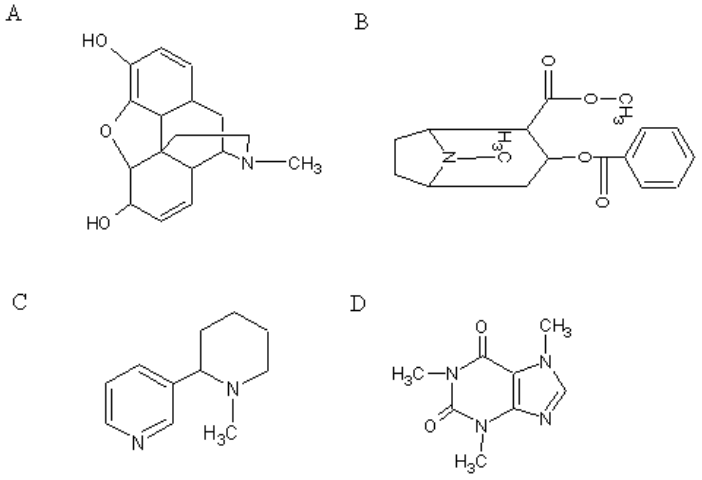


Figure 7: Structures of (a) morphine, (b) cocaine, (c) nicotine and (d) caffeine.

Alkaloids are found in approximately 20% of vascular plant species and are thought to be effective defences against browsing animals. Pyrrolizidine alkaloid (isolated from *Heliotropium subulatum* extracts) shows antimicrobial activity against both fungal and bacterial species (Craig, 1998).

Biologically active carbazole alkaloids (from *Murraya koenigii*) display mosquitocidal and anti-microbial activities as well as exhibiting topoisomerase I and II inhibition activities (Ramsewak et al., 1999). Although these compounds are lethal when administered in high doses, they have pharmacological uses as medicines, stimulants or sedatives at lower doses. Another medically useful alkaloid, digoxin, is produced within the leaves of the plant genus Digitalis. This cardiac glycoside is used as an antiarrhythmic agent to control heart conditions such as atrial fibrillation, atrial flutter and sometimes heart failure (van Veldhuisen and de Boer, 2009).

Many Australian plants contain bioactive alkaloids. The bark of Australian Acacia species (family Fabacea, subfamily Mimosoideae) in particular has been shown to contain high levels of nitrogenous tannins. For example, *Acacia mearnsii* (Black Wattle) bark contains 20-40% tannins by weight, of which up to 70% are proanthocyanidins (Tindale and Roux, 1969). The phytochemistry and known medicinal bioactivities of these and other plants is discussed separately in more detail in later sections of this volume.

2. Australian Plant Evolution

Australian flora is unique, with many species not occurring naturally in any other part of the world. Prior to the mid-Jurassic period (about 170 million years ago) Australia was part of a super continent called Gondwana which contained most of today's southern hemisphere land masses as well as India and Arabia (which are today in the northern hemisphere) (Meert, 2003; Cattermole, 2000). Free movement of living organisms was possible throughout Gondwana and biodiversity patterns were uniform throughout the supercontinent. Indeed, the Jurassic flora of Australia is thought to be very similar to other regions of Gondwana (Adam, 1992). During the late Jurassic period East Gondwana

(Australia, Antarctica, India and Madagascar) split from West Gondwana (Africa and South America) (Meert, 2003). Approximately 120 million years ago India and Madagascar split from East Gondwana and began to move north. Australia split from Antarctica more than 40 million years ago effectively isolating it from the rest of the world. This isolation allowed Australia's flora to evolve separately from that of other regions of the world.

The Greening of Gondwana (White, 1998) provides an in depth study of the evolution of Australian plants from the time of the supercontinent to present day. During the Cretaceous period, Australia experienced warm, moist conditions and rainforests were prevalent across much of the continent. Later, in the Tertiary period, Australia became drier and there was an increase in flora evolution and many new species arose to adapt to the environmental conditions. Eucalypts and Acacias are thought to have evolved during this time in response to the dry conditions and nutrient deficient soils. Approximately 15 million years ago as Australia and South East Asia moved closer together, an invasion of plant taxa from the north occurred, accounting for the taxonomic similarities between South East Asian and Australian northern tropical rainforest plants. Apart from this invasion, Australia's isolation has resulted in a high degree of endemism. Many of Australia's plants are already known to have medicinal properties and some have been used by Australian Aborigines for over 40 000 years. Whilst the world looks towards South American rainforests for new wonder drugs, the possibility exists that the unique plants that have evolved in the harsh Australian conditions may also hold the key to the treatment of many diseases and medical conditions.

2.1. Australian Medicinal Plant Use

The usage of Australian plants for the treatment of illness and injury falls into four main categories:

2.1.1. Indigenous Australian (Aboriginal) Ethnopharmacology.

Prior to European settlement in Australia, the Aboriginal people used a variety of plant medicines to help maintain their health (Barr et al., 1993; Lassak and McCarthy, 2006). It has been suggested that Aborigines needed relatively little medication prior to the arrival of European settlers due to their generally good health (Lassak and McCarthy, 2006). Some of the commonly used Aboriginal medicinal plants are outlined in Table 2. This is not a complete listing. Many of the early reports insufficiently or incorrectly described the taxonomy of the medicinal plants. Furthermore, many plants had different uses for different Aboriginal groups in different regions of Australia. Where plant identity or usage is in doubt, listings were omitted. Plants used by European or later settlers and Australian native plants used exclusively in other parts of the world are dealt with elsewhere in this volume.

Aborigines treated their occasional bouts of diarrhoea and dysentery with astringents such as Eucalyptus astringents. Fever was treated with a wide variety of plants, dependent on what was locally available. Toothache was relatively common due to a tough, fibrous diet, particularly amongst the elderly, and was treated by a wide variety of plant medications. Sore and infected eyes were some of the major problems faced by Australian Aborigines. Arguably the major health threat faced by Aborigines was bacterial infection (Roth, 1903). The commonness of this complaint is reflected in the number of plants Aborigines used as antiseptics. Much of the information about the antimicrobial activities of Australian plants is anecdotal although research into the antiseptic nature of Australian plants is receiving recent attention (Cock, 2008; Palombo and Semple, 2001; Setzer et al., 2000). However, still only a few of the Aboriginal medicinal plants have undergone rigorous

scientific investigation to confirm their antimicrobial activities. One study (Palombo and Semple, 2001) examined a panel of plant extracts commonly used by Australian Aboriginals and found approximately 20% of the samples tested were able to inhibit bacterial growth. This group has also demonstrated the antiviral activity of the same panel of Australian plants (Semple et al., 1998). There are many other Australian plants, some used by Australian Aborigines, that have not been properly examined for antibacterial activity.

With the arrival of European settlers, infectious diseases (eg. measles, mumps, chicken pox and venereal diseases) were introduced and caused major health problems in a population with no prior exposure (Lassak and McCarthy, 2006). The Aborigines actively sought and developed plant medications in an attempt to combat these introduced illnesses. See for example, the relatively large number of plant medications used to treat venereal diseases by the Aborigines (Table 2), all of which were incorporated into the Aboriginal pharmacopea following European settlement.

Table 2: Botanical names of plant species used by Australian Aborigines and their traditional medicinal uses.

Botanical Name	Plant Part(s) Used	Ethnomedicinal Use	Reference(s)
Amaryllidaceae			
Crinum flaccidum	bulb	antiseptic	Lassak and McCarthy (2006), Levitt (1979)
Crinum pedunculatum	whole plant	marine stings	Webb (1959)

Crinum uniflorum	whole plant	antiseptic	Levitt (1979)
Apiaceae			
Centella asiatica	leaf	skin diseases, leprosy, syphilis, prickly heat	Hurst (1942), Webb (1959), Maiden (1889)
Apocynaceae			
Alyxia buxifolia	bark	dysentery	Webb (1948)
Marsdenia australis	seeds	oral contraceptive	Reid and Betts (1979)
Ochrosia elliptica	bark	malaria	Webb (1948)
Rhyncharrhena linearis	seeds	oral contraceptive	Reid and Betts (1979)
Tabernaemontana orientalis	sap, fruit	antiseptic, skin sores	Webb (1959), Roth (1903)
Araceae			
Colocasia macrorrhiza	leaf	sores, burns, ulcers	Webb (1948)
Asclepiadaceae			
Sarcostemma viminale	stem	skin sores, eye complaints	Latz (1995), Barr *et al*., (1993), Smith (1991), Webb (1969)
Asteraceae			
Ageratum conyzoides	whole plant	skin sores	Webb (1959)
Centipeda cunninghamii	whole plant	cold, skin infections	Zola and Gott (1992), Johnston and Cleland (1943)
Centipeda minima	whole plant	sore eyes, colds	Reid and Betts (1979)
Centipedia thespidioides	whole plant	colds, sore throat, sore	Webb (1969)

		eyes	
Cymbonotus lawsonianus	leaves	cuts, antiseptic	Maiden (1889)
Pseudognaphalium luteoalbum	whole plant	general illness	Palmer (1883)
Pterocaulon serrulatum	leaves	cold, antiseptic, fever, headache	Webb (1948)
Pterocaulon sphacelatum	aerial portions of plant	cold, respiratory infections, skin sores, eye complaints	Latz (1995), Barr *et al.* (1993), Smith (1991)
Araucariaceae			
Araucaria cunninghamii	resin	kidney complaints	Maiden (1898)
Boraginaceae			
Trichodesma zeylanicum	whole plant	skin sores, diuretic, snake bite	Reid and Betts (1979), Bailey (1881)
Burseraceae			
Canarium australianum	bark	diarrhoea, stomach pain	Roth (1903)
Canarium muelleri	resin	cuts, skin sores, ulcers	Bailey (1909)
Cabombaceae			
Brasenia schreberi	leaves	dysentery	Maiden (1889)
Caesalpiniaceae			
Cynometra ramiflora	root, leaves	purgative	Maiden (1889)

Erythrophleum chlorostachys	bark, root	wounds, antiseptic	Reid and Betts (1979), Webb (1948)
Lysiphyllum carronii	bark	wounds, antiseptic	Reid and Betts (1979)
Senna odorata	leaves	laxative	Webb (1948)
Senna pleurocarpa	leaves, seed pods	laxative	Lassak and McCarthy (2006)
Campanulaceae			
Isotoma petraea	whole plant	respiratory complaints	Barr *et al*. (1993), Smith (1991)
Capparidaceae			
Capparis lasiantha	flower, whole plant	cough remedy, snake bite insect bites/stings	Reid and Betts (1979)
Cleome viscosa	whole plant	colds, rheumatism, pain	Reid and Betts (1979)
Casuarinaceae			
Casuarina equisetifolia	bark	astringent, diarrhoea, dysentery, mouthwash	Levitt (1979), Maiden (1889)
Chenopodiaceae			
Capparis uberiflora	bark, roots	cuts, skin sores	Roth (1903)
Chenopodium cristatum	whole plant	antiseptic, abscesses	Webb (1969)
Dysphania rhadinostachya	leaves	colds, headache	Reid and Betts (1979)
Convolvulaceae			
Convolvulus angustissimus	whole plant	diarrhoea, stomach pain	Webb (1969)
Evolvulus alsinoides	stems, roots, leaves	pain, dysentery, fever	Johnson and Cleland (1943), Maiden (1889)

Merremia tridenta	whole plant	sores, antiseptic	Roth (1903)
Cucurbitaceae			
Mukia maderaspatana	whole plant	skin sores, pain relief	Latz (1995), Low (1990) Silberbauer (1971)
Cycadaceae			
Cycas media	seeds	antiseptic	Hegnauer (1962)
Cyperaceae			
Cyperus bifax	roots	gonorrhoea	Webb (1948)
Eleocharis dulcis	whole plant	wounds, antiseptic	Levitt (1979)
Lepidosperma gladiatum	stem	cold	Gott (1992)
Lepidospermum viscidum	stem	cold	Gott (1992)
Schoenoplectus validus	roots	astringent, diuretic	Bailey (1883)
Dennstaedtiaceae			
Pteridium esculentum	stems, leaves	insect bites, rheumatism	Hegnauer (1962), Webb (1948)
Eucryphiaceae			
Eucryphia lucida	bark (resin)	antiseptic	Hegnauer (1966)
Euphorbiaceae			
Acalypha wilkesiana	leaves, shoots	skin sores, antiseptic	Webb (1969)
Breynia cernua	bark	dysentery	Webb (1959)
Beyeria lechenaultii	aerial portions of plant	fever, general illness tuberculosis	Webb (1969)

Breynia stipitata	leaves	sore eyes	Webb (1959)
Euphorbia alsiniflora	whole plant	dysentery, fever	Lassak and McCarthy (2006)
Euphorbia atoto	flowers, sap	sore throat	Reid and Betts (1979)
Euphorbia australis	whole plant	skin sores, antiseptic	Latz (1995), Reid and Betts (1979)
Euphorbia coghlanii	sap	skin sores, skin cancer	Reid and Betts (1979)
Euphorbia drummondii	whole plant	skin sores, genital sores,	Latz (1995), Reid and Betts (1979)
		fever, dysentery	Webb (1969), Maiden (1889)
Euphorbia hirta	whole plant	asthma, emphysema,	Reid and Betts (1979), Webb (1969)
		intestinal worms, dysentery,	Maiden (1889)
		colic warts	
Euphorbia mitchelliana	flowers	diarrhoea	Webb (1969)
Excoecaria parvifolia	bark	pain, general illness	Lassak and McCarthy (2006)
Mallotus mollissimus	sap	dysentery	Webb (1959)
Petalostigma pubescens	fruit, bark, antiseptic,	fever, malaria, antiseptic,	Reid and Betts (1979), Webb (1969)
		sore eyes, toothache	Maiden (1889)
Petalostigma quadriloculare	fruit, bark, antiseptic,	fever, malaria, antiseptic,	Reid and Betts (1979), Webb (1969)
		sore eyes, toothache	Maiden (1889)
Securinega malanthesoides	leaves	pain, severe illness, itches	Reid and Betts (1979)
		rash, skin sores, leprosy	
		chicken pox	

Fabaceae

Crotalaria eremaea	aerial portions of plant	general illness	Barr et al. (1993), Goddard and Kalotas (1988)

Crotalaria cunninghamii	bark, leaves	headache, sore eyes	Reid and Betts (1979)
Daviesia benthamii	root	cold, cough	Gott (1992)
Daviesia latifolia	leaves	fever, hydatid remedy	Webb (1948)
Erythrina verspertilio	leaves	sedative, sore eyes, pain	Reid and Betts (1979), Webb (1969)
Sophora tomentosa	roots, seeds	bilious sickness	Bailey (1883)

Flagellariaceae

Flagellaria indica	leaves	wounds, antiseptic, sore eyes, contraceptive	Webb (1969), Webb (1959), Maiden (1889)

Goodeniaceae

Goodenia ovata	leaves	diabetes	Webb (1948)
Goodenia varia	leaves	sedative	Lassak and McCarthy (2006),
Scaevola spinescens	stem, leaves	skin sores, boils, pain relief, urinary problems	Lassak and McCarthy (2006), Webb (1969), Cleland and Johnston (1939)
Scaevola taccada	fruit, leaf	tinea, skin sores	Lassak and McCarthy (2006), Webb (1959)

Gyrostemonaceae

Codonocarpus cotinifolius	stem, leaves	skin sores, pain relief, respiratory complaints	Barr *et al*. (1993), Smith (1991)

Haemodoraceae

Haemodorum ensifolium	whole plant	snake bite	Webb (1969)

Haemodorum spicatum	whole plant	dysentery	Webb (1948)
Hernandiaceae			
Gyrocarpus americanus	roots, leaves	cuts, antiseptic, rheumatism	Reid and Betts (1979), Webb (1969)
Lamiaceae			
Ajuga australis	whole plant	skin sores, boils	Lassak and McCarthy (2006),
Basilicum polystachyon	aerial portions of plant	fever	Lassak and McCarthy (2006),
Prostanthera striatifloria	aerial portions of plant	respiratory infection, skin sores, malaise	Latz (1995), Barr *et al*. (1993), Smith (1991)
Clerodendrum floribundum	wood	pain	Webb (1969)
Clerodendrum inerme	bark, leaves	skin sores, antiseptic	Webb (1959)
Mentha australis	whole plant	colds, coughs, headache	Webb (1969)
Mentha diemenica	whole plant	menstrual disorders, stomach pain, diuretic insecticide	Hager (1930), Maiden (1889)
Plectranthus congestus	leaves	general internal complaints	Roth (1903)
Prunella vulgaris	leaves	cuts, antiseptic, fever	Gildemeister and Hoffmann (1961) Ewart (1930)
Lauraceae			
Litsea glutinosa	bark, leaf	skin sores, scabies, pain infections, antiseptic	Webb (1969), Webb (1959)
Lecythidaceae			

Barringtonia calyptrata	leaves	fever, pain	Webb (1969)
Planchonia careya	leaves, stems, roots, bark	skin sores, antiseptic,	Levitt (1979), Reid and Betts (1979)
		general illness	Reid and Betts (1979), Bailey (1909)
			Roth (1903)
Liliaceae			
Dianella ensifolia	roots	painful urination	Webb (1948)
Dianella revoluta	root	cold, general illness	Bonney (1994)
Lobeliaceae			
Pratia purpurascens	whole plant	snake bite	Maiden (1889)
Loranthaceae			
Amyema maidenii	whole plant	genital inflammation	Cleland and Johnston (1939)
Amyema quandang	leaves	fever	Maiden (1898), Palmer (1883)
Malvaceae			
Hibiscus tiliaceus	bark, wood	antiseptic	Levitt (1979)
Lavatera plebeia	leaves	boils	Campbell (1973)
Menispermaceae			
Cissampelos pareira	root	laxative	Webb (1948)
Tionspora smilacina	stems	pain	Reid and Betts (1979)
Mimosaceae			
Acacia auriculoformis	leaves	antiseptic, allergy rash	Pennacchio *et al*. (2005), Barr

			(1993)
Acacia beauverdiana	ash from burnt wood	pain	Reid and Betts (1979)
Acacia bivenosa	bark	cough colds	Cribb and Cribb (1981)
			Reid and Betts (1979), Webb (1969)
Acacia cuthbertsonii	bark	pain	Reid and Betts (1979)
Acacia decurrens	bark	dysentery	Lassak and McCarthy (2006),
			Woolls (1867)
Acacia falcata	bark	skin diseases	Maiden (1889)
Acacia holosericea	roots	laryngitis	Reid and Betts (1979)
Acacia implexa	bark	skin diseases	Maiden (1913)
Acacia kempeana	bark, leaves	chest infection, cold,	Latz (1995), Barr *et al.* (1993),
		general illness	O'Connell *et al.* (1983)
Acacia leptocarpa	leaves	sore eyes	Reid and Betts (1979)
Acacia ligulata	bark, leaves	chest infection, cold,	Latz (1995), O'Connell *et al*, (1983),
		general illness	Webb (1969)
Acacia melanoxylon	bark	rheumatism	Lassak and McCarthy (2006),
Acacia monticola	roots, twigs	colds, coughs	Reid and Betts (1979)
Acacia tetragonophylla	stem, leaves	cough, wound treatment,	Reid and Betts (1979)
		dysentery	
Acacia transluscens	leaves, twigs	skin sores, headache	Reid and Betts (1979)

Moraceae

Ficus coronata	sap, bark	wounds, antiseptic	Roth (1903)
Ficus opposita	leaves, sap	ringworm	Webb (1959)

Myoporaceae

Eremophilia alternifolia	stem, leaves	general illness, pain respiratory infection,	Palombo and Semple (2001) Barr *et al*. (1993), Smith (1991), Goddard and Kalotas (1988)
Eremophila bignoniiflora	fruit	laxative	Webb (1948)
Eremophilia cuneifolia	leaves	colds	Reid and Betts (1979)
Eremophilia duttonii	stem, leaves	respiratory infection, sore throat and ears, eye inflammation	Palombo and Semple (2001) Latz (1995), Barr *et al*. (1993), Smith (1991), O'Connell *et al*. (1983)
Eremophilia fraseri	leaves	colds, rheumatism, toothache	Reid and Betts (1979)
Eremophilia freelingii	stem, leaves	cough, pain fever, cuts diarrhoea	Palombo and Semple (2001) Barr *et al*. (1993), Goddard and Kalotas (1988), Silberbauer (1971)
Eremophilia latrobei	stem, leaves	respiratory infection, cough, sore throat, malaise	Palombo and Semple (2001) Latz (1995), Barr *et al*. (1993), Smith (1991), O'Connell *et al*. (1983)
Eremophilia longifolia	stem, leaves	respiratory infection, eye wash, skin sores, boils	Latz (1995), Barr *et al*. (1993), Smith (1991)
Eremophilia maculata	leaves	cold	Pennacchio *et al*. (2005), Maiden (1889)
Eremophilia sturtii	stem, leaves	respiratory infection, cough, cuts, sore eyes, general illness	Palombo and Semple (2001) Barr *et al*. (1993), Smith (1991), Goddard and Kalotas (1988)
Myoporum debile	whole plant	venereal diseases	Webb (1948)

Myoporum platycarpum	bark	laxative	Maiden (1889)
Myrtaceae			
Angophora costata	bark (gum)	diarrhoea	Lassak and McCarthy (2006), Lauterer (1895)
Asteromyrtus symphyocarpa	leaves	liniment, headache, pain, colds, sore eyes	Lassak and McCarthy (2006),
Corymbia polycarpa	bark (gum)	dysentery	Webb (1959)
Corymbia tessellaris	bark	dysentery	Roth (1903)
Eucalyptus camaldulensis	bark (gum), leaves	diarrhoea	Campbell (1973), Maiden (1922)
Eucalyptus drepanophylla	bark	skin sores, antiseptic	Webb (1969)
Eucalyptus gummifera	bark (gum)	astringent, skin sores, venereal diseases, ring-worm antiseptic, cuts, skin sores	Webb (1948)
Eucalyptus haemastoma	bark (gum)	dysentery, cuts, wounds, antiseptic	Lassak and McCarthy (2006),
Eucalyptus maculata	bark (gum)	bladder infections	Lauterer (1895)
Eucalyptus papuana	bark	colds, sore eyes	Reid and Betts (1979)
Eucalyptus pilularis	bark (gum)	astringent	Maiden (1911)
Eucalyptus racemosa	bark (gum)	dysentery, cuts, wounds, antiseptic	Lassak and McCarthy (2006), Webb (1948)
Eucalyptus resinifera	bark, leaf	syphilis, diarrhoea, dysentery astringent	Maiden (1907), Roth (1903), Lauterer (1895)
Eucalyptus sclerophylla	bark (gum)	dysentery, cuts, wounds, antiseptic	Lassak and McCarthy (2006),
Eucalyptus signata	bark (gum)	dysentery, cuts, wounds,	Lassak and McCarthy (2006),

		antiseptic	
Eucalyptus tetrodonta	bark, wood, leaves	diarrhoea, fever, headache, influenza	Webb (1969)
Eucalyptus terminalis	bark (gum)	diarrhoea, chest pains	Reid and Betts (1979)
Eucalyptus viminalis	leaves	laxative	Maiden (1922)
Melaleuca alternifolia	leaves	antiseptic, cuts, skin sores	Lassak and McCarthy (2006),
Melaleuca cajuputi	bark, twigs, leaves	pain, coughs, cold, asthma, colic, rheumatism, ear and tooth ache	Lassak and McCarthy (2006),
Melaleuca quinquenervia	leaves	headaches, colds, coughs, general illness	Lassak and McCarthy (2006), Maiden (1889)
Syzygium suborbiculare	bark, root, fruit	stomach pain	Webb (1959)
Myristicaceae			
Myristica insipida	bark	ringworm	Webb (1959)
Orchidaceae			
Cymbidium canaliculatum	stems, bulbs	dysentery	Webb (1959)
Cymbidium madimdum	stems, bulbs	dysentery	Roth (1903)
Papilionaceae			
Canavalia rosea	roots	pain, colds	Reid and Betts (1979)
Vigna vexillata	roots	laxative	Webb (1969)

Piperaceae

Piper novae-hollandiae	whole plant	gonorrhoea, stimulant	Webb (1959), Webb (1948), Maiden
		oral pain	(1889)

Pittosporaceae

Pittosporum phylliraeoides	fruit, wood, leaves	cough, cold, skin disorders	Latz (1995), Reid and Betts (1979)
		pain	Webb (1969)

Poaceae

Cymbopogon ambiguus	leaves	respiratory infections, pain,	Latz (1993), Barr *et al.* (1993),
		fever, skin disorders, eye wash	O'Connell et al. (1983)
Cymbopogon bombycinus	whole plant	whole plant	Maiden (1889)
Cymbopogon obtectus	aerial portions of plant	respiratory infections	Barr *et al.* (1993), Smith (1991)
Phragmites australis	leaves	sore throat	Gott (1992), Clarke (1987)

Proteaceae

Grevillea pyramidalis	bark	skin sores, antiseptic	Reid and Betts (1979)
Hakea suberea	bark	skin and mouth sores	Barr *et al.* (1993), Smith (1991)
Persoonia falcata	bark, leaves	sore throats, colds, sore eyes	Webb (1969), Webb (1959)
Xylomelum scottianum	bark, leaves	internal pain	Webb (1969)

Ranunculaceae

Clematis glycinoides	leaves	colds, headache	Clarke (1987)

Clematis microphylla	aerial portions of plant	sores, gastric disorders	Clarke (1987)
Rhamnaceae			
Alphitonia excelsa	leaves, bark, root	sore eyes, headache, pain	Webb (1969)
Alphitonia petriei	bark	pain	Webb (1969)
Ventilago viminalis	bark, root	toothache, rheumatism cuts, skin sores	Reid and Betts (1979)
Rhizophoraceae			
Rhizophora mucronata	bark	astringent	Maiden (1889)
Rosaceae			
Rubus parvifolius	leaves	astringent, diarrhoea	Woolls (1867)
Rubus rugosus	leaves	stomach upsets	Lassak and McCarthy (2006),
Rubiaceae			
Morinda reticulata	root	oral contraceptive	Webb (1959)
Oldenlandia galioides	whole plant	snake bite	Webb (1948)
Timonius timon	wood, bark	sore eyes, colds, fever	Webb (1969)
Rutaceae			
Flindersia maculosa	resin	diarrhoea	Maiden (1889)
Geijera parvifolia	leaves	pain, toothache	Lassak and McCarthy (2006), Maiden (1889)
Melicope vitoflora	bark	toothache, pain	Webb (1969)

Santalaceae

Exocarpos aphyllus	stem	sores, cold	Webb (1969)
Santalum acuminatum	seeds, leaves	liniment, skin sores, gonorrhoea	Levitt (1979), Reid and Betts (1979), Maiden (1904)
Santalum lanceolatum	stem, bark, leaves	cold, sore throat, venereal diseases, malaise	Barr *et al.* (1993), Smith (1991)
Santalum spicatum	bark	cough	Reid and Betts (1979), Webb (1969)

Sapindaceae

Dodonaea lanceleolata	leaves	pain	Reid and Betts (1979), Webb (1969)
Dodonaea viscosa	roots, leaves	pain, toothache	Webb (1969)
Planchonella pohlmanniana	leaves, twigs	boils	Webb (1959)

Scrophulariaceae

Scoparia dulcis	whole plant	malaria, fever, stomach pain, influenza, skin sores	Webb (1969), Maiden (1889)
Stemodia grossa	leaves	colds, headache, pain	Reid and Betts (1979)
Stemodia lythrifolia	whole plant	headaches	Reid and Betts (1979)
Striga curviflora	whole plant	skin disease	Roth (1903)

Smilacaceae

Ripogonum papuanum	bark, roots	stingray injuries	Webb (1959)

Solanaceae

Solanum lasiophyllum	roots	poultice for swelling	Reid and Betts (1979)
Sterculiaceae			
Sterculia quadrifida	leaves, bark	wounds, antiseptic,	Webb (1959)
Thymelaeaceae			
Pimelea microcephala	stem, leaves	throat and chest infections	Cleland and Johnston (1939), Koch (1897)
Tiliaceae			
Grewia latifolia	roots	diarrhoea	Maiden (1889)
Grewia retusifolia	fruit, root, leaves	diarrhoea, dysentery, boils, toothache, eyewash	Lassak and McCarthy (2006), Webb (1969)
Urticaceae			
Dendrocnide excelsa	bark, leaves	rheumatism	Maiden (1925), Maiden (1889)
Urtica incisa	leaves	venereal ulcers	Clarke (1987)
Verbenaceae			
Verbena officinalis	whole plant	fever, rheumatism, pain, venereal diseases	Maiden (1889), Woolls (1867)
Vitaceae			
Ampelocissus acetosa	fruit juice	snake bite antidote	Bailey (1909)
Zingiberaceae			
Curcuma australasica	unknown	contraceptive	Webb (1959)

2.1.2. Settler/Immigrant Ethnopharmacology

European settlers arriving in Australia bought with them a tradition of herbal drug usage from their countries of origin. In particular, aromatic and bitter tasting remedies were highly reputed by early European settlers (Lassak and McCarthy, 2006). Many European remedies of the time were based on plant preparations. When European settlers arrived in Australia, they actively sought out Australian plants with similar aromatic and/or bitter taste characteristics to the plants from their homelands (Maiden, 1889). The search for plants with these characteristics was fortuitous as the bitter taste and 'sharp' aroma of some plants is often due to the presence of nitrogenous containing alkaloids. Many studies have demonstrated the medicinal value of alkaloids when used in small doses (Jansen et al., 2006; Sener et al., 2003; Citoglu et al., 1998; Yui et al., 1998). However, these same alkaloids can be toxic in larger doses (Jansen et al., 2006; Dweck, 2001; Hall et al., 2001; Weniger et al., 1998; Nanayakkara et al., 1988). Hence caution is necessary when using alkaloid containing plant preparations.

Unlike indigenous ethnomedicinal usage, settler plant usage is well documented (Bailey, 1909; Roth, 1903; Maiden, 1889; Woolls, 1867; Bailey, 1883; Bailey 1881). Such literature is invaluable as it indicates plants that early European settlers deemed medicinally important and point to plants that should be investigated as possible sources of phytomedicines. Surprisingly, few of these plants have been thoroughly scientifically investigated to date. The known plants used by settlers are summarised in Table 3. This by no means is a complete listing. Where plant identity or usage is in

doubt, listings were omitted. Plants used exclusively by overseas populations and not by immigrants to Australia are discussed in a later section.

Table 3: Botanical names of plant species used by Australian settlers/immigrants and their medicinal uses.

Botanical Name	Plant Part(s) Used	Ethnomedicinal Use	Reference(s)
Apocynaceae			
Alstonia constricta	bark	tonic fever, malaria	Webb (1948), Maiden (1889)
Alyxia buxifolia	bark	dysentery	Webb (1948)
Asclepiadaceae			
Sarcostemma viminale	stem	skin sores, eye complaints warts, rashes	Latz (1995), Barr et al., (1993), Smith (1991), Webb (1969)
Asteraceae			
Acmella grandiflora	roots	toothache (introduced by Chinese immigrants)	Webb (1959)
Cymbonotus lawsonianus	whole plant	antiseptic	Maiden (1889)
Brassicaceae			
Rorippa islandica	whole plant	scurvy	Lassak and McCarthy (2006)
Burseraceae			

Canarium muelleri	resin	cuts, skin sores, ulcers	Bailey (1909)
Caesalpiniaceae			
Chamaecrista absus	seed	ophthalmic (Egypt)	Webb (1948)
Chenopodiaceae			
Atriplex nummularia	whole plant	scurvy, blood diseases	Lassak and McCarthy (2006)
Monimiaceae			
Atherosperma moschatum	bark	laxative, tonic, diuretic	Lassak and McCarthy (2006), Maiden (1889)
Daphnandra micrantha	bark	heart disease	Maiden (1922)
Doryphora sassafras	bark	tonic	Maiden (1889)
Euphorbiaceae			
Euphorbia alsiniflora	whole plant	dysentery, fever	Lassak and McCarthy (2006)
Omalanthus populifolius	leaves	wounds (Chinese settlers)	Webb (1948)
Gentianaceae			
Sebaea ovata	whole plant	dysentery	Woolls (1867)
Lamiaceae			
Mentha satureioides	whole plant	colds, coughs, aches, pain	Webb (1948), Maiden (1889)
Myrtaceae			

Eucalyptus gummifera	bark	antiseptic	Maiden (1907)
Eucalyptus terminalis	bark (gum)	diarrhoea, chest pains	Reid and Betts (1979)
Melaleuca cajuputi	leaves	coughs, colds, stomach cramps, colic, asthma, neuralgia, rheumatism, toothache, earache	Hager (1930)
Melaleuca quinquenervia	leaves	headaches, colds, coughs,	Lassak and McCarthy (2006)
		general illness	Maiden (1889)

Portulacaceae

Portulaca oleracea	whole plant	blood cleanser	Lassak and McCarthy (2006)

Proteaceae

Isopogon ceratophyllus	bark	tonic	Maiden (1889)

Ranunculaceae

Clematis glycinoides	leaves	colds, headache	Hegnauer (1969), Webb (1948)
Clematis microphylla	aerial portions of plant	sores, gastric disorders	Clarke (1987)

Rosaceae

Rubus parviflorus	whole plant	astringent, diarrhoea	Woolls (1867)

Rubiaceae

Nauclea orientalis	bark	malaria, fever	Webb (1948), Roth (1903)
Oldenlandia galioides	whole plant	snake bite (Chinese	Webb (1948)

		settlers)	
Rutaceae			
Flindersia maculosa	resin	diarrhoea	Maiden (1889)
Smilacaceae			
Smilax glyciphylla	leaves	tonic, coughs, blood purifier	Webb (1969), Maiden (1889)
Winteraceae			
Tasmannia lanceolata	bark	scurvy	Ewart (1930)

There is considerable overlap between the plants used by early European settlers and Aborigines. For example, many plants of the family Myrtaceae (especially Eucalypts and Melaleucas) were used by both groups, especially as antiseptic agents and to treat colds and coughs. It is not clear how much the early European settlers learnt from Aborigines. In fact, some early reports indicate that the new settlers were largely unwilling to try Aboriginal treatments (Lassak and McCarthy, 2006). The language barrier also prevented communication of plant medications between the Aboriginal and settler populations. Even when settlers did learn of medicinal plants from Aborigines, they were not always effective as the method of preparation and usage of plant medicines is also important to their effect. Lassak and McCarthy (2006) describes a case where an early settler, having heard of Aborigine usage of *Planchonia careya* bark as an antiseptic, prepared the medication by shredding the hard outer bark into water and making an infusion. Instead, the Aborigines used to prepare an

infusion from only the inner bark. The settler's preparation proved of little use, possibly due to these preparation differences.

Later migration to Australia by people from diverse regions has also bought a wealth of further knowledge of plant medicinal use. All world populations have developed their own plant based medical systems. In particular, Asian emigration bought a far wider understanding of the therapeutic potential of plants. Plant medicinal use in India (eg. Ayurveda) and traditional Chinese medicinal plant use are particularly well documented (Patwardhan et al, 2005; Khan and Balick, 2001) and will not be dealt with here. Similarly, African (Iwu, 1993), Middle Eastern (Ghazanfar, 1994), North American (Moerman, 1998) and South American (Roth and Lindorf, 2002) populations have well established phytomedicinal systems. Immigrants from these regions have bought with them their own systems of medicinal plant use, all of which have added to our understanding of Australian plant medicinal potential.

2.1.3. The Usage of Australian Native Plants By Overseas Populations

Many Australian plant species are widely distributed around the world, occurring both naturally and as introduced species. Some species occur naturally in South East Asia and India and as far away as Africa and the Middle East. Other species have been introduced into a variety of locations as commercially useful species (eg. Eucalypt introduction into Portugal and North America) and in some cases are considered invasive (Santos, 1997). There is often overlap between plant usage in Australia and in overseas populations. For example, *Euphorbia atoto* was used by Australian Aborigines as well as by Indian and Arabian healers as a herbal medicine (Reid and Betts, 1979; Bailey, 1883). However, there are no records of the therapeutic use of some plants in Australia which have been used

medicinally in other parts of the world. Table 4 summarises the use of Australian native plants in overseas populations. This is by no means a complete listing. Where plant identity or usage is in doubt, listings were omitted.

Table 4: Botanical names of plant species used by overseas populations and their medicinal uses.

Botanical Name	Plant Part(s) Used	Ethnomedicinal Use	Reference(s)
Adiantaceae			
Adiantum aethiopicum	whole plant	astringent, chest infections (Europe)	Hager (1930), Maiden (1889)
Amaranthaceae			
Deeringia amaranthoides	leaves	measles (Indonesia)	Webb (1948)
Anacardiaceae			
Semecarpus australiensis	juice, nut	rheumatism, warts, asthma (India)	Maiden (1889)
Apocynaceae			
Alstonia scholaris	bark	diarrhoea, general illness (India)	Maiden (1889)
Cerbera manghas	nuts, bark, leaves	narcotic, purgative, laxative	Maiden (1889)

		(Java)	
Araceae			
Colocasia macrorrhiza	leaves	rubefacient, sores, burns, ulcers, sunburn (India)	Maiden (1889)
Eclipta prostrata	roots	liver complaints (India), tonic (Sri Lanka)	Hurst (1942), Bailey (1909) Bailey (1883)
Asteraceae			
Ageratum conyzoides	whole plant	wounds (Nigeria)	Adesogan and Okunade (1979)
Wedelia calendulaceae	whole plant	tonic (Sri Lanka)	Webb (1948), Bailey (1909)
Boraginaceae			
Trichodesma zeylanicum	whole plant	diuretic, snake bite (India)	Bailey (1881)
Caesalpiniaceae			
Cynometra ramiflora	root, leaves	purgative, leprosy, scabies (India)	Webb (1948), Maiden (1889)
Capparidaceae			
Cleome viscosa	leaves, roots, whole plant	fever, diarrhoea, cuts, ulcers	Webb (1949), Bailey (1909),
	seeds	ear disease (India, Vietnam) skin irritations (USA, Vietnam)	Maiden (1889)
Calophyllum inophyllum	seeds	rheumatism, leprosy	Roth (1903), Maiden (1889)

		(India)	
Casuarinaceae			
Casuarina equisetifolia	bark	astringent, diarrhoea, (China)	Maiden (1889)
Commelinaceae			
Cyanotis axillaris	whole plant	abdominal swelling (India)	Webb (1949)
Convolvulaceae			
Operculina turpethum	roots	purgative (India)	Webb (1948), Bailey (1883)
Cucurbitaceae			
Diplocyclos palmatus	whole plant	laxative (India)	Webb (1948)
Trichosanthes palmata	fruit	antiseptic (India)	Bailey (1881)
Cyperaceae			
Scleria lithosperma	whole plant	kidney inflammation (India)	Bailey (1881)
Euphorbiaceae			
Acalypha wilkesiana	leaves	sedative	Paijmans (1976)
Euphorbia atoto	sap	ulcers, antiseptic	Bailey (1883)
Mallotus philippensis	seed pods	skin complaints, leprosy (India, Middle East)	Webb (1948), Bailey (1883)
Fabaceae			

Abrus precatorius	roots, leaves, seeds	coughs, (India), ophthalmic (India, Brazil)	Maiden (1889)
Caesalpinia bonduc	seeds, leaves, roots	tonic (India), astringent (Vietnam)	Maiden (1889)
Mucuna gigantea	bark	rheumatism (India)	Webb (1948), Bailey (1883)
Pongamia pinnata	seed, leaves	skin diseases, scabies, herpes, rheumatism, ulcers (India)	Maiden (1889)
Sesbania sesban	leaves	boils (India)	Bailey (1883)

Hydrophyllaceae

Hydrolea zeylanica	leaves	antiseptic (India)	Bailey (1881)
Ottelia alismoides	whole plant	anti-venom (India)	Bailey (1881)

Lauraceae

Cassytha filiformis	whole plant	ulcers, sore eyes (India)	Maiden (1889)
Cinnamomum laubatii	bark, leaves	diuretic, stimulant (India)	Maiden (1889)

Lecythidaceae

Barringtonia acutangula	leaf	skin sores, diarrhoea, laxative (India)	Maiden (1889)
Barringtonia racemosa	root, bark, seeds	laxative, ulcers, skin diseases (India)	Maiden (1889)

Lythraceae

Ammannia baccifera	leaves	rheumatism, fever (India)	Maiden (1889)

Malvaceae

Sida rhombifolia	leaves, roots	rheumatism, diarrhoea	Webb (1969), Webb (1948), Bailey (1881)
Thespesia populnea	fruit, bark	scabies, skin diseases (India)	Maiden (1889)

Meliaceae

Melia azedarach	fruit, root, bark	leprosy, malaria (India) purgative (USA)	Webb (1948), Maiden (1908)
Toona ciliata	bark	dysentery, fever	Webb (1948), Maiden (1889)

Nyctaginaceae

Boerhavia diffusa	root, whole plant	expectorant, asthma, diuretic (India)	Hegnauer (1969), Webb (1948)

Nelumbonaceae

Nelumbo nucifera	leaf, stem	diarrhoea (India)	Maiden (1889)

Olacaceae

Ximenia americana	roots	diarrhoea	Webb (1948)

Orchidaceae

Dockrilla treetifolium	leaves	headache, pain (South Pacific islands)	Maiden (1889)

Plumbaginaceae			
Plumbago zeylanica	bark, root	dyspepsia, skin lesions (India), leprosy (South Africa)	Webb (1948)
Polygonaceae			
Persicaria barbata	leaves, seeds	pain, sedative, diuretic, astringent (India)	Webb (1948), Bailey (1883), Bailey (1881)
Portulacaceae			
Portulaca oleracea	whole plant	internal complaints (India)	Webb (1949)
Rhamnaceae			
Ziziphus oenoplia	bark, fruit	antiseptic (India)	Webb (1949)
Rubiaceae			
Morinda citrifolia	leaves, bark, roots	antiseptic, ulcers (India)	Webb (1948), Maiden (1889)
Sapindaceae			
Allophylus serratus	roots	diarrhoea (India)	Maiden (1889)
Dodonaea viscosa	leaves	stomach disorders (South Africa), stimulant (Peru)	Webb (1948)
Scrophulariaceae			
Bacopa monniera	leaves	rheumatism, diuretic, laxative, tonic (India),	Hegnauer (1973), Bailey (1909), Bailey (1883)

		laxative (Sri Lanka)	
Scoparia dulcis	whole plant	malaria, fever	Webb (1969), Maiden (1889)
Simaroubaceae			
Ailanthus triphysa	bark	tonic, dyspepsia, dysentery	Hegnauer (1973), Bailey (1909)
		bronchitis, asthma (India)	
Brucea javanica	seeds	dysentery (Java), malaria (China)	Bailey (1909)
Thymelaeaceae			
Wikstroemia indica	bark, leaves	antiseptic, coughs (Fiji)	Maiden (1889)
Verbenaceae			
Clerodendrum inerme	leaves, bark	wounds (New Guinea), fever (Guam)	Webb (1959), Webb (1948)
Violaceae			
Hybanthus enneaspermus	roots	urinary disorders (India)	Bailey (1881)
Vitaceae			
Cayratia trifolia	juice	snake bite (India)	Bailey (1909)

2.1.4. Plants Not Currently Used Medicinally But Containing Bioactive Components

Many plants for which no medicinal use has been previously reported may be considered potential therapeutic agents due to their chemical compositions. Recent studies have reported a variety of Australian native plants to be high in antioxidants (Netzel et al., 2007; Netzel et al., 2006). In particular, *Davidsonia pruriens* (Davidson plum) (Figure 8a), *Eugenia carissoides* (Cedar Bay cherry), *Kunzea pomifera*, *Citrus microcitrus* (finger lime) (also known as *Microcitrus australasica*), *Pleiogynium timorense* (Burdekin plum), *Podocarpus elatus* (Illawarra plum) (Figure 8b), *Rubus moluccanus* (Molucca raspberry), two *Szyzygium* species (*Szyzygium australe* (bush cherry) and *Szyzygium luehmannii* (riberry)), *Tasmanian lanceolata* (Tasmanian pepper) and *Terminalia ferdinandiana* (Kakadu plum) (Figure 8c) were found to be good sources of ascorbic acid and other antioxidants. Indeed, *Terminalia ferdinandiana* was reported as having ascorbic acid levels per gram of fruit more than 900 times higher than blueberries. All of these plants are also reported to have high levels of phenolic compounds and anthocyanins (Netzel et al., 2007; Netzel et al., 2006).

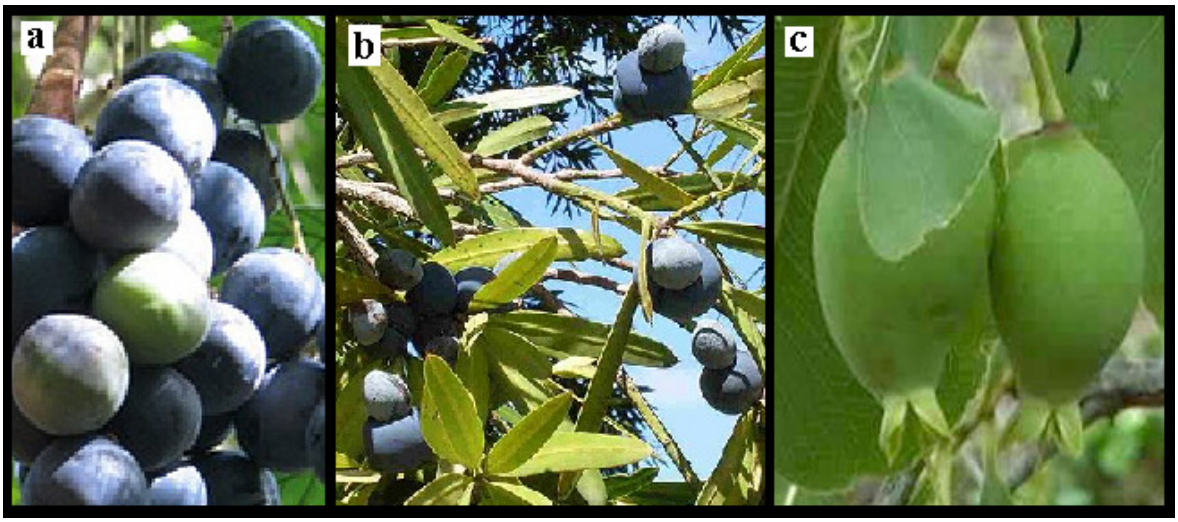


Figure 8: (a) *Davidsonia pruriens* (Davidson plum), (b) *Podocarpus elatus* (Illawarra plum), *Terminalia ferdinandiana* (Kakadu plum). Photos (b) and (c) were accessed from Wikipedia Commons on 21

January 2011 and are adapted and reproduced here with the relevant permissions **(**http://en.wikipedia.org/wiki/Terminalia_ferdinandiana **;** http://en.wikipedia.org/wiki/Podocarpus_elatus **).** Photo (a) was taken by Dr Ian Cock in Brisbane, Australia in 2009.

Antioxidants have been associated with the prevention of cancer (Lambert et al., 2005; Hertog et al., 1996), cardiovascular disease (Geleijnse et al., 2002) and neurological degenerative disorders (Youdim et al., 2002). They are also linked with anti-diabetic bioactivities (Matsui et al., 2002) and have been associated with the reduction of obesity (Tsuda et al., 2003). Antioxidants can directly scavenge free radicals, protecting cells against oxidative stress related damage to proteins, lipids and nucleic acids (Rice-Evans, 2001; Rice-Evans et al., 1996). Therefore, the Australian plants identified by the Netzel studies (Netzel et al., 2007; Netzel et al., 2006) have potential for the treatment of a variety of diseases and disorders and their potential bioactivities warrant further investigation. Indeed, preliminary studies have demonstrated the broad spectrum antiseptic potential of *Terminalia ferdinandiana* (Cock and Mohanty, 2011).

Similarly, plants rich in flavonoids have a wide range of potential medicinal uses. Numerous medicinal plants contain levels of flavonoids found to be useful in treating disorders of the peripheral circulation (Mills and Bone, 2000) and that are anti-inflammatory (Mills and Bone, 2000), antispasmodic (Robbers and Tyler, 2000) and anti-allergic (Mills and Bone, 2000). Flavonoids also are inhibitory towards a variety of human pathogens including bacteria, fungus and viruses (Bylka et al., 2004). Therefore, plants found to possess high flavanoid levels may prove useful in combating these

diseases/medical conditions. Plants containing high levels of other chemical agents (eg. alkaloids and terpenes) may also prove useful medicinal agents.

3. Some Useful Australian Medicinal Plants

Although scientific investigation into the usage of Australian medicinal plants is still in its infancy, some plants have already proved useful. In particular, the Eucalypts and Melaleucas have proved valuable medicinally and commercially. This volume will attempt to summarise the current state of research in this field and point to possible future research directions. To provide a background, a selection of Australian plants that have already proved to be useful medicinal/therapeutic products will be examined. This is not a complete examination of all noteworthy plants but will give an indication of the potential for discovery of new commercially important medicinal products. To begin, the essential oil producing plants which currently form the bulk of the commercialisation of Australian medicinal plants will be discussed. Examples of plants used for the commercial production of essential oils include the Eucalypts, Melaleucas, Leptospermums and *Backhousia citriodora*.

3.1. Eucalyptus Species

Perhaps no other plant personifies Australia to the same degree as do the Eucalyptus species (Figure 9). Eucalyptus is a diverse genus of trees in the family Myrtaceae. Of the more than 700 species that comprise this genus, most are endemic to Australia. A smaller number are also native to New Guinea, Indonesia and the Philippines. Eucalypts can be found in almost every region of the Australian continent. They have also been widely introduced into drier subtropical and tropical

regions in areas as diverse as Africa, the Middle East, India, USA and South America. In many of these areas these trees are considered invasive (Santos, 1997) whilst in other areas they are prized for their commercial applications.

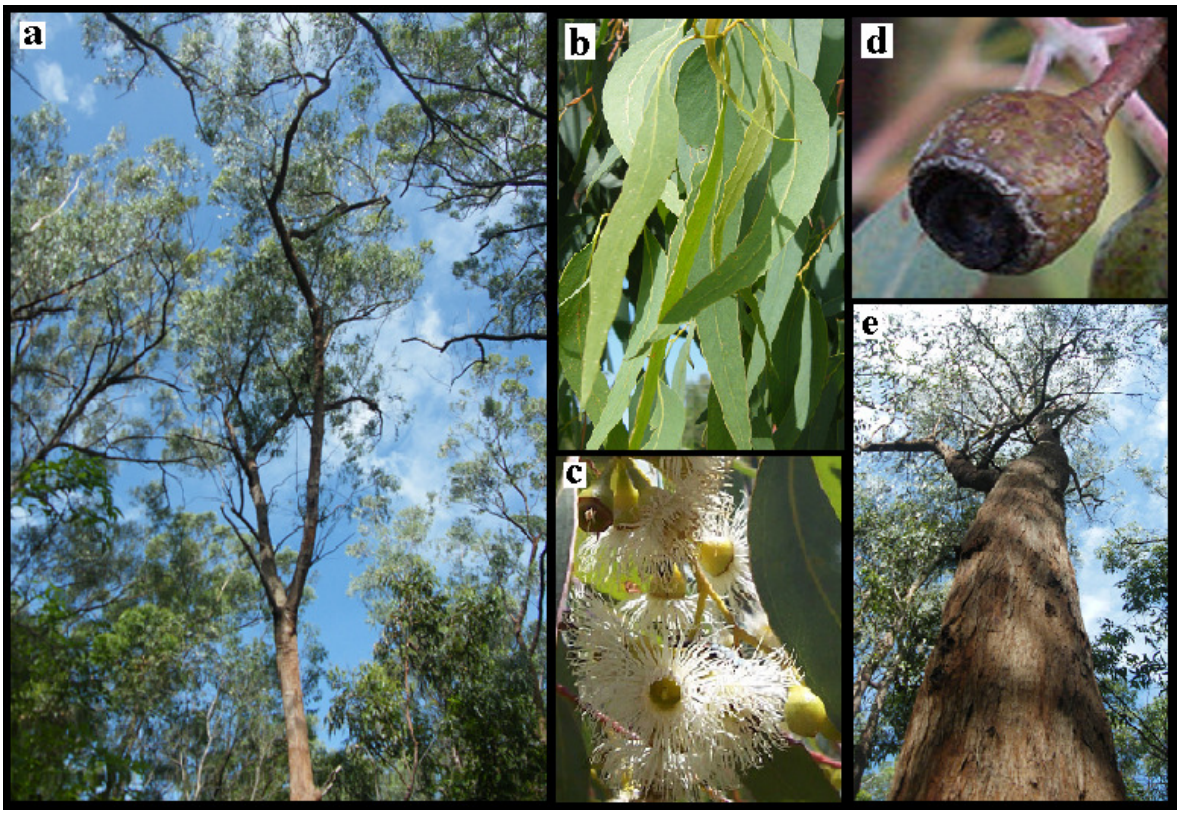


Figure 9: (a) Eucalyptus forrest with *Eucalyptus major* in the centre, (b) *Eucalyptus major* leaves, (c) *Eucalyptus major* flowers, (d) Eucalyptus fruit (gum nut) from unverified species and (e) *Eucalyptus baileyana*. Pictures were taken in Toohey Forrest, Australia by Dr Ian Cock.

Eucalypts are valued for their wood and some are also valuable sources of proteins, tannins, gum and dyes, although their most valuable product is the Eucalyptus oil that is readily distilled from their leaves (Sartorelli, 2007; Trivedi and Hotchandani, 2004). Essential oils from some Eucalyptus species (eg. *Eucalyptus pulverulenta*) comprise up to 90% cineole (Brophy et al., 1985; Foley and Lassak,

2004). The structure of cineole is shown in Figure 10. Essential oils from other plants containing cineole (eg. *Heteropyxis natalensis* Harv) have previously been demonstrated to have good antimicrobial properties (Gundidza et al., 1993). Eucalyptus oil is used extensively in cleaning and deodorising products as well as in cough drops and decongestants (Sartorelli, 2007). Eucalyptus oil also has insect pest repellent properties and is a component in many commercial pesticides (Fradin and Day, 2002).

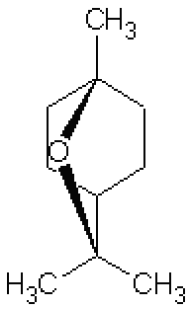


Figure 10: Chemical structure of 1,8-cineole, the major oil component of Eucalyptus leaves.

Australian Eucalyptus species also had a role as traditional bush medicines for Australian Aborigines. Several species have been reported to be used to prepare antiseptic washes (Lassak and McCarthy, 2006; Harborne and Baxter, 1995). The resinous exudate from the trunk of *Eucalyptus maculata* was also taken internally to cure bladder infections (Lassak and McCarthy, 2006). Oils from several Eucalyptus species have been used for the treatment of upper respiratory tract infections, colds, influenza, sinus congestion (Harborne and Baxter, 1995) and pulmonary infections (Low et al., 1974). Recent studies have confirmed the antimicrobial activity of oils from many Eucalyptus species (Cock, 2008; Sartorelli, 2007; Delaquis et al., 2002; Oyedeji et al., 1999).

3.2. Melaleuca Species

Melaleuca (family Myrtaceae) is a diverse genus of trees and shrubs, most of which are endemic to Australia (Page and Olds, 2004). Figure 11 shows *Melaleuca quinquenervia* (paper bark) trees as well as bark, leaves and flowers. A few Melaleuca species are also indigenous to Papua New Guinea and Indonesia and some species are found in coastal regions of South East Asia. Many species have papery bark that easily peels from the trunk (Figure 11b) which early Aborigines had many uses for, including medicinal uses (eg. stemming blood flow from wounds) (Lassak and McCarthy, 2006). Other parts of the plant, particularly the leaves, were also used by indigenous Australians as medicines, especially in the treatment of coughs and colds and as antiseptic agents (Lassak and McCarthy, 2006; Maiden, 1889). European settlers also have a long history of Melaleuca medicinal use (Lassak and McCarthy, 2006). In fact, it is reported that the early English explorer Captain Cook and his party used the leaves of *Melaleuca alternifolia* as early as 1770 (Cook, 1777) to make a tea and referred to this plant as “Tea Tree”, a name that is still used to this day. With the advent of European settlement in Australia, *Melaleuca alternifolia* became a valued bush medicine. However, it wasn’t until after World War 1 that scientific study demonstrated the medicinal potential of this plant. Studies in the 1920’s (Penfold and Grant, 1925a, b) showed Tea Tree leaf oil to be approximately 12 times stronger as an antiseptic agent than carbolic acid (the standard at the time).

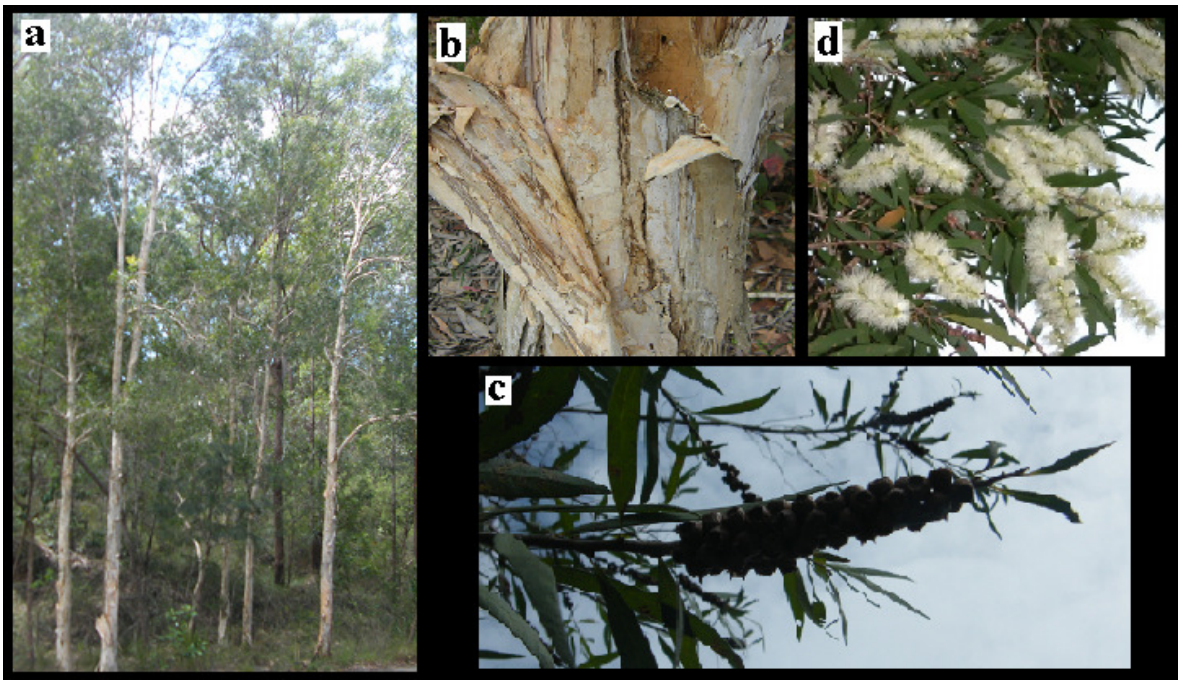


Figure 11: *Melaleuca quinquenervia* (a) group of trees, (b) close up of the "paper" bark, (c) unopened flowers and (d) flowers and foliage. Pictures were taken at various times throughout 2010 in Toohey Forrest, Australia by Dr Ian Cock.

Like the Eucalypts previously described, many Melaleuca species are valued for their oils which are also rich in 1, 8-cineole (Figure 10) as well as a variety of other terpenes and sesquiterpenes. The structures of some of the major terpenes present in Melaleucas are shown in Figure 12. Melaleuca essential oils have well known antiseptic properties and are valued commercially as antibacterial agents. Recent interest in Australian bush foods has also seen Melaleuca oils used in the food and flavouring industries and there is scope for commercial development in this area. Melaleuca oils as natural food additives not only provide a pleasing flavour but also inhibit microbial food spoilage.

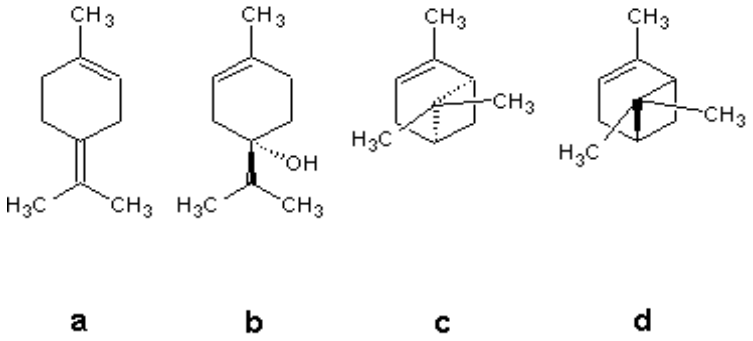


Figure 12: Chemical structures of (a) terpinolene, (b) terpinene-4-ol, (c) α-pinene and (d) β-pinene, major phytochemical component of Melaleuca essential oils.

3.3. Leptospermum Species

Leptospermum (family Myrtaceae) is a genus of more than 80 species that are widely distributed in Australia, with a few species also native to New Zealand and Malaysia (Thompson, 1983). The antiseptic properties of several Leptospermum species are well known (Lassak and McCarthy, 2006). Particularly well studied are the antimicrobial properties of *Leptospermum scoparium* (Manuka) (Figure 13), a species endemic to eastern Australia (Brophy et al., 1991) and New Zealand (Wardle, 1991). This species has been traditionally used medicinally for many ailments. The leaf vapour was used for colds and coughs, the gum exudates for scalds and burns, aqueous bark and seed extracts for infections and inflammation and the leaves for urinary complaints (Brooker et al., 1987). Honey derived from *L. scoparium* is also known as a good antibacterial agent (Weston et al., 2000; Allen et al., 1991). The medicinal properties of other Leptospermum species are less well studied although some are also known to have been used by Australian Aborigines as antiseptic agents (Lassak and McCarthy, 2006). Reports have demonstrated the antibacterial and antifungal activity of

Leptospermum petersonii (lemon scented tea tree) (Davis and Ward, 2003; Lis-Balchin et al., 1996) and *Leptospermum amboinense* (Setzer et al., 2000).

Figure 13: *Leptospermum scoparium* (a) entire plant and (b) close up of foliage and flowers. Photos were accessed from Wikipedia (http://en.wikipedia.org/wiki/Leptospermum_scoparium) on 17 January 2010 and are adapted and reproduced here with the relevant permissions.

Research into the medicinal value of other Leptospermum species is less extensive and much still needs to be done to identify their antimicrobial potential. Many plants of this genus are known to contain a mixture of terpenes including 1, 8-cineole and terpinen-4-ol (Figure 14) (Porter and Wilkins, 1999; Carr, 1998). Both 1, 8-cineole and terpinen-4-ol are thought to have antimicrobial activity (Simić et al., 2005; Mondello et al., 2006).

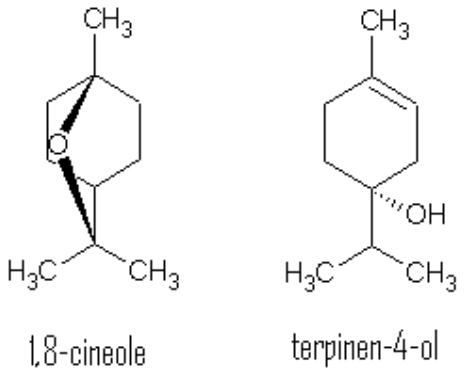


Figure 14: Chemical structures of (a) 1, 8-cineole and (b) terpinene-4-ol, terpene components of Leptospermum leaves.

3.4. Eremophila Species

Eremophila is a large, diverse genus of plants with more than 210 species which mainly inhabit arid and semi-arid areas in the central regions of mainland Australia, preferring relatively poor soils and dry conditions (Page and Olds, 2004). They are commonly referred to by a variety of names including poverty plant, emu bush, fuchsia bush, terpentine bush and tar bush. Figure 15 shows Eremophila whole plants, leaves and flowers. Eremophilas were widely used by Australian Aborigines in a number of roles including as adhesives and sealants as well as being used as medicinal agents (Richmond, 1993). As well as using Eremophila decoctions and extracts as liniments (Richmond and Ghisalberti, 1994), Aborigines used them as antiseptic agents to treat cuts, open sores, sore throats and ear infections (Barr et al., 1993).

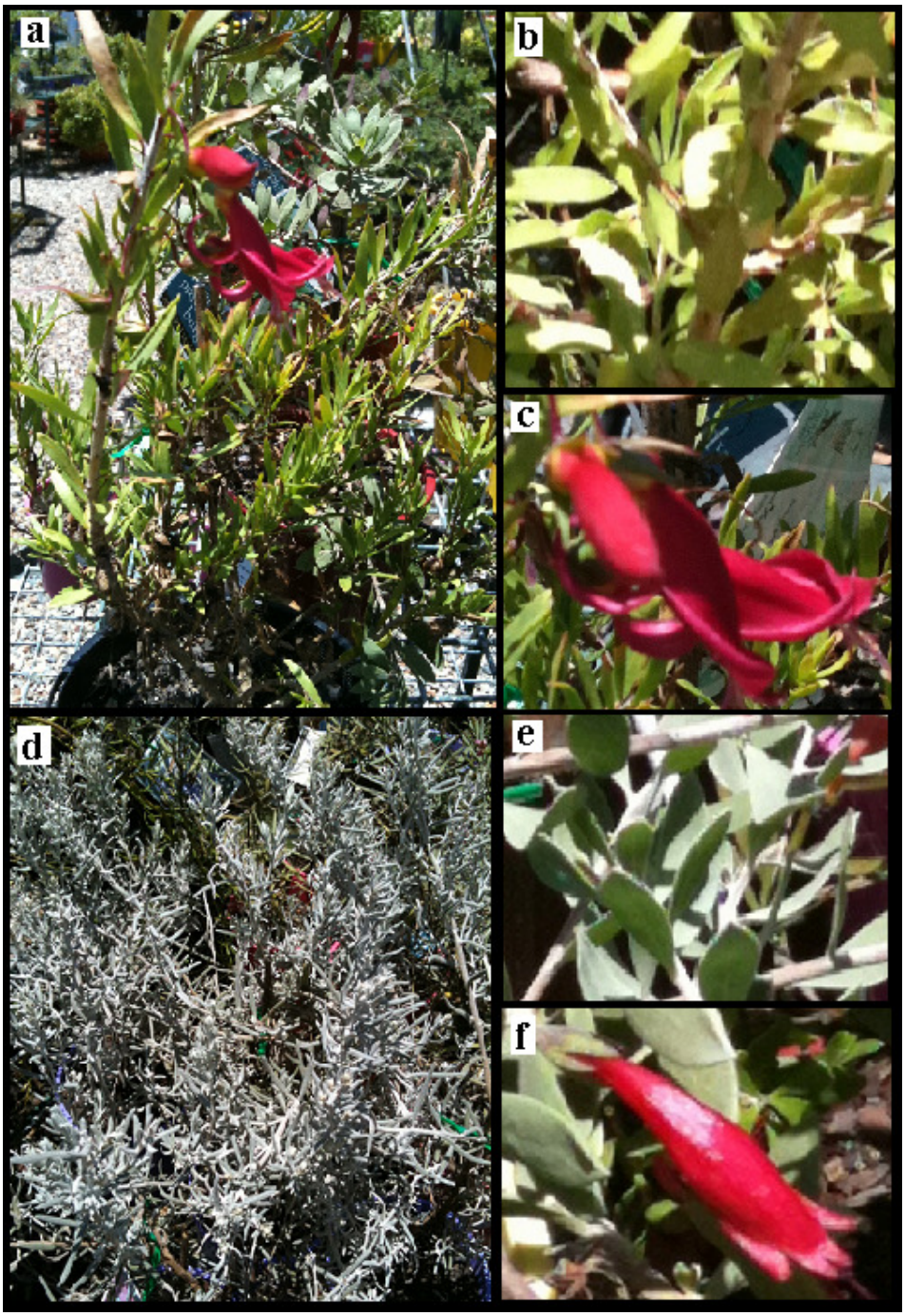


Figure 15: (a) *Eremophila maculata* whole plant, (b) *Eremophila maculata* foliage, (c) *Eremophila maculata* flower, (d) *Eremophila nivea* whole plant, (e) *Eremophila glabra* foliage and (f) *Eremophila glabra* flower. Pictures were taken at Nielsen's Native Nursery, Brisbane, Australia in January 2011 by Dr Ian Cock.

Perhaps one of the most promising genus' of the medicinal Australian plants, Eremophila species have received much recent attention as potential therapeutic agents. Recent studies (Pennachio et al., 2005; Pennachio et al., 1996; Pennachio et al., 1995), describe the cardioactive effects of Eremophila extracts. Studies have also shown various Eremophila species to have antiseptic properties, particularly towards Gram-positive bacteria (Pennachio et al., 2005; Palombo and Semple, 2001), thus confirming the validity of traditional Aboriginal medicinal usage. Much is still to be learnt about the active constituents and the mechanisms of action of Eremophilas, although at least one of the active components is known. Pennachio et al. (1996) isolated a phenylethanoid glycoside called verbascoside (Figure 16a) which they showed to significantly increase heart rate and contractile force in isolated rat hearts. Eremophilas are also known to produce the cyanogenic glycoside prunasin (Figure 16b) and the sesquiterpenes 10, 11-dehydromyoporone (Figure 16c) and 10, 11-dehydromyodesmone (Figure 16d) (Blackburne et al., 1972) and various alkaloids (Aplin and Cannon, 1971), any of which may potentially be responsible for the antiseptic nature of Eremophila species.

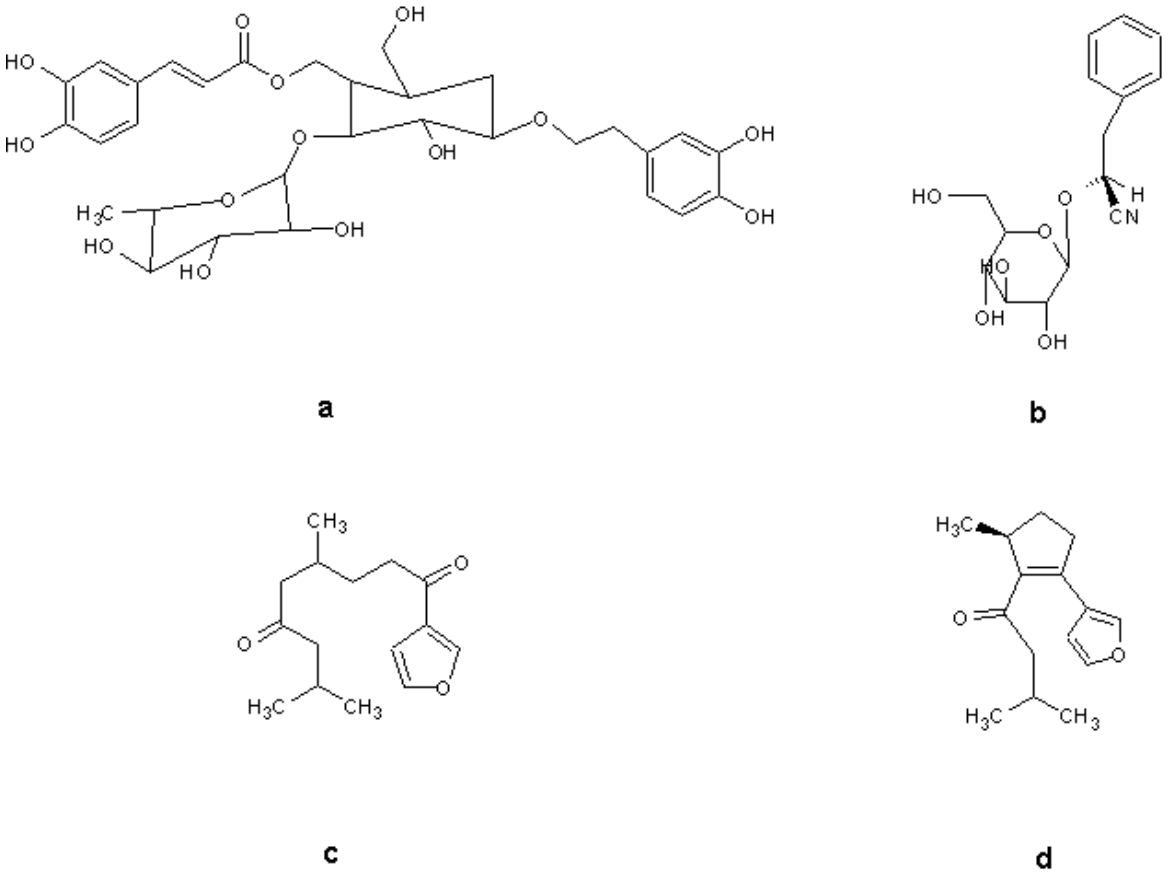


Figure 16: Chemical structures of (a) verbascoside, (b) prunasin, (c) 10, 11-dehydromyoporone and (d) 10, 11-dehydromyodesmone, the major phytochemical components of Eremophilas.

3.5. *Backhousia citriodora*

Backhousia citriodora (lemon myrtle) is an Australian plant, native to subtropical areas of eastern Australia. Figure 17 shows *Backhousia citriodora* whole plants, leaves and flowers. The leaves of this plant are widely used as a bush food and as a component of toiletries and cosmetics (Hegarty et al., 2001). Studies in this laboratory (Cock, 2008) and elsewhere (Wilkinson et al., 2003; Ryan et al.,

2000) have demonstrated the antibacterial activity of *B. citriodora* leaves. Interestingly, no definitive ethnobotanical reports of Australian Aboriginal medicinal use of *B. citriodora* were found in the literature, although the leaves are known to have been used in cooking. Most of the studies of *B. citriodora* antibacterial potential focus on the essential oil of the leaves (Wilkinson et al., 2003; Ryan et al., 2000). In most plants of this species, more than 90% of the oil is citral (Figure 18), a mixture of neral (α-citral) and geranial (β-citral) (Opdyke, 1976). Both neral and geranial have previously been reported to have potent antibacterial activity against a variety of bacteria (Wilkinson et al., 2003; Inouye et al., 2001; Kim et al., 1995).

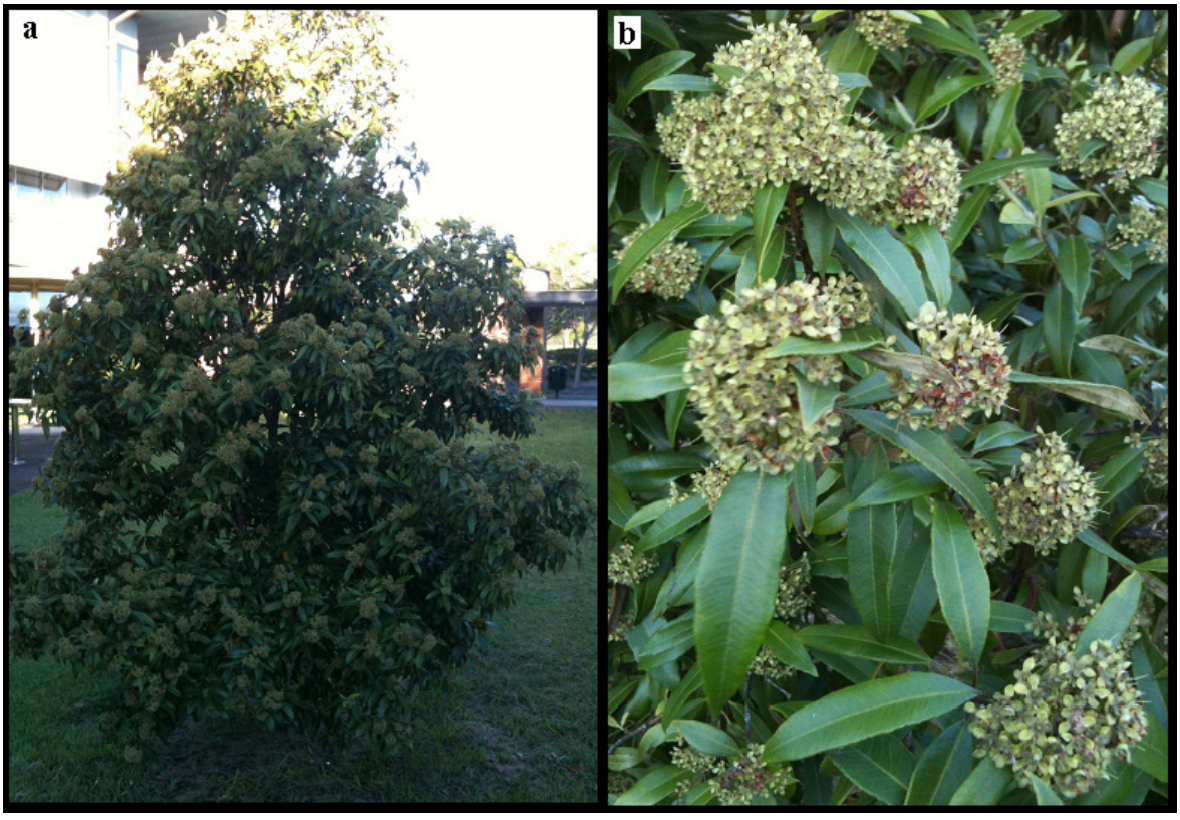
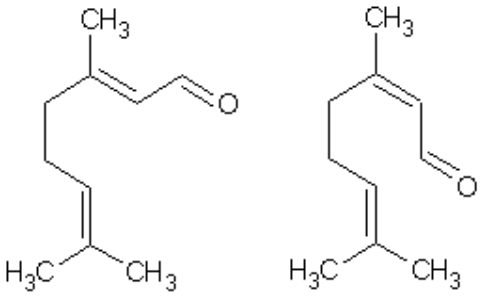


Figure 17: *Backhousia citriodora* (a) whole plant and (b) foliage and flowers. Photos were taken in January 2011 in Brisbane, Australia by Dr Ian Cock.



neral (α-citral) geranial (β-citral)

(a) (b)

Figure 18: Chemical structures of (a) neral (α-citral) and (b) geraniol (β-citral), the major oil components of *B. citriodora* leaf essential oils.

3.6 Callistemon Species

The genus Callistemon (family Myrtaceae) consists of 34 species endemic to Australia. Some species have also been introduced to other areas such as USA (Gilman, 1999) and Africa (Nel et al., 2004; Macdonald et al., 2003) where they are considered invasive species. They are closely related to Melaleucas and have similar leaf and flower morphology (Wrigley and Fagg, 1993; Elliot and Jones, 1982). Callistemons are commonly referred to as 'bottlebrushes' due to the appearance of their

flowers. Figure 19 shows *Callistemon citrinus* whole plants, leaves and flowers. They occur naturally in temperate regions of Australia, particularly on the east and south-west coasts.

Figure 19: (a) *Callistemon citrinus* tree, (b) *Callistemon citrinus* foliage and unopened flowers, (c) *Callistemon citrinus* flower. Photos (a) and (c) were accessed from Wikipedia Commons (http://en.wikipedia.org/wiki/Callistemon_citrinus ; http://en.wikipedia.org/wiki/Callistemon) on 17 January 2011 and are adapted and reproduced here with the relevant permissions. Photo (b) was taken by Dr Ian Cock in Brisbane, Australia in January 2011.

Callistemon flowers were used as a food source by Australian Aborigines. The flowers were sucked for their nectar or used to make sweet drinks (Nash, 2000). Callistemon species also had roles as

traditional bush medicines for Australian Aborigines (Jirovetz et al., 1997). The leaves were used to cure respiratory tract infections. *Callistemon rigidus* leaves have also been used to cure coughing, bronchitis and respiratory tract infections in Cameroon, China and various other parts of Asia (Jirovetz et al., 1997). Unfortunately, most of our understanding of the medicinal potential of Callistemon species is anecdotal with few species being properly studied by rigorous scientific investigation. Recent reports have confirmed the antibacterial activity of a *Callistemon rigidus* (Sanjai and Charu, 2006; Saxena and Gomber, 2006). These preliminary studies have confirmed the need for further investigation. It has been postulated that terpenes in the leaves may be responsible for the efficacy of Callistemons in traditional treatments (Jirovetz et al., 1997).

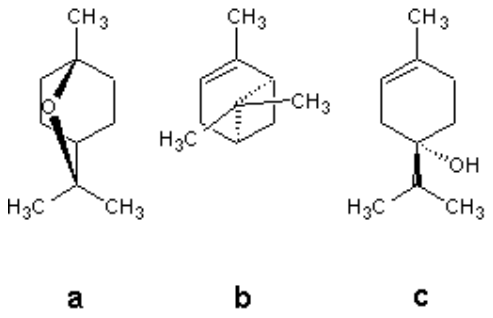


Figure 20: Chemical structures of (a) 1, 8-cineole (b) pinene and (c) terpinene-4-ol, components of Callistemon leaves.

Callistemons have been shown to contain some of the same components found in other Australian plants with demonstrated antimicrobial activities (Figure 20). 1, 8-cineole (Figure 20a) is a major constituent of Callistemon leaves (Ming et al., 1998; Misra et al., 1997) and has been shown in other plants (Eucalypts, Melaleucas, Leptospermums) to kill bacteria and fungi. Likewise, Callistemon

leaves also contain the terpenes pinene (Figure 20b) and terpinene-4-ol (Figure 20c) (Change-Ming et al., 1998; Misra et al., 1997), either of which may also be responsible for the antiseptic properties of Callistemon species.

3.7. Acacia Species

The Acacia genus (family Fabaceae, subfamily Mimoaceae) consists of over 1200 species, more than 700 of which are indigenous to Australia (Ali, 1998). Other species are spread throughout tropical to warm temperate regions of Africa, India and the Americas. Figure 21 shows an *Acacia aulocarpa* tree (Figure 21a) and flowers (Figure 21b), as well as *Acacia complanta* foliage (Figure 21c) and seed pods (Figure 21d). Acacias have also been introduced into other countries for ornamental and economic purposes. Most Acacia species produce quality wood and some are also valuable sources of proteins, tannins, gum, perfumes, paint, ink and flavouring agents (Arias et al., 2004; Seigler, 2003). For Australian Aborigines, Acacia seed formed an important part of their diet, providing an easily obtainable, high energy food (Hegarty and Hegarty, 2001; Latz, 1995) that could easily be ground to a flour, mixed with water and eaten either raw or cooked to produce a type of unleavened bread. Other parts of some Acacia species are also eaten. Several species exude a sugary gum from wounds to the stem and branches (Arias et al., 2004; Hegarty and Hegarty, 2001) whilst others are hosts for edible grubs often referred to as witchetty grubs by non-Aboriginal Australians (Kalotas and Goddard, 1985).

Figure 21: (a) *Acacia aulocarpa* tree, (b) *Acacia aulocarpa* foliage and flowers, (c) *Acacia complanta* foliage, (d) *Acacia complanta* with open seed pods. Pictures were taken at various times throughout 2010 in Toohey Forrest, Australia by Dr Ian Cock.

Australian Acacia species also had roles as traditional bush medicines for Australian Aborigines. Several species have been reported to be used to prepare antimicrobial washes and lotions (Lassak and McCarthy, 2006). *A. nilotica* was traditionally used by Aborigines for ailments such as diarrhoea and was reported to have antihyperglycemic (Ahhtar and Kahn, 1985), antimicrobial (Abd-El-Nabi, 1992) molluscicidal (Hussein, 1984), antihypertensive and antiplatelet aggregatory activities (Shah et al., 1997). Unfortunately most of our understanding of the medicinal potential of Australian Acacia species is anecdotal with few species being properly studied. One South American Acacia species (*A. aroma*) has been shown to demonstrate antibacterial activity against both Gram-positive and Gram-negative bacteria (Arias et al., 2004). Amongst the Australian Acacia species studied, *A. kempeana*, *A. tetragonophylla* (Palombo and Semple, 2001), *A. linarioides*, *A. brachystachya*, *A. lineate*, *A. trineura* and *A. olliquinervia* (Ali, 1998) have been reported to have to have antibacterial activity. A

potent cyclooxygenase-1 inhibition by extracts of *A. ancistrocarpa* has also been reported (Li et al., 2003).

Much is still to be learnt about the active components and mechanisms of action of Acacias, although they are known to contain a number of biochemicals of medicinal interest including alkaloids, cyanogenic glycosides, cyclitols, diterpenes, phytosterols, saponins, and tannins (Seigler, 2003). The alkaloid β-Phenethylamine (Figure 22a) and related amines have been reported in a number of Australian Acacias including *A. adunca*, *A. cultriformis*, *A. floribunda*, *A. hakeoides*, *A. harpophylla*, *A. kettlewelliae*, *A. linifolia*, *A. longifolia*, *A. lunata*, *A. podalyriaefolia*, *A. pravissima*, *A. prominens*, and *A. suaveolens* (Fitzgerald, 1964; White, 1944a, b). 2-methyl-1, 2, 3, 4-tetrahydro-β-carboline (Figure 22b) has also been reported for some species (Poupat, et al., 1976). Maslin et al. (1987) report that 96% of Australian Acacias contain the cyanogenic cyanides prunasin (Figure 22c) and sambunigrin (Figure 22d). Acacias are known to contain a number of terpenes such as the diterpenes labd-13-en-3β, 8α, 15-triol (Figure 22e) and 3β, 8α-dihydroxylabd-13-en-15-oic acid (Figure 22f) (Forster et al., 1985). Many species also contain phytosterols and saponins including α-spinasterol (Figure 22g) (Mahato, 1989). Common flavonoids in Acacia species include the flavan-3-ols catechin (Figure 22h), epicatechin and epigallocatechin (Tindale and Roux, 1969). Acacia bark contains high levels of tannins. *A. mearnsii* (Black Wattle) bark has been reported to contain 20-40% tannins by weight, of which up to 70% are proanthocyanidins (Figure 22i) (Tindale and Roux, 1969).

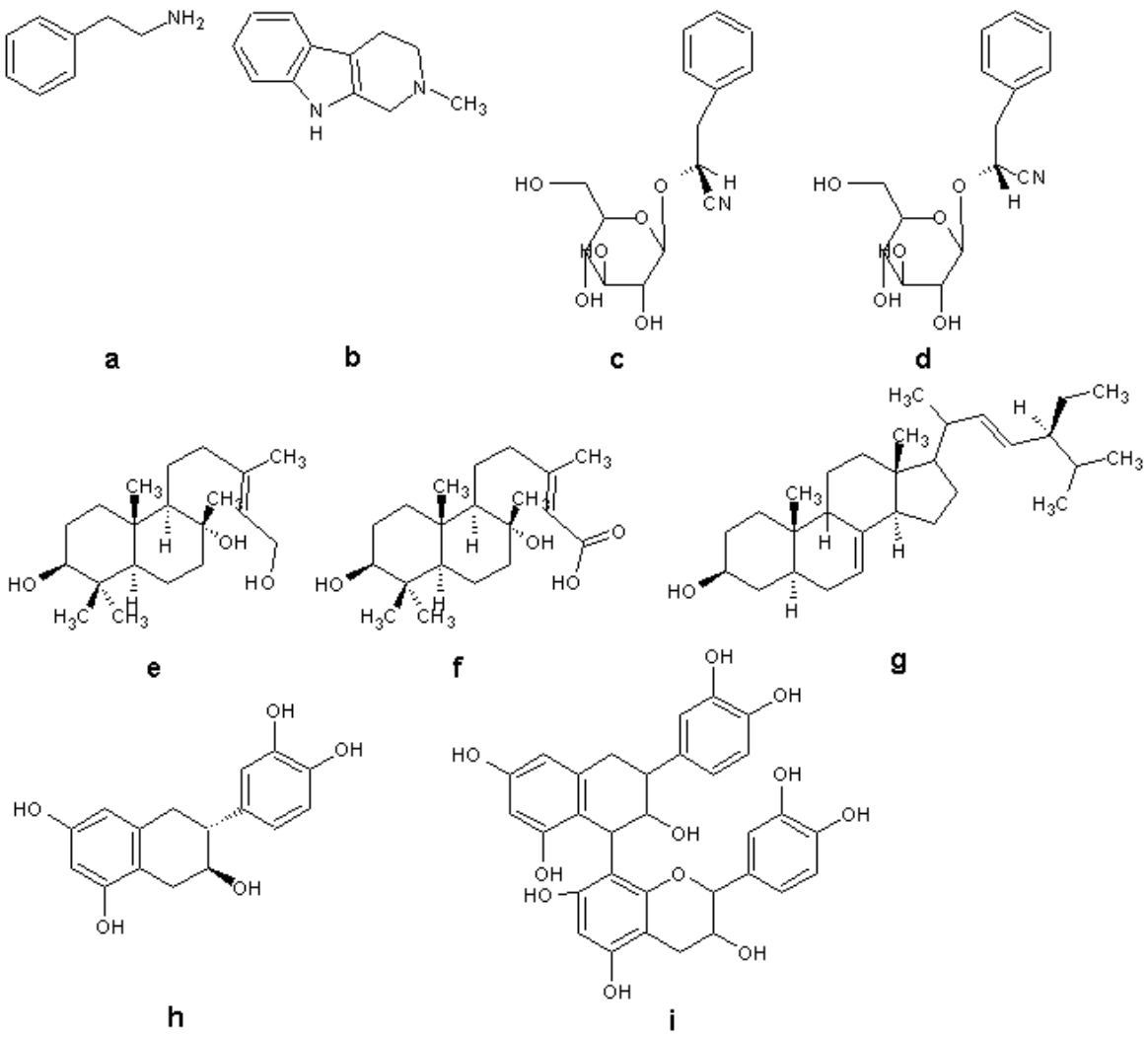


Figure 22: Chemical structures of (a) β-Phenethylamine, (b) 2-methyl-1, 2, 3, 4-tetrahydro-β-carboline, (c) prunasin, (d) sambunigrin, (e) labd-13-en-3β, 8α, 15-triol, (f) 3β, 8α-dihydroxylabd-13-en-15-oic acid, (g) α-spinasterol, (h) catechin and (i) and proanthocyanidin from Acacias.

3.8. *Scaevola spinescens*

Scaevola spinescens (family Goodeniaceae) (commonly known as currant bush, maroon bush and fanflower) (Figure 23) was used by Australian Aborigines as a medical plant to treat a variety of

conditions (Lassak and MacCarthy, 2006; Ghisalberti, 2004; Leyland, 2002). An infusion of the roots was used to treat stomach pain and urinary disorders. A decoction of crushed stem was used to treat boils, rashes and skin disorders. The whole plant was burnt and the fumes inhaled to treat colds. Leaves and twigs were steamed and sores treated by exposure to this steam.

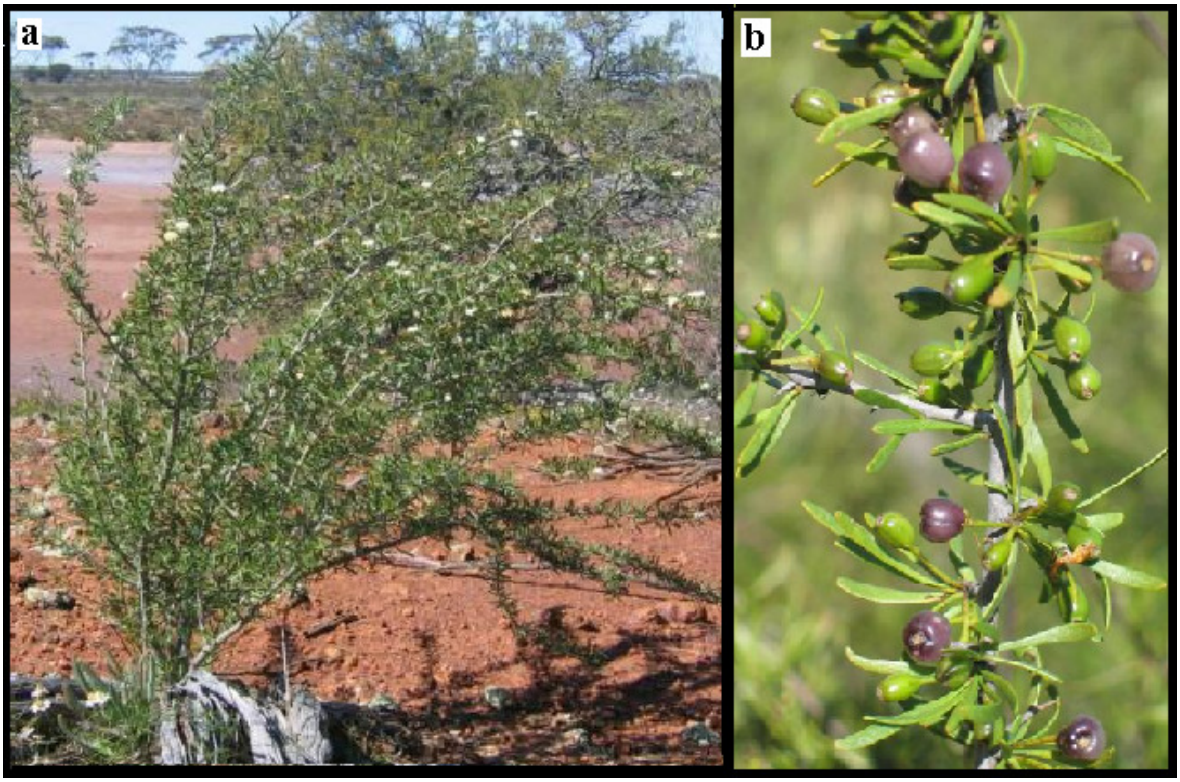


Figure 23: *Scaevola spinescens* (a) whole plant and (b) foliage and berries. Photos were taken and copyrighted by Jeanie Cargo and are reproduced here with the photographer's permission.

Despite its range of traditional medicinal uses, the phytochemistry and therapeutic potential of *S. spinescens* has not been extensively studied. A study by Semple et al. (1998) examined 40 different Australian plants for antiviral bioactivities (Semple et al., 1998). The study found that *S. spinescens* leaf extracts were capable of inhibiting greater than 25% of human cytomegalovirus (CMV) late

antigen production. More recently, studies have detected antiviral bioactivity of *S. spinescens* methanolic extract against MS2 bacteriophage (Cock and Kalt, 2010a). These studies demonstrate the antiviral potential of *S. spinescens* and provide support for the traditional Aboriginal use of *S. spinescens* infusions to treat viral diseases.

S. spinescens also had uses in the treatment of various cancers. This ethnopharmacological knowledge was traditionally passed on by word of mouth instead of by written record and unfortunately much of our understanding of Aboriginal medicinal usage has been lost as Aboriginal society has merged into mainstream Australian society. Accounts exist of aqueous extracts of *S. spinescens* root bark being used to cure cancer (as reviewed in Ghisalberti, 2004), although their efficacy has yet to be verified in controlled laboratory studies. Annecdotal accounts have also credited *S. spinescens* with anticancer activity (Bushfoods, 2010) although these also have yet to be verified by rigorous scientific examination.

Whilst individual bioactive compounds are yet to be identified, *S. spinescens* has been reported to contain high yields of a number of taraxerene type pentacyclic triterpenoids (Kerr et al., 1996). In particular, high levels of 14-taraxerene-3,28-diol (1; myricadiol) (Figure 24) were isolated from *S. spinescens* in the Kerr et al. study. Similar pentacyclic triterpenoids isolated from *Alchornea latifolia* have been linked with cytotoxic activity towards Hep-G2 and A-431 human cancer cell lines and are potent inhibitors of topoisomerase II (Setzer et al., 2000). Taraxerene triterpenoids from *Laggera pterodonta* have also been shown to have antiviral activity against herpes viruses (Kuljanabhagavad et al., 2009). Studies have also demonstrated the antibacterial activity of pentacyclic triterpenoids from a variety of other plants (Ahmad et al., 2008; Shai et al., 2008; Djoukeng et al., 2005).

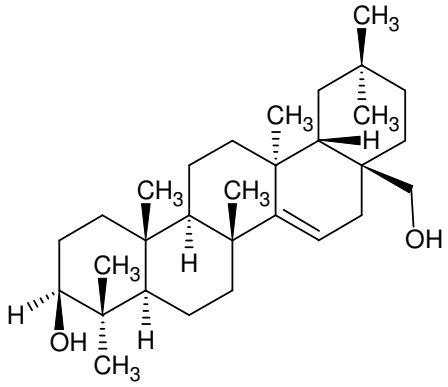


Figure 24: Chemical structure of the pentacyclic triterpenoid 14-taraxerene-3, 28-diol (1; myricadiol) from *S. spinescens*.

3.9. *Pittosporum phylliraeoides*

Pittosporum phylliraeoides (family Pittosporaceae) (figure 25), commonly known as 'cattle bush' or 'gumbi gumbi' is a native Australian plant that was used by Aborigines for a variety of purposes including improving circulation, as a birth control measure and as an anti-cancer agent. It has been proposed that *P. phylliraeoides* contains haemolytic saponins that hydrolyse to form the triterpenoid compounds phyllyrigenin (Figure 26a) and barrigenol (figure 26b) (Lassak and McCarthy, 2006; Chopra et al, 1965; Knight and White, 1961). It has also been suggested that as well as saponins, polyphenols and phytoestrogens are also present within *P. phylliraeoides* (Lassak and McCarthy, 2006) and these may also be responsible for the therapeutic potential of this plant.

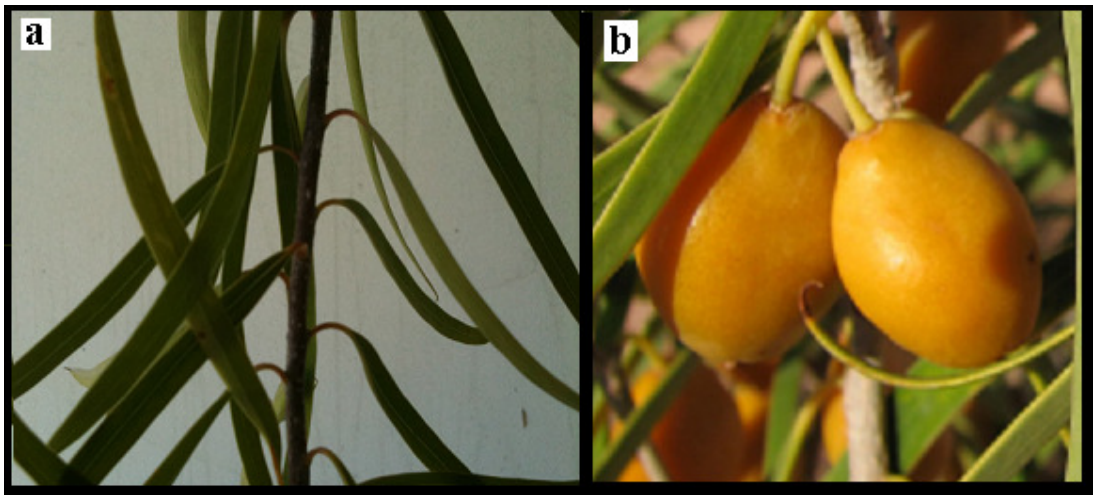


Figure 25: *Pittosporum phylliraeoides* (a) foliage and (b) fruit. Pictures were taken in Brisbane, Australia by Dr Ian Cock.

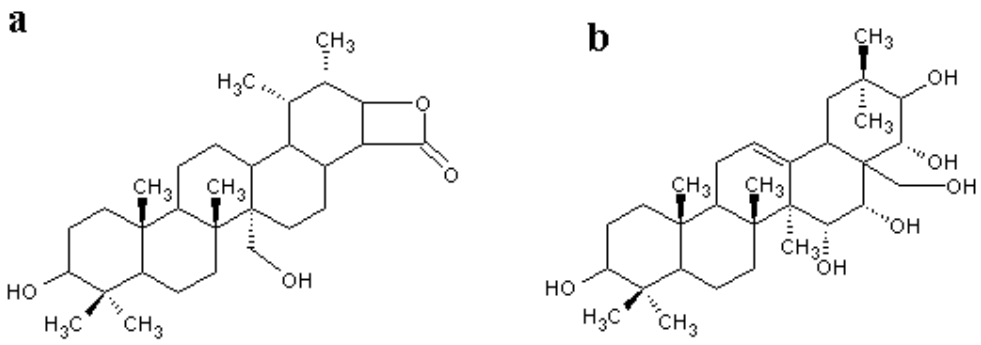


Figure 26: Chemical structures of (a) phyllyrigenin and (b) barrigenol from *Pittosporum phylliraeoides*.

3.10. *Duboisia myoporoides*

Duboisia myoporoides (Figure 27), commonly known as Corkwood, contains the tropane alkaloid scopolamine within its leaves. Scopolamine (Figure 28) is an anticholinergic agent capable of blocking the neurotransmitter acetylcholine in the central and the peripheral nervous systems. In minute doses (~330µg); scopolamine has been used for the treatment of nausea, motion sickness, intestinal cramping, ophthalmic purposes, as an anti-depressant, and in conjunction with narcotic painkillers (Renner et al., 2005; Furey and Drevets, 2006).

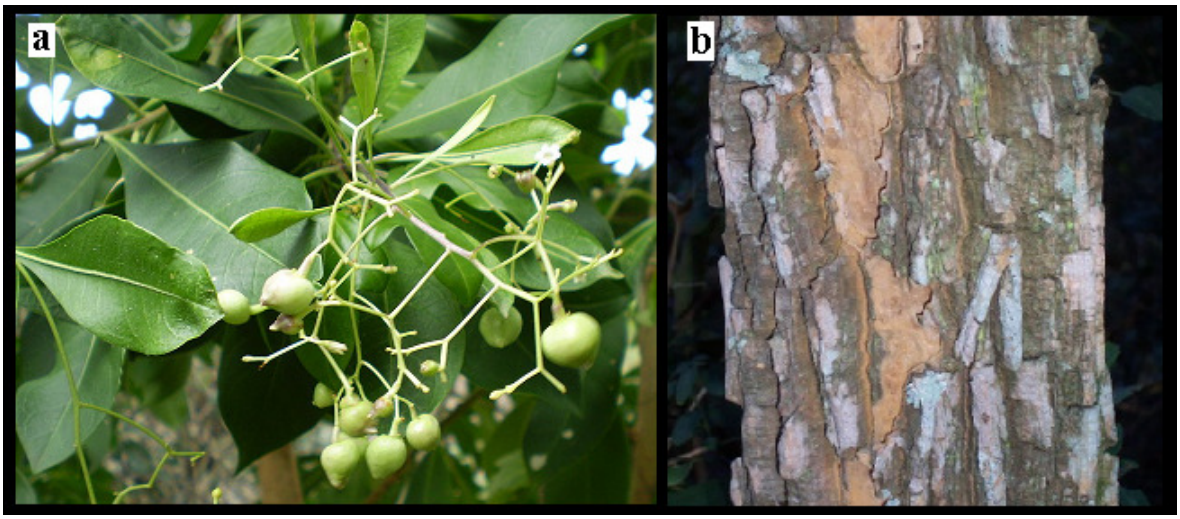


Figure 27: *Duboisia myoporoides* (a) foliage and fruit and (b) bark. Photographs were accessed from Wikipedia Commons (http://en.wikipedia.org/wiki/Duboisia_myoporoides) on 20 January 2011 and are adapted and reproduced here with the relevant permissions.

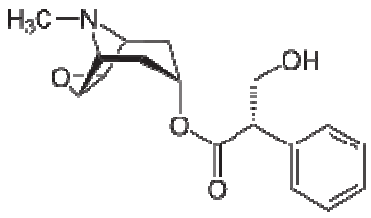


Figure 28: Chemical structure of scopolamine, a component of *Duboisia myoporoides* leaves.

3.11. Planchonella Species

The genus Planchonella (family Sapotaceae) consists of approximately 100 species, 18 species of which are native to Australia. Nomenclature within this genus can be somewhat confused with many species often included in the genus Pouteria (eg *Planchonella queenslandica* (Figure 29a) and *Pouteria queenslandica* are the same species). *Planchonella thyrsoidea* has been shown to contain pyrrolizidine alkaloids (Figure 30a) which have toxic properties (Culvenor, 1967). Triterpene acids have also been shown to be present in the leaves of *Planchonella duclitan* and have shown cytotoxicity toward human colorectal carcinoma cell line HT29 and human breast carcinoma cell line MCF-7 (Lee et al., 2005). Studies into *Planchonella vitiensis* have documented the presence of α-Spinasterol (Figure 30b) within the heartwood (Cambie et al., 1997). Anecdotal evidence also indicates the presence of alkaloids in *Planchonella pohlmanniana* (yellow box) and an infusion of twigs and leaves were used by north Queensland Aborigines as a poultice for boils. The species *Planchonella queenslandica* is currently under investigation within my laboratory.

Figure 29: (a) *Planchonella queenslandica* foliage and (b) *Planchonella australis* trunk. Photographs were accessed from Wikipedia Commons (http://en.wikipedia.org/wiki/Planchonella_queenslandica and http://en.wikipedia.org/wiki/Pouteria_australis) on 20 January 2011 and are adapted and reproduced here with the relevant permissions.

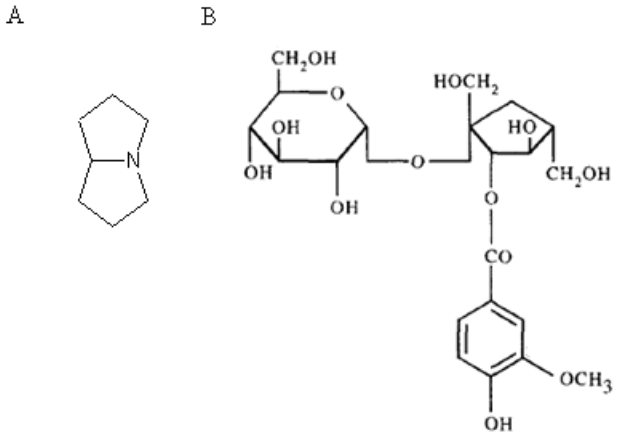


Figure 30: Structure of (a) pyrrolizidine alkaloid and (b) α-Spinasterol, secondary metabolites present in the Planchonella genus.

3.12. Petalostigma Species

The genus Petalostigma (family Picrodendraceae) consists of seven species, two of which have been investigated for medicinal properties (Kalt and Cock, 2011). These two species, *Petalostigma pubescens* (commonly known as 'quinine tree') and *Petalostigma triloculare*, differ slightly in terms of leaf and fruit shape and size but otherwise have similar morphology. Although the common name

suggests quinine is present within the fruit or leaves, there is no scientific evidence to support this. However, an infusion of bark or fruit in water is known to have been used by Aborigines to relieve sore eyes, and as an antiseptic (Lassak and McCarthy, 2006). Fruit was also held in the mouth to relieve toothache (Lassak and McCarthy, 2006). Studies within my laboratory have demonstrated the toxicity and broad spectrum antiseptic properties of the leaves and fruit (Kalt and Cock, 2011) and antiviral bioactivities (Kalt and Cock, in preparation) of both plants. Further work is needed to determine the potential of the other species of this genus.

Figure 31: *Petalostigma pubescens* (a) whole plant, (b) foliage and immature fruit and (c) ripe fruit. Pictures were taken in January 2011 in Toohey Forrest, Australia by Dr Ian Cock.

Active constituents are not fully characterised but the fruit contains a definite bitter substance, possibly an alkaloid (Lassak and McCarthy, 2006). Investigation into the chemical composition of *Petalostigma pubescens* heartwood has identified five tricyclic diterpenes: 5,9-syn-rosanes petalostigmone (Figure 32a), erythroxylane petalostigmone (Figure 32b), norditerpene lactone (Figure 32c), pubescenone (Figure 32d), and ent-cleistanthane diterpene sonderianol (Figure 32c) (Grace et al., 2006).

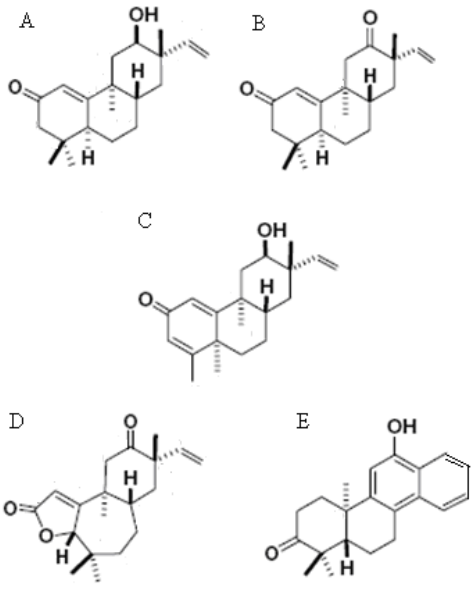


Figure 32: Structure of the five tricyclic diterpenes present within *Petalostigma pubescens* heartwood: (a) 5,9-syn-rosanes petalostigmone, (b) erythroxylane petalostigmone, (c) norditerpene lactone, (d) pubescenone and (e) ent-cleistanthane diterpene sonderianol.

4. Current Investigations of Australian Medicinal Plants

Our understanding of the medicinal potential of Australian medicinal plants is in its infancy and significantly more research into the phytochemical composition of Australian plants with therapeutic potential is required:

- To isolate bioactive compounds for direct use as drugs. Examples of medicines derived from plants internationally include atropine, ephedrine, digoxin, digitoxin, morphine, reserpine, tubocurarine, taxol, vinblastine and vincristine. These compounds have come into use through research of indigenous remedies (Fabricant et al., 2001). Bioactivity studies of Australian plant extracts and essential oils may ultimately also provide a wealth of new therapeutic agents.

- To produce bioactive compounds of novel/known structures as guide compounds for semi-synthesis of patentable compounds of higher activity and lower toxicity. Such a protocol has previously led to the manufacture of many therapeutic drugs based on phytochemicals purified from plants internationally (eg. metformin, nabilone, oxycodon, physostigmine, quinidine, emetine (and other narcotic analgesics), taxotere, teniposide, verapamil, and amiodarone (Fabricant et al., 2001)).

- Research enables us to use phytochemical agents as pharmacological tools in understanding the normal physiology of the human body. Previous international studies have used natural pharmaceuticals such as lysergic acid diethylamide (LSD) as a pharmacological tool to investigate the synaptic mechanism in the lateral geniculate of the brain (Bishop et al., 1958). Other known phytochemicals used for similar investigations include atropine (extracted from *Atropa belladonna*), amphetamine (a semi-synthetic analogue of the plant

derivative ephedrine), d-tubocurarine (a natural neuromuscular blocking agent derived from the South American plant *Chondrodendron tomentosum*), strychnine (an alkaloid isolated from *Strychnos ignatii)*, veratrine and veratridine (neurotoxic steroidal alkaloids derived from plants of the family Liliaceae), mescaline (a psychedelic alkaloid derived from peyote cactus (*Lophophora williamsii*)) and yohimbine (a alkaloid stimulant derived from *Pausinystalia yohimbe*) (Fabricant et al., 2001; Bishop et al 1958). Purified phytochemicals from Australian plants may provide similar insights.

- Finally these studies enable us to use the whole plant or part of it as an herbal remedy eg. cranberry, echinacea, feverfew, garlic, ginkgo biloba, St. John's wort (Fabricant et al., 2001). With regard to Australian plants, herbal remedies currently used mainly relate to the essential oil producing plants previously discussed (eg. Eucalypts, Melaleucas, Leptospermums).

Phyto-pharmacological research should embrace a multidisciplinary (pharmacological, botanical and chemical) approach towards documentation of indigenous medical knowledge, scientific study of plant derived medicines and the search for pharmacologically unique principles from existing ethnopharmaceutical remedies. Many Australian plants have not been previously examined for their usefulness as medicines. Research requires exhaustive testing to ascertain pharmacological and toxicological mechanisms of action and, if possible, clinical studies on their efficacy.

New phytopharmaceutical discovery requires the identification of medicinally useful plants, the isolation of compounds from those plants, and bioactivity testing. It is also essential that any potential new plant-derived pharmaceutical be subjected to toxicological examination to evaluate its

worth as a therapeutic agent. Generally, phytopharmaceutical discovery involves the following steps:

1. Correct identification of the plant used/tested.
2. Collection and preparation of the plant material.
3. Extraction or essential oil production.
4. Fractionation of the extracts/oils by separation techniques.
5. Purity control and analysis of the isolated compounds
6. Structural discovery by a combination of diverse techniques including spectroscopic (UV/VIS, IR, MS, NMR), physical (X-ray crystallography) and chemical techniques (derivative formation etc).
7. Synthesis or semi-synthesis of the product.
8. Structure/activity analysis by structural modification
9. Pharmacological and toxicological testing

4.1. Plant Selection

Australia has a large quantity of unique plants, many of which have either not been scientifically investigated as medicinal sources, or have only received preliminary examination. Considering the number of Australian plants which have not yet been studied, thought needs to be given to the choice of plant for testing. A number factors need to be considered:

1. Ethnopharmacology.

With the wide choice of plants yet to be studied, often a good starting point is to begin with plants previously used by traditional healers. Australian Aborigines had a good understanding of the botany in their local areas and used a variety of plant medicines to help maintain their health (Barr et al., 1993; Lassak and McCarthy, 2006). Unfortunately, most Aboriginal knowledge of plant usage was not documented, instead being passed from one generation to the next entirely orally. As Aboriginal society has been increasingly assimilated into non-Aboriginal society, much of the cultural identity and traditional knowledge has been lost. Only a handful of individuals remain with extensive knowledge of traditional medicines and then, not in all regions. For example, many Northern Territory Aborigines still live traditional lives and ethnopharmaceutical knowledge is still available (Lassak and McCarthy, 2006). However, in other areas of Australia where Aborigines have either left their traditional lands and/or abandoned their traditional lifestyles, much of this traditional knowledge has already been lost. Efforts need to be made to safeguard the remaining knowledge.

Aborigines lived as separate populations in widely varied geographical areas of Australia with different botanical profiles. As such, these different groupings developed different ethnopharmacologies, dependent on the plants available and the requirements of the local populations. For example, indigenous populations living in the hot, humid conditions of Northern Queensland would be faced with conditions ideal for bacterial growth. Scratches and skin abrasions could readily become sceptic if left untreated. It is not surprising that Northern Queensland Aborigines sought ways of treating these infections. In fact, in an early report of Australian plant use (Roth, 1903), nearly a quarter of the knowledge of antiseptic plants was obtained from Northern Queensland Aborigines. Other Aborigine populations from other regions of Australia were faced with different environmental stresses and had different plant species available. For example, Aborigines from the coastal regions of Northern New South Wales and Southern Queensland used *Crinum*

pedunculatum (Figure 33) to treat marine stings whilst Aborigines from central Australia had no such knowledge of this plant, nor its potential use. It is unlikely, with such varied knowledge across the indigenous populations, that we will ever be able to determine the full extent of medicinal knowledge indigenous people had.

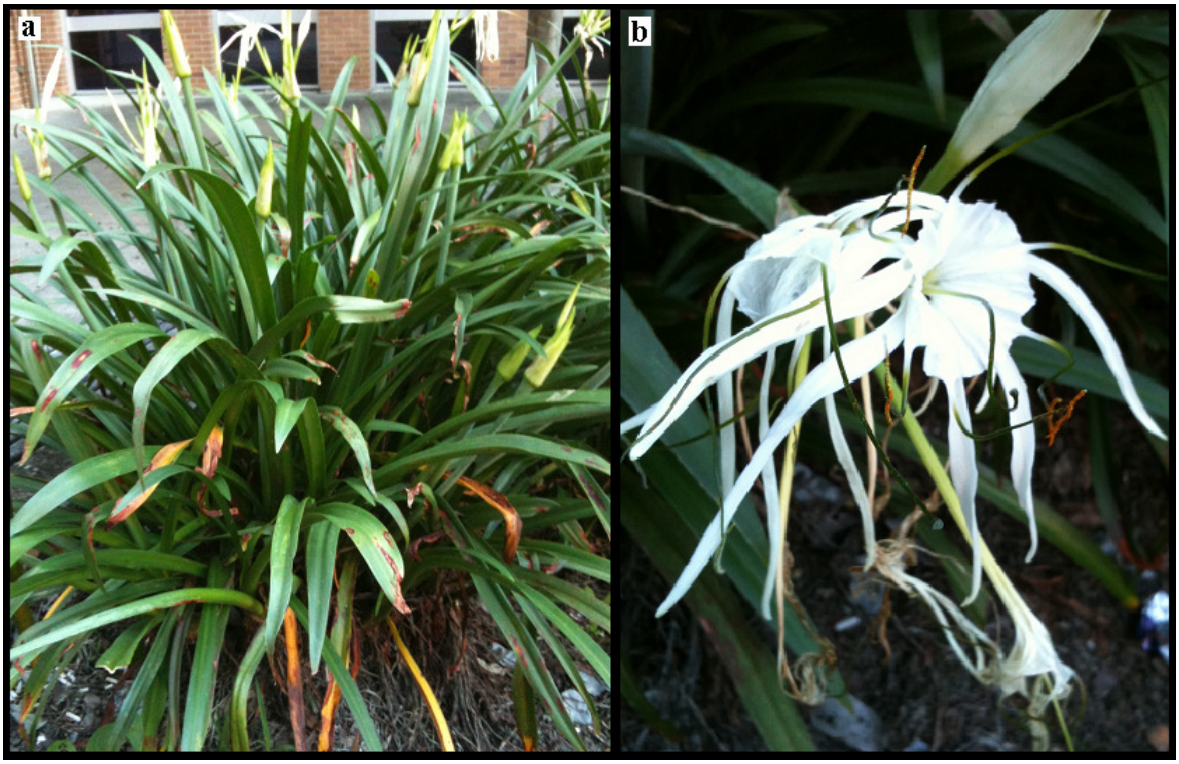


Figure 33: *Crinum pedunculatum* (a) whole plant and (b) flower. Pictures were taken in January 2011 in Brisbane, Australia by Dr Ian Cock.

2. Field observations

The researchers own field observations are often valuable in selecting a plant species for testing. Plants which grow despite environmental stresses, such as plants in tropical rainforests where there are an abundance of insects, fungi and bacteria, may have adapted to produce molecules with bioactivities to protect themselves. *Ficus coronata* (a native fig) for example, is a tree that usually grows in coastal rainforest areas of Queensland, Northern Territory and northern New South Wales (Page and Olds, 2004). Growing in these hot, humid conditions (which provide an ideal environment for bacterial and fungal growth) would on its own make further examination of *F. coronata* warranted. This, coupled to the ethnopharmacological knowledge that north Queensland Aborigines used the sap from this plant as an antiseptic (Lassak and McCarthy, 2006), makes this plant an ideal candidate for further investigation.

Early studies into the antiseptic properties of Eucalyptus leaves also originated through field observations. A team of Japanese researchers noticed that collected leaves of *Eucalyptus gunnii* have an almost total absence of microbes not only inside the leaf, but also on their surface (Egawa et al, 1977). These researchers examined *Eucalyptus gunnii* leaves and the leaves of other Eucalyptus species for antiseptic agents. Not only did they isolate three antifungal agents (gallic acid and two phenolic compounds) from *Eucalyptus gunnii* leaves but they also isolated antifungal agents from more than half of the Eucalyptus species they tested.

In my own laboratory, studies based on field observations have yielded interesting results into the medicinal potential of *Xanthorrhoea johnsonii* (Figure 34). *X. johnsonii* are long lived with some plants being estimated at more than 550 years of age (Boorsboom, 2005; Stanley et al., 1989; Bulow-Olsen et al., 1982). However, *X. johnsonii* are also extremely slow growing with the growth rates estimated as low as 0.88 cm/year (Bulow-Olsen et al., 1982; Lamont and Downes, 1979). Due to its

slow growth rate, it was thought likely that *X. johnsonii* may have developed chemical protective mechanisms to deter foraging animals which could potentially threaten their survival. The number of animals that use *X. johnsonii* as a food source is low and even when animals use *X. johnsonii* as a food, the leaves are generally not ingested. Indeed, in the only reports we found of grazing animals foraging on *Xanthorrhoea johnsonii* leaves, cattle eating the leaves were said to become uncoordinated and lose condition, become dehydrated, and in severe cases die following ingestion (McKenzie, 1997; Everist, 1978; Hall, 1956; Hurst, 1942). Studies undertaken in my laboratory identified an interesting bioactivity for *X. johnsonii* leaf extracts (Cock and Kalt, 2010b). The leaves were found to have an apparent anaesthetic effect, similar to the effects previously described for tubocurarine, dimethyltubocurarine and alcuronium (collectively known as curare, a South American arrow poison) from *Chondrodendron tomentosum* (Bisset, 1989; Bisset, 1992a; Bisset, 1992b)

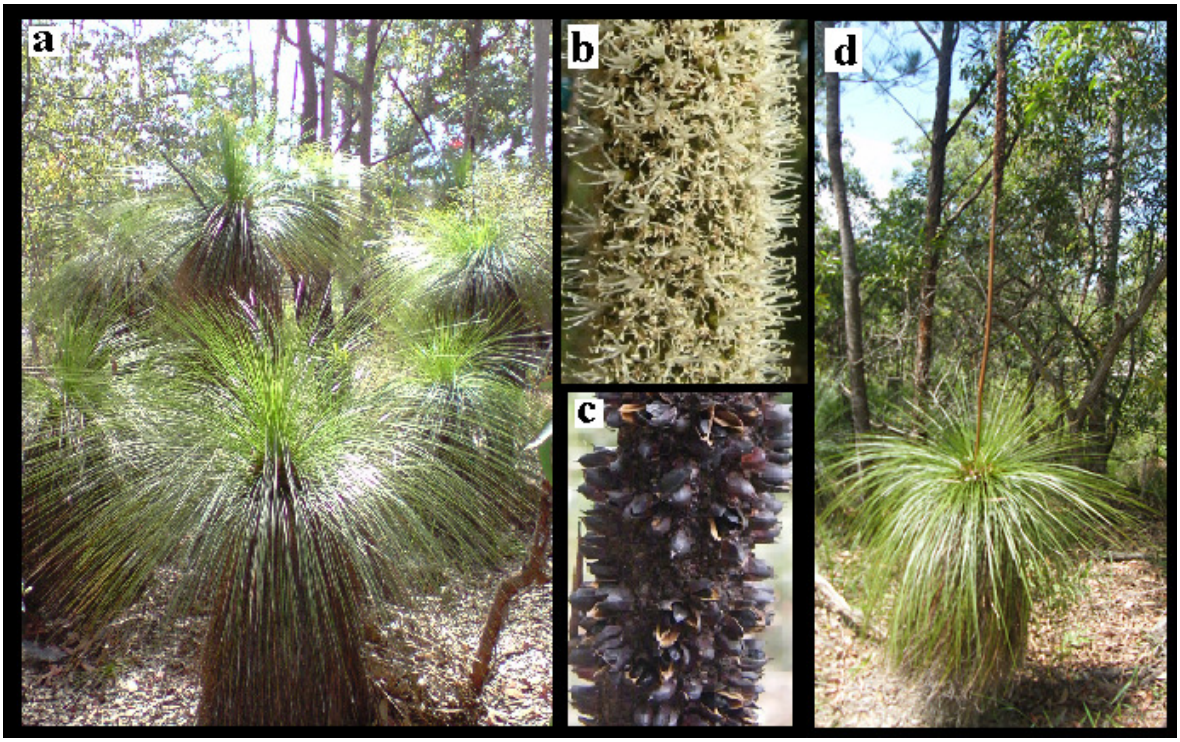


Figure 34: *Xanthorrhoea johnsonii* (a) plants, (b) close-up of flowers, (c) close-up of seeds and (d) a single plant with a flower spear. Pictures were taken at various times throughout 2010 in Toohey Forrest, Australia by Dr Ian Cock.

3. Taxonomic considerations

Many Australia plants are related to plants from other regions of the world that are know to produce pharmaceutical phytochemicals. For example, *Adansonia digitata* (baobab) is widespread across much of the African continent (Page and Olds, 2004). The fruits and seeds of this plant contain tartaric acid and are used by African populations as a remedy for dysentery (Watt and Breyer-Brandwijk, 1962) and as an antiseptic agent (Hussain and Deeni, 1991). A related *Adansonia* species, *Adansonia gregorii* (Figure 35), is native to far north Western Australia (Page and Olds, 2004). No reports of any similar bioactivities were found for this plant in the literature, neither was any reference to ethnopharmacological use found. Preliminary antibacterial screening in my laboratory has shown antibacterial activity for *Adansonia gregorii* flowers towards a limited panel of bacteria (Cock, 2008). Further investigation of this plant is warranted.

Figure 35: *Adasonia gregorii* tree (cultivated) in summer with full leaf growth (Photograph by Dr Ian Cock).

Azadirachta indica (commonly known as Neem tree) is another example of a plant of international origin with well characterised bioactivities and phytochemistry. *A. indica* (a member of family Meliaceae) is native to tropical and semi-tropical regions of Southern Asia. Products made from Neem claim a wide variety of therapeutic properties including anthelmintic, antifungal, antidiabetic, antibacterial, antiviral, anti-fertility, and sedative properties, and are commonly prescribed for skin diseases such as chicken pox and acne in India (Nahak and Sahu, 2010; Vishnukanta, 2008). Indeed, the wide range of ailments that are claimed to be treatable by *A. indica* products has resulted in it being commonly described as "Divine Tree," "Heal All," "Nature's Drugstore," "Village Pharmacy" and "Panacea for all diseases". Azadirachtin (a triterpene limonoid) (Figure 36a) has been isolated

and characterised from *A. indica* seeds. Azadirachtin has been shown to exhibit toxicity to some insects yet low toxicity to mammals and anti-fertility activity in mice (Mandal and Dhaliwal, 2007; Coria et al., 2008).

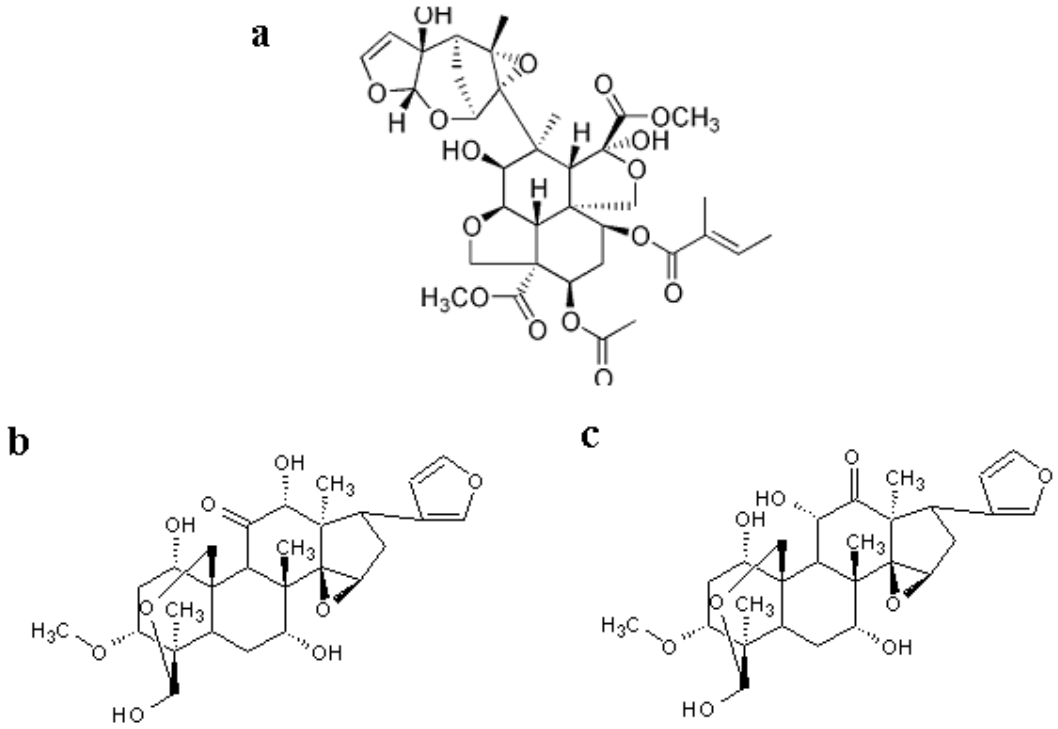


Figure 36: The structure of (a) azadirachtin, a triterpene limonoid from *Azadirachta indica* and (b) 12-hydroxiamoorastatin and (c) meliartenin from *Melia azedarach.*

Melia azedarach var. *australasica* (family Meliaceae) (Figure 37) is a species closely related to *A. indica*. *M. azedarach* has a wide distribution, occurring naturally in Australia, India, China, parts of South East Asia and the Pacific Islands. Recent studies have shown that extracts from *A. indica* and *M. azedarach* have similar toxicities towards the cabbage moth *Plutella xylostella* (Charleston et al., 2006). Whilst the phytochemistry of *M. azedarach* has not yet been extensively examined, a recent study has isolated two limonoid isomers (12-hydroxiamoorastatin (Figure 36b) and meliartenin

(Figure 36c)) from *M. azedarach*. Both these limonoids were found to have similar ED_{50} values towards *P. xylostella* as azadirachtin isolated from *A. indica.* Further work is necessary to determine if *M. azedarach* and *A. indica* share other bioactivities.

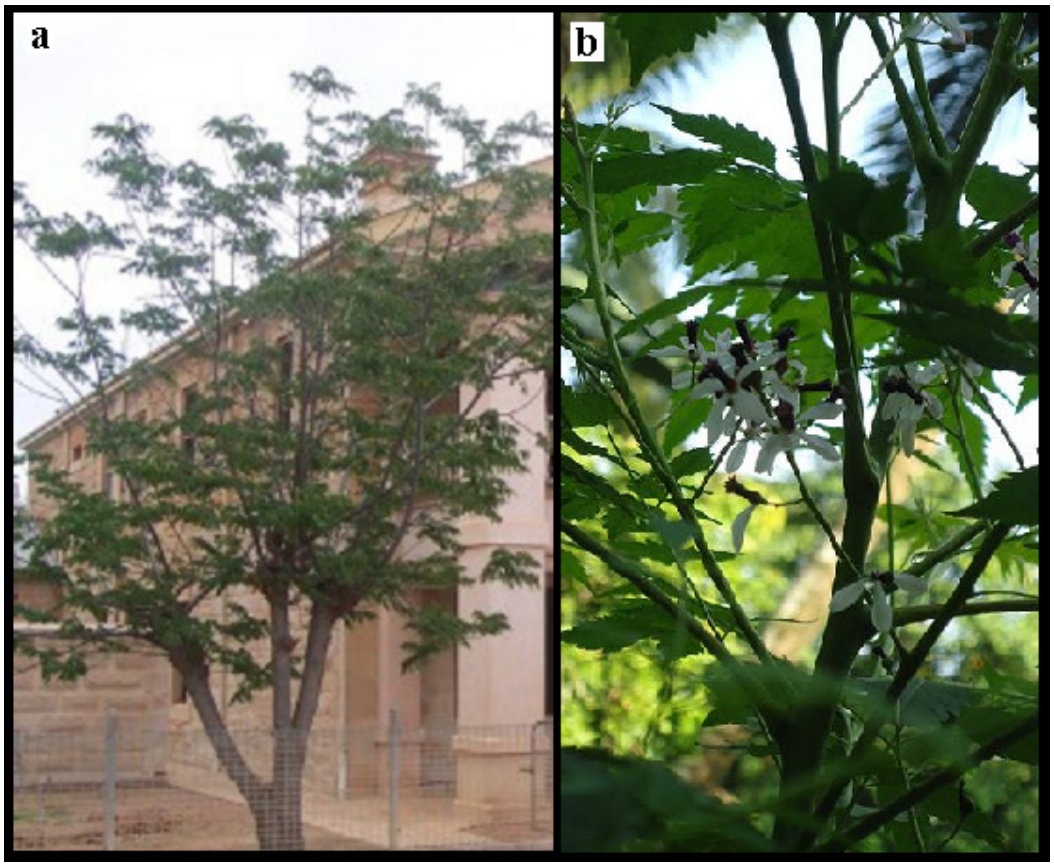


Figure 37: *Melia azedarach* (a) whole tree and (b) leaves and flowers. Photographs were accessed from Wikipedia Commons (http://en.wikipedia.org/wiki/Melia_azedarach) on 24 January 2011 and are adapted and reproduced here with the relevant permissions.

4. Random selection

Random selection should not be overlooked when choosing plants for biotesting. Given the number of Australian plants that have not yet been investigated, the possibility exists that random testing could well result in exciting new discoveries. Indeed, recent antimicrobial studies within my laboratory revealed a wealth of previously unreported antibacterial activities from a wide variety of randomly selected plants (Cock, 2008)

Many new diseases and medical conditions that early Australians were not exposed to or did not know about are now a part of our everyday lives. HIV, Alzheimer's disease, Parkinson's disease, multiple sclerosis and many cancers were not major health concerns for Aborigines nor early European settlers. Whilst neither modern medicine nor Australian ethnopharmacology has provided answers for these and other diseases, random testing may.

4.2. Screening For Pharmaceutical Usefulness

Once a researcher has selected plant material for testing, a relatively simple assay is required to determine whether that plant has therapeutic (or toxic) actions. Even when a plant preparation is found to have desirable effects, these effects need to be further localised in specific extracts and individual fractions. Medicinal plant preparations may contain hundreds of different constituents. Therefore, even when a plant preparation with a desired bioactivity is found, only a fraction of the compounds in that preparation may be useful. It is essential that the researcher has relatively simple and rapid tests available to enable the screening of high sample numbers. These tests should also be sensitive enough to detect activities in the low concentrations that some substances may be in plant preparations. The targets for biological testing can be divided into six broad groupings:

1. Lower organisms (eg. Bacteria, fungi, viruses). Testing for antibacterial or antifungal activity is relatively simple. A crude plant extract or a purified component can be placed in contact with the microorganism (eg. by disc/plate hole diffusion assays or broth growth inhibition assays) and the inhibition of microbe growth or death is observed. Antiviral activity is easily determined using the plaque reduction assay (Cock and Kalt, 2010a; Gentry and Aswell, 1975). With the development of new antibiotic resistant strains of bacteria and fungi, the development of new antimicrobial agents is of high priority.

2. Invertebrates (eg. insects, crustaceans, molluscs). Some plants have insecticidal and/or repellent properties. These plants have potential roles in the prevention of tropical parasitic diseases (eg. Malaria, Ross River and Dengue fevers). Other plants may act as molluscicides and be useful for controlling molluscs. Medicinally, these plants would have potential uses in controlling diseases that spread using a mollusc host for all/part of their lifecycle (eg. Bilharzia, a disease that affects large numbers of people in developing countries). These plants would also have applications as pesticides.

Invertebrate assays are also useful in toxicity screening assays. Whilst many laboratories use cell culture assays (which are expensive and have inherent difficulties) or whole animal assays (which have ethical constraints as well as being time consuming and expensive), invertebrate bioassays may provide a convenient, rapid detection alternative. The *Artemia* nauplii (brine shrimp) bioassay developed by Meyer et al (1982) has been routinely used in my laboratory and by other researchers in this field (Setzer et al., 2000). This assay is an efficient, inexpensive and relatively rapid way to detect toxic compounds, requiring only low amounts of sample (<20 mg). This test correlates well

with cytotoxic activity of some human tumours and therefore has the potential to detect new antitumour agents (McLaughlin et al., 1998).

3. Cell cultures. Cell culture assays are of particular importance in cancer research where it is important to find molecules that are cytotoxic to tumour cells or inhibit their growth but not to normal cultured cells. Many substances have proved cytotoxic to isolated cancer cells (Jansen et al., 2006; Dweck, 2001; Hall et al., 2001; Weniger et al., 1998; Nanayakkara et al., 1988). Unfortunately, most of these are also toxic to normal cells. Potential anticancer therapeutics need to be tested against both tumour and normal cell lines to evaluate their usefulness as chemotherapeutic agents.

4. Isolated organs. Pharmacological testing often utilises isolated animal organs. Perfused frog heart has been used (El Bardai et al., 2003; Hotta et al., 1994) to study cardiac glycosides. Similarly, perfused liver, guinea pig heart, chicken veins etc. have been routinely used for pharmacological testing (Rang et al., 2003).

5. Whole animal bioassays. The testing of potential therapeutic agents on live animals is still an important step in the development of new therapeutic agents as they give a true indication of the drug's affect on a whole organism. Whilst a drug may have a desired effect in one or more of the other assays, they may still have limited potential due to unforeseen factors. Whilst an isolated plant compound may prove cytotoxic in cell culture assays, they may be of limited use as a chemotherapeutic agent due to other problems (eg. they may not reach/be transported to the

target tissue). Whole animal tests are invaluable, even if only as a final step in the testing of a potential new medicinal agent. However, where practical, other testing protocols should be utilised before resorting to whole animal testing. Not only are there ethical concerns, but whole animal testing can be expensive (high animal numbers are needed to get statistically significant results), require specialised animal facilities and expertise and require long assay times.

6. Isolated subcellular systems (eg. enzyme or receptor bioassays). When the causes of a disease are known it is possible to make direct use of the receptors and/or enzymes known to be implicated in this condition. For example, when testing anti-cancer drugs, inhibitors of topoisomerases I and II and protein kinase C as well as substances that affect tubulin polymerisation are potential targets. Likewise, testing substances for the ability to inhibit cyclooxygenase or lipooxygenase enzymes (involved in inflammation) would aid in the discovery of novel anti-inflammatory drugs. Tests of this type are usually very sensitive and very specific so allow screening of large numbers of samples using only small sample quantities.

5. Toxicity, Crossreactivity And The Safe Use Of Medicinal And Aromatic Plants

Whilst many users are turning to plant based medicines due to their perception of being safer than allopathic drugs, it is important to realise that dangers are also inherent with natural medicines. Indeed, it has often been stated that medicines are toxins taken at low doses. Even when a particular phytochemical within a plant preparation has a medicinally desirable effect, it may also be toxic at higher doses. An example is the cardiac glycoside digoxin which is present in plants of the genus Digitalis. Digoxin is an antiarrhythmic agent which is used to control heart atrial fibrillation, atrial flutter and sometimes heart failure (van Veldhuisen and de Boer, 2009). It is a very useful drug in

therapeutic doses. However, at higher doses, it may cause excessive slowing of the rate of heart beat (bradycardia) or even block contraction and may be life threatening (The Digitalis Research Group, 1997). The perception of the safety of plant preparations may result in the user taking higher doses than would otherwise be achieved with pure, allopathic medicines, without thought of overdosing or unwanted side effects.

Many individuals who use plant based medicines self-diagnose their conditions and will prescribe plant preparations for themselves. An incorrect diagnosis may be dangerous, particularly as plant medicines often contain multiple bioactive compounds. It is therefore possible that an inappropriate or even dangerous remedy is prescribed. It is also noteworthy that many drugs actually have enhanced effects in the presence of other drugs. Similarly, the functioning of some drugs may be blocked or decreased in the presence of other drugs (including phytochemicals). For example, St Johns wort is a perennial herb indigenous to Europe which is often used to treat depression (Gupta and Möller, 2003) as well as a variety of other conditions. It has been well established that administration of St Johns wort will counteract the effects of warfarin in some patients (Henderson et al., 2002). Warfarin is a anticoagulant that is often prescribed for preventing thrombosis and embolism. Therefore the counteracting effect of St Johns wort in patients prescribed warfarin could potentially have fatal results. Furthermore, a phytochemical that has a desirable effect on a target tissue may in fact also have an undesirable effect in other tissues (eg. liver or kidney). It is important to realise that there has been limited scientific studies into the safety and effectiveness of most plant based remedies. It is necessary to understand the mechanism of action and cross reactivity of any drug before using multiple drugs or preparations in conjunction. This is routinely undertaken before allopathic drugs are released to the market, yet no such requirement exists for natural therapeutics.

Unlike allopathic medicines, many natural medicines are not effectively regulated. This means that different plant based medicinal preparations will contain different types and quantities of phytochemicals. Whilst some herbal preparations do contain standardised quantities of one (or even several phytochemicals) other chemicals within the preparation are often not standardised. For example, commercially available Aloe vera juices often note levels of several important phytochemicals (eg. Aloe emodin, barbaloin) without fully detailing the levels of other components. This is also true of Australian plant based essential oil medications. Eucalyptus oil products may provide the levels of 1, 8-cineol, but will rarely detail the levels of other phytochemicals. Likewise, the recent interest in *Terminalia ferdinandia* due to its high levels of vitamin C has resulted in the standardisation and reporting of vitamin C levels in commercial preparations and products. However, *T. ferdinandia* fruit also contains a number of other phytochemicals which may impact on the usage and efficacy of this fruit, yet these are rarely measured and reported.

Care also needs to be exercised in specialised cases (eg. in pregnant women). In an effort to avoid drugs, pregnant women often use natural therapeutics as they believe them to be harmless. During pregnancy, the maternal bloodstream is shared with the foetal bloodstream. Thus toxic chemicals ingested by the mother will be shared with the foetus. As the foetus generally will not have developed the same tolerances as the mother, acute toxicity may develop in the foetus without being evident in the mother. Furthermore, some chemicals including phytochemicals, may be mutagenic. These chemicals would be likely to have more profound effects in a developing foetus than to the mother. Many women quite sensibly quit smoking and drinking alcohol during pregnancy for this very reason, without considering the effects of the natural therapeutics they are also taking. Similarly, toxic phytochemicals may also be present in the breast milk of women taking plant therapeutics. The same precautions should be exercised by breastfeeding women as during pregnancy. Children, elderly people, immunocompromised individuals, and those suffering severe

allergies to specific drugs are other examples of people who should exercise caution with natural medications, as indeed they should for any medication.

6. Conclusion

Plants have been the basis of traditional medicines throughout the world for thousands of years and continue to provide us with new remedies to existing and emerging diseases and medical conditions. Traditionally, plant based medicines have been used as crude formulations such as infusions, tinctures and extracts, essential oils, powders, poultices and other herbal preparations. These same plant medicines now serve as the basis for the discovery of new drugs. Active compounds have been isolated from medicinal plants, beginning with the isolation of the narcotic analgesic morphine from the opium poppy in the early 1800's (Kinghorn, 2001), through the early discoveries of drugs such as codeine, quinine, cocaine and digitoxin (many of which are still widely used). Plants continue to provide us with new drugs for both existing and new medical conditions and are vital to drug discovery (Verpoorte, 1998). Higher plants are well known producers of an enormous variety of chemically complex, biologically active compounds (Gentry, 1993; McChesney, 1993). Indeed, approximately 25 % of all prescription drugs currently in use were originally derived from plants (Walsh, 2003; Hostettmann and Hamburger, 1993; Newman et al., 2000). 75 % of these drugs were discovered by an examination of traditional medicines (Walsh, 2003; Newman et al., 2000; Harvey, 1993). Furthermore, plant derived drugs and their semi-synthetic analogues comprise nearly 75 % of all new anticancer drugs marketed between 1981 and 2006 (Newman and Cragg, 2007). Yet despite the importance of plant derived medications, only approximately 10 % of the estimated 250,000 species worldwide have been screened for one or more bioactivities (Walsh, 2003; Hostettmann and Hamburger, 1993; Harvey, 2000; Verpoorte, 1998).

As most of these phytotherapeutic studies have centred on ethnomedicines from other parts of the world (particularly Ayurvedic medicinal plants from India, Chinese traditional medicinal plants and African ethnobotanicals), Australian plants remain relatively unstudied. Given the unique nature of many Australian plants and the diverse, and often harsh conditions in which they grow, it is surprising that more research is not undertaken in this field. In fact most research into medicinal plants involves an examination of plant species from other regions of the world. Even amongst phytochemical/natural therapeutics researchers in Australia, the greater emphasis appears to be on research into international plants. For example, the number of publications relating to Aloe vera medicinal properties greatly exceeds publications of Eucalypts medicinal properties, even amongst Australian researchers. Presumably this is due to the wealth of knowledge already available about international plants, providing a starting point for more advanced studies. Likewise, the documentation of medicinal plants in other cultures may make species selection a simpler process. However, Australia's harsh climatic conditions are likely to have resulted in Australian plants producing phytochemical protective mechanisms unique to their environment. Therefore, it is likely that Australian plants may produce unique phytochemicals that may result in new therapeutic agents and may provide the starting point for the development of novel drugs. There are quite a number of promising plants, some of which have been described in this volume, for which rigorous scientific studies are required. It is hoped that this text may help to stimulate interest in Australian medicinal plants and may provide a starting point for further studies in this field.

Glossary

Alkaloid: a bitter tasting nitrogenous phytochemical found in some plants. Certain alkaloids (eg quinine and scopolamine) are medicinally useful in low doses. However, in higher doses, alkaloids are often toxic.

Allopathic: a medicinal system which aims to treat illness with remedies that induce effects differing from and counteracting those produced by the disease itself. Western medicinal systems are nearly exclusively allopathic.

Analgesic: a drug which alleviates or reduces pain.

Anthocyanidin: a class of antioxidant flavonoid which also act as common plant pigments.

Antibacterial: a medicine or agent that prevents the growth of, or kills bacteria.

Anticancer: a drug or treatment with cancer inhibiting or overcoming properties.

Anticholinergic: a substance that blocks or opposes the action of the neurotransmitter acetylcholine.

Anticoagulant: am medicine or substance that prevents or retards the clotting of blood.

Antidiabetic: a medicine capable of counteracting or overcoming the effects of diabetes.

Antifungal: a medicine or agent that prevents the growth of, or kills fungi.

Antiinflammatory: a medicine or substance capable of counteracting or overcoming the effects of inflammation.

Antimalarial: a medicine or agent that prevents or counteracts malaria.

Antimicrobial: a medicine or agent that prevents the growth of, or kills microbes.

Antioxidant: a molecule or substance capable of slowing or preventing the oxidation of other molecules.

Antipyretic: a medicine capable of reducing fever.

Antispasmodic: a medicine capable of preventing or relieving spasms and convulsions.

Antiseptic: any substance or medicine which prevents or retards the growth of microorganisms.

Antithelmintic: a medication that causes the expulsion of parasitic worms from the body by either stunning or killing them.

Antitumour: a drug or treatment capable of inhibiting tumour growth. Usually referred to in connection with cancer.

Antiviral: a medicine or agent that prevents the reproduction or spread of virus. Antiviral medicines may directly destroy the bacteria, or block one or more steps in their replicatory cycle.

Aphrodisiac: a medicine capable of inducing sexual desire or enhanced sexual performance.

Aromatic chemical: a compound containing a six membered carbon ring structure with conjugated double bonds. This structure allows electrons to freely cycle between carbon atoms, resulting in a stable structure with charge delocalisation.

Ascorbic acid: vitamin C.

Asthma: a respiratory disorder resulting from chronic inflammation of the lungs in which the airways may suddenly and unexpectedly narrow.

Astringent: a substance that constricts tissues, blocking secretion of fluids such as mucus.

Atherosclerosis: the build up of waxy plaque on the inner surface of blood vessels.

Ayurvedic medicine: a philosophy and healing system developed in India over thousands of years. It uses an integrative approach to healthcare, often using botanical preparations and lifestyle intervention. Ayurveda focuses on prevention rather than curative action.

Bactericide: an agent which kills bacteria.

Bioassay: any technique used to compare the biological activity of a substance on a test organism with those of a standard preparation.

Bronchitis: An inflammation of the respiratory tubes and tissues.

Chalcone: an aromatic ketone that as well as being a secondary metabolite in its own right, is an intermediate in the biosynthesis of flavonoids.

Cardiac glycosides: steroidal glycosides which exert effects on the heart in small amounts (eg digitonin). However, in higher doses, cardiac glycosides are often toxic.

Carminative: a medicine which relieves colic or flatulence.

Cathartic: purgative.

Colic: acute abdominal pain (especially in infants).

Contraceptive: a medicine of treatment (either chemical or physical) capable of blocking conception.

Coumarin: a bicyclic aromatic compound found in many plants which give them characteristic aromas. 1,2-benzopyrone is the parent coumarin compound from which other coumarins are derived.

Cyclitol: a cycloalkane having at least three hydroxyl groups attached at different carbon atoms of the ring structure.

Cytotoxic: any substance that is toxic to cells.

Decoction: an aqueous extract obtained by boiling plant material in water.

Depilatory: hair removing.

Diabetes: a group of medical conditions characterised by high blood glucose levels, either as a result of the individuals inability to produce enough functional insulin, or an inability to respond to the insulin which is produced.

Diaphoretic: A medicine or agent which increases perspiration.

Diarrhoea: an abnormally fluid, frequent bowel discharge.

Diterpene: see terpene.

Diuretic: a medicine or agent which increases urinary output.

Dysentery: disease characterised by severe diarrhoea, often containing mucus and/or blood. Often associated with abdominal pain.

Dyspepsia: indigestion, characterised by heartburn, discomfort or nausea.

Eczema: an acute or chronic inflammation of the skin, characterised by redness, itching and the outbreak of oozing vesicles which become encrusted and scaly.

Embolism: a blood clot or fatty deposit that floats in the bloodstream and obstructs blood flow.

Emetic: a medicine or agent which causes vomiting.

Emmolient: a medicine used for soothing and softening the skin.

Emphysema: an enlargement of the air vesicles within the lung, resulting in decreased respiratory function.

Endemic: native to a particular location and not found naturally occurring elsewhere.

Essential oil: a volatile oil obtained by steam distillation plant materials. Common essential oils include those from Australian native plants of the Eucalyptus and Melaleuca genuses.

Ethnopharmacology: the use of traditional medicines by specific ethnic and cultural groups.

Expectorant: a medicine which promotes the secretion of bronchial mucus, resulting in the expulsion of phlegm from the lungs.

Febrifuge: a medicine which reduces fever.

Fever: an increased body temperature, often a symptom of infection.

Flavonoid: a large class of plant secondary metabolites which have antioxidant effects and limit oxidative damage. Flavonoids are often also responsible for the colour of plants.

Free radical: an atom (usually an oxygen atom) or group of atoms with at least one unpaired electron. Free radicals are extremely chemically reactive and in order to stabilise themselves, they remove electrons from nearby molecules thereby oxidising those

molecules. Free radicals have been implicated in many degenerative diseases and cancer.

Germicide: a substance that kills microorganisms.

Glycoside: any substance in which a sugar residue is bound to a non-carbohydrate moiety, usually a small organic molecule such as a flavonoid, coumarin, steroid or terpene.

Gondwana/Gondwanaland: The name of the southern most of the two precursor supercontinents (the other being Laurasia) formed from the split of the land mass Panagea. Gondwana later split to form Australia, Africa, South America, Antarctica, India and Arabia.

Gonorrhoea: a common sexually transmitted disease caused by the bacterium *Neisseria gonorrhoeae*.

Hemolytic: causing the breaking open of red blood cells and the release of haemoglobin.

Hemostatic: an agent that stops bleeding.

Hydatid: a cyst filled with fluid which forms as a consequence of a infestation of tapeworm larvae.

Hydrolysis: the addition of a water molecule to a compound resulting in the splitting of that molecule into two (or more) smaller fragments.

Hyperglycemic: a higher than normal blood glucose level.

Hypertensive: having a higher than normal blood pressure.

Hypoglycemic: a lower than normal blood glucose level.

Hypotensive: having a lower than normal blood pressure.

Inflammation: a response of body tissues to injury, infection or irritation. Inflammation is characterised by pain, swelling, redness and heat.

Infusion: a solution obtained by the steeping or soaking of plant material in water (eg tea).

Invasive: an invasive species is capable of invading a habitat that it does not naturally occur in, to the detriment of the native species.

Isoprene: an unsaturated five carbon hydrocarbon which is readily polymerised. Isoprene units form the structural basis of terpenes.

Kino: the gum exudates obtained from various plants and trees (especially Eucalypts) in response to mechanical damage.

Lactagogue: a medicine or compound that induces or increases the secretion of milk.

Lactation: the secretion of milk from the mammary gland.

Laryngitis: an inflammation of the mucus membrane of the larynx.

Laurasia: The name of the northern most of the two precursor supercontinents (the other being Gondwana) formed from the split of the land mass Panagea. Laurasia later split to form most of Asia, Europe and North America.

Laxative: a medicine or substance that causes evacuation of the bowels.

Leprosy: or Hansen's disease, is a chronic disease of the skin and nerves, caused by the bacteria *Mycobacterium leprae* and *Mycobacterium lepromatosis*. It is manifested as lesions in the skin, mucous membranes and peripheral tissues.

Linament: a medicated liquid treatment for topical application to the skin.

Malaise: a general feeling of physical discomfort, fatigue or unease.

Malaria: a mosquito-borne infectious disease caused by protozoans of the genus Plasmodium. Symptoms include fever, shivering, joint pain, vomiting and convulsions.

Monoterpene: see terpene.

Morphology: the form, structure and configuration of an organism.

Mucilage: a gelatinous substance secreted by plants and some microorganisms.

Narcotic: a drug that relieves pain and produces numbness and stupor.

Nephritic: of or relating to the kidneys.

Nephritis: an inflammation of the kidneys.

Ophthalmia: an inflammation of the eye.

Oxidation: a chemical reaction where electrons are transferred from a substance to an oxidising agent. Oxidation reactions may produce free radicals which can cause cellular damage (also see oxidative stress)

Oxidative stress: disturbances in the normal redox state of cells may result in an imbalance between the production of reactive oxygen species (ROS) and the biological systems ability to detoxify the reactive species or to repair the damage induced by ROS.

Palsy: the loss of controlled movement of a body part. It is characterised by an uncontrolled tremor.

Pangaea: an early supercontinent which contained all or nearly all of the current land masses. Pangaea split during the Triassic era to produce the southern supercontinent (Gondwana) and the northern supercontinent (Laurasia).

Parasitic: a relationship between organisms of different species where one organism derives benefit (nourishment) at the expense of the other.

Phenolic compound: secondary metabolites which contain one or more phenol group incorporated into their structure.

Phytochemical: any chemical compound derived from plants which has biological activity, but is not nutritive.

Phytoalexins: are chemically diverse antibiotics produced by plants in response to pathogen infection.

Polyphenol: a group of organic compounds produced by plants characterised by the presence of more than one phenol moiety per molecule. Examples include flavonoids and tannins. Polyphenol compounds tend to be colourful and have antioxidant properties.

Polyterpene: see terpene.

Poultice: a soft, moist mass applied topically to a sore, aching, inflamed or lesioned part of the body to soothe.

Proanthocyanidin: a class of flavanols found in many plants. They are reputed to have beneficial health effects due to their free radical scavenging capacity.

Proteolytic: a substance which hydrolyses proteins into peptides and/or amino acids by cleaving peptide bonds.

Pruritus: severe itching sensation resulting from an irritation of the sensory nerve endings. It has many possible causes including allergy, infection, lymphoma and diabetes.

Psychoactive: a drug or substance that acts primarily on the central nervous system, altering brain function, resulting in changes in perception, mood, consciousness or behaviour.

Pulmonary: relating to the lungs.

Purgative: a medicine or substance that causes evacuation of the bowels.

Quinones: a class of organic compounds derived from aromatic compounds which have two carbonyl groups in the same six membered ring. Quinones are usually yellow/red coloured and often function as electron carriers.

Reactive oxygen species (ROS): highly reactive oxygen containing compounds resulting from incomplete cellular reduction processes. ROS induce oxidative stress and damage to cellular components and have been linked with aging and a variety of disease states and degenerative conditions.

Reduction: a type of chemical reaction in which electrons are added to an atom or ion.

Rheumatism: a painful disorder of the joints, muscles or connective tissues.

Ringworm: a condition caused by a fungal infection of the skin.

Rubefacient: a medicinal agent for topical application which increases blood flow and reddens the skin in the area applied.

Saponin: a class of chemical compound (steroidal or triterpenoid) which are natural surfactants and form soapy lathers when agitated with water.

Scabies: a contagious skin infection caused by the parasitic mite *Sarcoptes scabieri*. It is characterised by an intensively itchy rash caused by an inflammatory hypersensitivity reaction.

Scurvy: an inability to synthesise collagen and connective tissue due to a deficiency of vitamin C. Symptoms include weakness, nausea, spongy gums, loose and bleeding teeth, hair loss and eventually death.

Secondary metabolite: organic compounds produced by plants that have no direct involvement in the growth, development or reproduction of that plant. Secondary metabolites are often involved in plant defence mechanisms and their production is often increased in response to stress.

Sedative: a drug that reduces excitability and induces calm.

Sesterterpene: see terpene.

Sesquiterpene: see terpene.

Steam distillation: a type of distillation used for isolating the volatile compounds from botanical material to produce essential oils. Material is boiled in water (or has steam passed through it) and the steam is condensed to recover the volatile compounds.

Steroid: a class of organic compound consisting of seventeen carbon atoms arranged in four fused rings, usually with additional functional groups attached. Many have important physiological functions.

Styptic: an astringent agent which stops bleeding by constricting blood vessels and other tissues.

Syphilis: a common sexually transmitted disease caused by the bacterium *Treponema pallidum*.

Tannin: a diverse class of astringent polyphenolic compounds of plant origin. They often play a role in protection against predation and microbial infection in plants.

Taxonomy: the classification of organisms into groups based on similarities of structure, origin, genetics etc.

Terpene: a large and varied class of substances derived from the five carbon molecule isoprene. Monoterpenes (the simplest terpenes) consist of two isoprene units, sesquiterpenes consist of three isoprenes, diterpenes of four, sesterterpenes of five, triterpenes of six and tetraterpenes (also called carotenoids) consist of eight isoprene units. Polyterpenes consist of long chains of many isoprene units. Terpenes are often modified chemically (eg by oxidation or by rearrangement of their carbon skeleton), and are generally called terpenoids (meaning terpene-like).

Terpenoid: see terpene.

Tetraterpene: see terpene.

Thrombosis: the formation of a blood clot in a vein or artery, causing loss of circulation.

Tincture: an alcoholic extract or solution which includes non-volatile compounds.

Tinea: a fungal disease of the skin.

Tonic: a medicine or compound that strengthens and invigorates.

Triterpene: see terpene.

Vermifuge: a medication or compound which causes the expulsion of parasitic intestinal worms such as tapeworms.

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