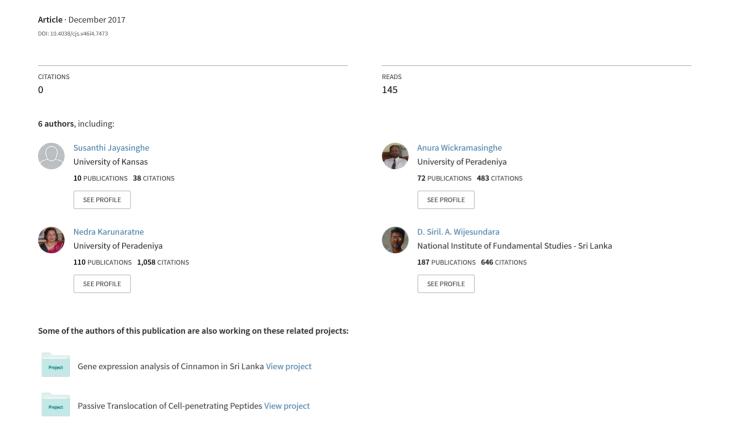
# The importance of harnessing the rich diversity of Sri Lankan flora for their medicinal value



#### **REVIEW ARTICLE**

### The importance of harnessing the rich diversity of Sri Lankan flora for their medicinal value

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**Abstract:** Ethnomedicine evolved from the traditional use of plant parts for treating various ailments. Historically, most medical breakthroughs have arisen based on the plant sources showing potential for curing many diseases. Even so, the therapeutic power and scientific validation of their modes of action remains unexplored. Sri Lanka being a biodiversity hotspot due to its high endemism and diversity has inspired the search for ethnopharmacological values which may give rise to drug leads or to the discovery of new bioactive compounds. This brief review aims to highlight the global importance of the exploration of traditional medicinal plants, current status and the progress of the studies on Sri Lankan medicinal plants, and the necessity to discover the medicinal value of the Sri Lankan plants.

Keywords: Plant medicines, Sri Lankan biodiversity, status and challenges, bioactive chemical space, screening, bioactive endemics.

#### INTRODUCTION

Because of the manifold biological activities and medicinal potentials of natural products, all human civilizations have amassed know-how and knowledge of their practical uses. For more than 5,000 years, Ayurveda has been practiced to promote wellness in India. From the Sanskrit words ayurs (life) and veda (knowledge), ayurveda originated from Hindu scriptures called the Vedas, and may have influenced Buddhist philosophy, Eastern and Western health care. In ancient Mesopotamia, circa 2600 BC, medicinal plant descriptions were written on clay tablets in cuneiform. About 1,000 plants and plant-derived substances were inscribed in these tablets, such as the oils of Cedrus species (cedar), the resin of Commiphora myrrha (myrrh) and the juice of the poppy seed Papaver somniferum (Newman et al, 2000). Many of these herbs and formulations are still used today. Such practices seem to have evolved, as shown by the inscriptions in the Egyptian Ebers Papyrus, dating from around 1550 BC, which contains about 800 complex prescriptions and more than 700 natural agents such as Aloe vera (aloe), Boswellia carteri (frankincense) and the oil of castor, Ricinus communis (Zhong and Wan, 1999). In what appears to be discriptions of curative agents for known disease conditions, the famous Greek physician, Hippocrates of Cos (circa 460-377 BC), collected more than 400 natural agents and described their use in his Corpus Hippocraticum. Here, he refers to melon juice as a laxative, explains the diuretic effect of the juice from Ornithogalum caudatum (squill) and illustrated the use of Atropa belladonna extract as an anesthetic. He also advised using an extract of Veratrum album (white hellebore) as an emetic and how to use olive oil to improve wound healing (Castiglioni, 1985). Later, Roman expanded physicians on this knowledge and added their own intuitions and experience. Pedanius Dioscorides (circa 40-90 AD) compiled De Materia Medica, which described the dosage and efficacy of about 600 plant-derived medicines which contributed to the development of pharmacology in Europe (Wermuth, 2003). Galen (129-200 AD), another Greek physician and pharmacist, recorded 540 plant-derived medicines and demonstrated that herbal extracts contain both beneficial and harmful compounds (Cai, 1992).

During ancient times in South Asia, where Ayurveda was practiced, the therapeutic effects of plants were recognized and documented in Materia Medica and Ola leaf manuscripts. Although in Sri Lanka, both the traditional system and the allopathic (Western) system are practiced, according to the WHO, over 70% of people in Sri Lanka, still benefit from the

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indigenous systems of medicine which use plant interventions (Anon., 1978). based 'Ayurveda', 'Deshiya Chikitsa', 'Siddha' and 'Unani' are systems widely practiced in Sri Lanka. Ayurveda and Deshiya Chikitsa systems use plant and herbal products, the former using approximately 2,000 plant species and the latter about 500. Long established preparations like 'arishta', 'kasaya', 'guli' and 'kudu' contain the majority of material derived from plants. 'Sinhalese Materia Medica' is a modern day list of a sizable number of Sri Lankan plants used in the above traditional preparations (Attygalle, 1917). Later, chemistry and the pharmacology of Sri Lankan and Indian plants was published by Chandrasena (1955) followed by the serial compilation by Jayaweera (1980-82) medicinal plants used in Sri Lanka.

#### SRI LANKA'S BIODIVERSITY

Sri Lanka is one of the most biologically diverse countries in Asia. Despite its small size of 6,524,540 hectares, Sri Lanka has a varied climate and topography, which has resulted in rich endemism distributed within a wide range of ecosystems. Its distinctive biological diversity is defined by the ecosystems, species and genera that occur in the island's diverse array of forests. wetlands, coastal, marine and agricultural systems. Sri Lanka's biodiversity is considered to be the richest per unit area in the Asian region with regard to mammals, reptiles, amphibians, fish and flowering plants. The global importance of the island's biodiversity has placed Sri Lanka together with the Western Ghats of India among the 34 biodiversity hotspots in the world (Myers et al., 2000).

### IDENTIFICATION OF FLOWERING PLANTS IN SRI LANKA

The most comprehensive description of Sri Lankan plants was carried out during the Colonial period by Trimen (1893-1931) and that was subsequently revised by Dassanayake and Fosberg (1980-2000). This latter attempt has helped to expand and modernize the National Herbarium at the Royal Botanical Garden in Peradeniya which safeguards the authentication of the plants. The National Herbarium currently contains about 165,000 specimens.

Globally, the angiosperms are the most diverse group of plants with an estimated number of 200,000 to 400,000 species (Thorne, 2002) belonging to 415 families. In Sri Lanka,

angiosperm flora has been recorded by several scientists since the colonial times. The earliest being Trimen's Handbook to the Flora of Ceylon (Trimen, 1893-1900). More recently, the revision of the Trimen's Flora (Dassanayake and Fosberg 1980-2000) described 3,771 species in 1,363 genera and that included many naturalized species. The total number of endemic species (including varieties and subspecies) was about 1,000 according to that revision. Compared to the rest of South Asia, angiosperm diversity in Sri Lanka is remarkably high due to multitudes of factors. Origin, affinities and biogeography of our flowering plants have been discussed by several authors in the past (Trimen, 1893-1900; Ashton and Gunatilleke, 1987).

One of the prominent attributes of Sri Lanka's angiosperm flora is its high endemicity. The Red List of Sri Lanka disclosed that there are 894 endemic angiosperm species in Sri Lanka distributed largely in the central and south west region (MOE, 2012). However, there may be more endemic species in the northeast and eastern areas of the country where the plant species have not undergone descriptions as the plants of south western regions. Sri Lanka has no endemic families endemic genera although 14 have described. The endemic genera Hortonia (Family: Monimiaceae) and Schumacheria (Family: Dilleniaceae) have probably been derived from the Gondwanaland flora of 100-120 million years ago (Somasekaram et al., 1997).

The relict rain forest plant taxa of Gondwana-Deccan ancestry are now found only in some isolated forest pockets in the Penninsular India and Southwestern Sri Lanka. Deccan flora evolved in isolation in the late Cretaceous and early Tertiary periods, during the drifting of the Indian plate (Somesekaram *et al.*, 1997). It has been hypothesized that biotic impoverishment, prior absence followed by colonization and later speciation has led to the tremendous endemic diversity in the island (Biswas, 2008). It is thus fitting that the World Conservation Monitoring Centre has also designated Sri Lanka as a biodiversity hotspot (Caldecott *et al.*, 1994).

Out of 3,154 indigenous species evaluated in the Red List, 1,386 (44%) are threatened (critically endangered, endangered or vulnerable). Out of the 186 families evaluated, 81 families have 50% or more threatened species and in 24 families all species are threatened.

Only 45 families do not consist of any threatened species. Out of all these, six species are believed to be extinct viz., Strobilanthes caudata (Acanthaceae). Blumea angustifolia (Asteraceae). Crudia zevlanica (Fabaceae). Rinorea bengalensis and Rinorea decora (Violaceae). Alphonsea hortensis (Annonaceae) and Doona ovalifolia (Dipterocarpaceae). These species are believed to be found only in cultivation at the National Botanic Gardens (extinct in the wild). However, Rinorea bengalensis and Rinorea decora have been rediscovered (MOE, 2012).

#### STATUS OF LOWER PLANTS

Our understanding of the diversity of lower plants such as lichens, mosses, liverworts and hornworts has been enhanced with more recent studies.

Brunbauer in 1984 compiled 15 articles based on published literature on Sri Lankan lichens (Brunbauer, 1984-1986) which included 550 species belonging to 122 genera and 48 families. According to the literature, 696 lichens had been recorded in 2006. Some recent investigations on lichens carried out in Sri Lanka indicate that the numbers of lichen species recorded from Sri Lanka may exceed 1000 species (Jayalal *et al.*, 2008); importantly, a number of new species have been recorded (Orange et al., 2001; Jayalal *et al.*, 2012; Weerakoon *et al.*, 2012).

Abewickrama and Jansen (1978a) published the first checklist of liverworts and hornworts of Sri Lanka, where they reported 183 species of the former and 5 species of the latter. Recently, Long and Rubasinghe (2014) have expanded this list to include 327 species of liverworts and 5 species of hornworts. Abewickrama and Jansen (1978b) also reported 569 species of mosses and high endemicity was noted (11%) among them. A recent study by Ruklani and Rubasinghe (2013) has added 12 new species of mosses.

#### GLOBAL BIODIVERSITY TREATIES

The United Nations Convention on Biological Diversity (CBD) has resulted from the Rio Earth Summit in 1992 in Brazil (Cragg *et al.*, 2012). The three main objectives of the CBD are the conservation of biological diversity, the sustainable use of its components, and the fair and equitable sharing of the benefits arising from

commercial and other utilization of genetic resources. The agreement covers all ecosystems, species, and genetic resources. It established expectations regarding access to and the use of biodiversity ('genetic resources') across national borders. In general, the CBD states that: (a) countries have sovereign entitlements over the genetic resources within their boundaries, (b) access to genetic resources by foreign groups obliges prior informed agreement from the appropriate authority in the country containing the genetic resource, (c) access on mutually agreed terms should be facilitated by the source country, (d) benefits from the use of genetic resources should be shared in a just and reasonable way with the source country, (e) the source country should participate in related research on the genetic resources, where feasible, and profit from technology transfer. The CBD was signed by most countries in the world (194 to date), including Sri Lanka, and has been extensively ratified (with the important exception of the United States). However, since the CBD necessitates individual countries to adopt appropriate laws and regulations to implement its principles, the impact of the CBD has been mixed. Importantly, the CBD did not offer exclusive recommendations addressing the use of traditional knowledge from one group of people by other groups or companies. This became the subject of the Nagova Protocol, which was approved in 2010 by the Conference of the Parties to the CBD. This Protocol gives enumerated proposals that cover access and benefit-sharing related to natural products and traditional knowledge. Although the Protocol has been signed by 92 countries (as of November 2014), it is only ratified by 30 countries, with Norway being the first 'developed' nation to do so. Fifty countries have to adopt the Protocol before it can become legal and binding. However, it can be considered as a realistic guide for those working on biodiversity making use of traditional knowledge.

### GLOBAL REASSESSMENT OF NATURAL PRODUCTS AS POTENTIAL DRUGS

After several decades of insufficient interest in natural products as drug candidates, today there is a progressively strong case for reevaluating natural products for drug discovery. Traditionally, natural products are a source of almost all medicinal preparations and, more recently, natural products have entered clinical

trials or provided lead compounds that have entered clinical trials, mainly as anticancer and antimicrobial agents (Harvey, 2008; Harvey and Gericke, 2011; Dias et al., 2012). comprehensive analysis of new medicines the US Food and approved by Drug Administration (FDA) between 1981 and 2010 (Newman and Cragg, 2012) showed that 34% of those medicines that were founded on small molecules were natural products or direct derivatives of natural products — comprising the statins, tubulin-binding anticancer drugs and immunosuppressants (Mishra and Tiwari, 2011; Carter, 2011; Cragg and Newman, 2013; Butler and Blaskovich, 2013). Although it seems ironic that despite success stories, there was diminished interest in natural products by the pharmaceutical industry. There have been several reasons for the lack of interests in natural products for drug discovery. There are genuine concerns regarding the United Nations Convention on Biological Diversity which pursues to regulate international access to natural products. The following may be the reasons why natural products became a source of low interest in drug discovery: (a) products assumption that natural incompatible with drug discovery approaches based on high-throughput screening (HTS) directed at molecular targets (Rishton, 2008); (b) unreliability of repeated isolation of known compounds and synthesis of natural products pharmaceutical manufacture being during impractical (Drewry and Macarron, 2010); (c) combinatorial chemistry has not provided all the lead compounds needed for effective lead discovery (Newman and Cragg, 2012).

However, it is now understood that the diversity within biologically relevant 'chemical space' is more significant than the size of the library of compounds. Natural product libraries show a wide range of pharmacophores rich in stereochemistry, and these attributes are considered important in contributing to their ability to deliver hits, even against proteinprotein interactions which are normally hard to achieve (Drewry and Macarron, 2010). In addition, natural products have the benefit over synthetic compounds since they are natural metabolites, and importantly, drugs have been implied to show the property of 'metabolitelikeness' (Hert et al., 2009). This means that they are both biologically active and will act as substrates for one or more of the many

transporter systems that can carry the compounds to their intracellular site of action.

Traditionally in natural-product research, concentrated extract samples were screened in bioassays (Quinn, 2012). Usually, these extracts complicated mixtures. Although, components present in the extract may reach the biological target of the assay, the concentration of some components may be too low to have measurable effects. In addition, the signal from the assay may be confused by interference or undesirable compounds, or by the additive or synergistic effects of mixtures of compounds. On the other hand, isolating each and every compound from a crude extract prior to screening is cumbersome, and too costly for large numbers of samples. Thus, the removal of artifacts prior to screening will be very useful: polyphenolic tannins are the usual nuisance compounds in plant extracts (Wall, 1996). Then, fractions which are less complex can be prepared for screening, allowing the scale to be reduced and the speed increased. The use of simplified fractions, together with sensitive techniques, has tackled the isolation and structure-elucidation bottleneck.

The Dictionary of Natural Products has records of about 200,000 plant secondary metabolites, including about 170,000 unique structures (after the removal of duplicates). Around 15% of the drug interventions in the www.ClinicalTrials.gov database are plantrelated, with approximately 60% of these 'drugs' being grouped from only 10 taxonomic families (Sharma and Sarkar, 2013). Notwithstanding these hits, it is very likely that the majority of plant species have not been systematically investigated in drug discovery campaigns. In addition, microorganisms exhibit a significance of biodiversity that betters those of eukaryotes, incomparable and have metabolic adaptability.

The study of metabolomics came about from the goal of qualitatively and quantitatively analyzing all metabolites in an organism within a given time frame and conditions. Metabolomics makes it possible for indirect monitoring of gene function and biochemical status of an organism. Thus, metabolomics and genomics can be used to optimize biosynthetic pathways to selectively produce biologically active natural products (Craig *et al.*, 2010).

In another approach, metabolomics has enabled the study of the effects of the complex mixtures contained in traditional herbal medicine (Youns et al., 2010). For example, Angelica sinensis tea-derived Chinese health products have been analyzed by chemometric-guided HPLC to give qualitative analysis on the individual compounds contained in overlapping profiles of co-eluting compounds (Li et al., 2013). Metabolomics with electrospray ionization quadrupole time-of-flight spectrometry (ESI-TOFMS) led to the isolation of an antitumour saponin from Panax ginseng (Mao et al., 2012).

Overexpression is a unique method to overcome the supply problems of minor metabolites (Stevens et al., Overexpression antisense-suppression and methods have been used in transgenic plants such as soybean where key gene-coding enzymes for flavonoids, isoflavanoids and terpenoids led to circumventing seasonal and geographical limitations (Wang et al., 2011; Lange and Ahkami, 2013).

### SCREENING STUDIES OF NARTURAL PRODUCTS IN SRI LANKA

The Department of Chemistry, University of Peradeniya initiated a research project aimed at chemical investigation of endemic plants of Sri Lanka in 1981, the first such large scale effort in this area. In this project, about 125 Sri Lankan plant species were investigated. Some of these efforts are highlighted in the publications below.

The family Clusiaceae, where several nonendemic species belonging to *Calophylum* and *Garcinia* are used in indigenous medicine in Sri Lanka (Attygala, 1917; Chandrasena 1955), emerged as a family rich in xanthones (Gunasekara *et al.*, 1981; Bandara *et al.*, 1986).

Among the family Dipterocarpaceae, Sri Lanka has 9 genera, with 58 species of which *Doona* and *Stemonoporus* are endemic (Kostermans, 1992). Almost all species of Dipterocarpaceae are endemic. A large number of sesquiterpenes and triterpenes have been reported from this family (Bandaranayake *et al.*, 1975).

Another family of high endemism is Flacourtiaceae (now under Achariaceae and Salicaceae). Here, 8 genera and nine species are endemic (Bandaranayake and Sultanbawa, 1969).

The presence of triterpenoids is the hallmark of this plant family (Gunasekera and Sultanbawa, 1973).

Two endemic plants of the family Celastraceae, namely Kokoona zeylanica Thw. and Salacia reticulata var. diandra Thw. have been extensively studied in Peradeniya. From the former, among a number of compounds isolated, tri- and tetra-oxygenated D:A-friedo-oleanan triterpenes (Gunatilaka and Nanayakkara, 1984), 27-hydroxy and 6β-hydroxy di- and trioxygenated D:A-friedo-oleanane triterpenes (Gunatilaka et al., 1983), phenolic D:A-friedo-24-noroleanane triterpenoids (Gunaherath and Gunatilaka, 1983) are noteworthy. The latter plant, commonly referred to as Kothala Himbutu, is erroneously named as Salacia reticulata var. diandra Thw. Significantly, this plant was first described by Thwaites as Salacia diandra as a distinct species endemic to Sri Lanka and it was later reduced to a variety of S. reticulata (Salacia reticulata var. diandra) by Lawson in 1875. However, in the Revised Handbook to the Flora of Ceylon (Dassanayake and Fosberg, 1980-2000) it has been listed as Salacia diandra Thw. A notable difference in S. diandra from S. reticulata is its solitary flowers, narrower leaves with entire margin and finer reticulation of veins and flowers with two stamens. Unlike S. reticulata, S. diandra is distributed in the Wet Zone (wetter parts of Ratnapura, Galle and Matara Districts). According to the National Red List, S. diandra is an endangered plant. Undoubtedly, this plant which is commonly known to be originating from India and Sri Lanka, is a plant endemic to Sri Lanka.

Following noteworthy screening endemics for their biological activity stand out: Antimicrobial and insecticidal activities of Sri Lankan plants were carried out by scientists from the University of Peradeniya; of particular importance are the work on endemics (Hewage et al., 1998; Kumar et al., 1989; ; Bandara et al., 1989; Bandara et al., 2015). In addition, biological activity of Sri Lankan lichens have also been determined (Thadhani et al., 2012). Antiradical and antilipoperoxidative effects of some plant extracts used by Sri Lankan traditional medical practitioners for cardioprotection were reported by Munasinghe et al., (2001). Arseculeratne et al., (1985) screened fifty medicinal plants for hepatotoxic activity. In a seminal study of oral hypoglycemic activity of some Sri Lankan plants, Karunanayake et al., (1984) reported the antidiabetic activity of Salacia diandra Thw. Sri Lankan alkaloids and their biological activity have been reviewed by Gunatilaka, (1999). Siriwardena et al., have reviewed biologically active compounds isolated from Sri Lankan flora (2015). The endemic genera, Hortonia and Schumacheria have extensively studied (Ratnayake et al., 2008; Ratnayake, 2009; Carr, 2012) and (Bandara et al., 2015). Twelve of the seventeen endemic Annonaceae plants were investigated for their bioactivity and the presence of Alkaloids (Weerasinghe et al., 2013; Puvenendran et al., 2010). Authors claimed that the remaining five species could not be collected due to their unavailability from the recorded sites, yet again highlighting the importance of investigating the medicinal value of Sri Lankan endemic species before it is too late.

Tropical lichens, particularly ones from Sri Lanka, continue to unfold a wide variety of biologically active phenolic compounds with iron chelating siderophore type activity (Karunaratne *et al.*, 2005; Kathirgamanathar *et al.*, 2006; Karunaratne *et al.*, 2002; Karunaratne *et al.*, 1992).

Out of the 30 patents covering the compounds and extracts of Salacia reticulata var. diandra (Kothala Himbutu) growing in Sri Lanka and India, several Japanese patents claim anti-diabetic properties of its extracts. The claims of these patents have been made despite the practice of using S. diandra in the treatment of high blood-sugar, which is part of the traditional knowledge of Sri Lanka; and furthermore its efficacy had been shown through work carried out by Karunanavake et al. (1984) prior to the approval of these patents. Although, the group in Peradeniya missed the antidiabetic principals found in the aqueous extract of the root of this plant, they published isolation

quinonemethides (Tezuka *et al.*, 1993; Tezuka *et al.*, 1994; Dhanabalasingham *et al.*, 1996) from the organic extracts of this plant.

More recently, Attanayake *et al.*, (2013) has reported the efficacy and dose response studies of oral antihyperglycaemic activity of eight Sri Lankan medicinal plant extracts, used in the treatment of diabetes in traditional medicine in diabetic rats.

## FUTURE DIRECTIONS AND CONCLUSIONS

Table 1 lists the endemic plants with reported medicinal activity. However, work on the endemic genera *Hortonia* and *Schumacheria* have shown that many more endemic plants can be added to this list (Ratnayake *et al.*, 2008; Bandara *et al.*, 2015).

Prior to about 1985-2000, biological activity determination of plant derived secondary metabolites were not routinely carried out. Thus, the numerous compounds reported in the above description were not tested for their biological activity. For example, xanthones triterpenoids have recently been reported for their antitumour activity (Pinto et al., 2005; Petronelli, 2009). Therefore, a strong case can be made for reinvestigating the plants that come under the families such as Guttiferae, Dipterocarpaceae and Celastraceae, particularly the endemic plants, for their biological activity. Thus, in Sri Lanka, since there has not been a large-scale systematic search for therapeutics from its flora so far, the potential of Sri Lankan endemic flowering plants (823) and the nonflowering plants such as lichens remain largely unknown. Therefore, variety, richness and abundance of flora in Sri Lanka in general make it a fertile testing ground for a systematic drug discovery program.

**Table 1:.** Endemic plants possessing medicinal properties (Jayaweera, 1980-82).

Plant Name	Family	Medicinal uses
Semecarpus coreacea Thwaites	Anacardiaceae	Used for scrofulous, venereal and leprous conditions; as a vesicant in rheumatism and sprains;
		used for piles, boils in the rectum, urinary diseases, nervous debility, skin diseases, sexual debility, and diseases of the liver and spleen; used as a vermifuge and for asthma and cancer.
Semecarpus gardneri Thwaites	Anacardiaceae	Used for dysentery, asthma, coughs and incipient tuberculosis; used as an emetic. Root with water is used for neuralgia and headache.
Vernonia zeylanica Less	Asteraceae	Used in bone fractures; leaves applied on suppuration of boils; with turmeric, used for eczema of the legs; leaves used for treatment of asthma, also as an emetic, particularly in cases of food poisoning.
Impatiens repens Moon	Balsaminaceae	Used in epilepsy, piles and hemorrhoids.
Canarium zelyanicum Blume	Burseraceae	Bark is astringent and antiseptic; a decoction is used for bleeding and spongy gums; an ointment is used for chronic ulcers and fistulae; used as an aromatic stomachic and astringent and against diabetes; useful for infective fevers and malaria; gum resin used for halitosis.
Calophyllum walkeri Wight	Clusiaceae	Oil from the seeds used on fractures and contusions.
Argyreia populifolia Choisy	Convolvulaceae	Used as an astringent and antiseptic; leaves used for treating weak and spongy gums; root applied to swellings caused by dog bite.
Dillenia retusa Thunb	Dilleniaceae	Fruit used for poultices, fractures and dislocations.
Dipterocarpus glandulosus Thwaites	Dipterocarpaceae	Resin oil used in rheumatic swellings and leprosy.
Dipterocarpus zeylanicus Thwaites	Dipterocarpaceae	Heartwood used for fever; gum resin used on chronic ulcers, sinuses and fistulae; it acts as a diaphoretic and expectorant; useful against pharyngitis, tonsillitis, bronchitis and pneumonia.
Sansevieria zeylanica (Linn.) Willd	Dracaenaceae	Root used for bile and gonorrhea.
Hydnocarpus venenata Gaertn	Flacourtiaceae	Oil used as application for cutaneous diseases and for leprosy.
Exacum trinerve (Linn.) Druce	Gentianaceae	Entire plant used for mild fevers.
Plectranthus zeylanicus Benth	Lamiaceae	Used for fevers, dysentery, diarrhea, vomiting and thirst; acts as a cholagogue and useful for acute and chronic congestion of the liver; used as a diuretic and diaphoretic.
Litsea longifolia Benth. & Hook.	Lauraceae	Bark used for treating nervous diseases and boils.

Plant Name	Family	Medicinal uses
F.		
Barringtonia ceylanica (Miers) Gard. Ex C.B. Clarke	Lecythidaceae	Tender leaves used for dysentery and bleeding from cuts; bark and leaves used for rat-snake bites, rat poisoning and on boils; seeds employed for treatment of itch, piles, tonsillitis and typhoid fever; bark used for gastric ulcers.
Munronia pumila Wight	Meliaceae	Given for fever, dysentery and purification of blood.
Horsfieldia iryaghedhi (Gaertn.) Warb.	Myristicaceae	Flowers and bark used for dysentery, hiccough and wasting .
Zeuxine regia (Lindl.) Trimen	Orchidaceae	Used for treating snake-bite poisoning.
Madhuca neriifolia (Thw.) H. J. Lam.	Sapotaceae	Used in skin disease, rheumatism, headache, as a laxative, for piles, hemorrhoids, is an emetic, and anti-earth worm.
Madhuca fulva (Thw.) J.F. Macbr	Sapotaceae	Leaves and bark are used on scalds and burns.
Amomum masticatorium Thwaites	Zingeberaceae	Rhizome is aromatic and carminative.

#### REFERENCES

- Abewickrama, B. A. and Jansen, M. A. B. (1978a). A check list of liverworts of Sri Lanka. *UNESCO:* Man and the Biosphere National committee for Sri Lankan Publication 1: 1-10.
- Abewickrama, B. A. and Jansen, M. A. B. (1978b). A check list of mosses of Sri Lanka. UNESCO: *Man and the Biosphere National committee for Sri Lankan Publication* 2: 1-25.
- Anon. (1978). The Promotion and Development of Traditional Medicine. World Health Organisation Technical Report, Geneva **622**: 10.
- Arseculeratne, S.N., Gunatilaka, A.A.L. and Panabokke, R.G. (1985). Studies of medicinal plants of Sri Lanka part 14: toxicity of some traditional medicinal herbs. *Journal of Ethnopharmacology* **13**(3): 323-335.
- Ashton, P.S. and Gunatilleke, C. V. S. (1987). New light on the plant geohraphy of Ceylon. I. Historical plant geography. *Journal of Biogeography* **14**: 249-285.
- Attanayake, A. P., Kamani, A. P. W. Jayatilaka, K. A. P. W., Pathirana, C. and Mudduwa, L. K. B. (2013). Study of antihyperglycaemic activity of medicinal plant extracts in alloxan induced diabetic rats. *Ancient Science of Life* **32**(4): 193-198.
- Attygala, J. (1917). Sinhalese *Materia Medica*, Gunesena & Co., Colombo.
- Bandara, B. M. R., Dharmaratne, H. R. W., Sotheeswaran, S. and Balasubramaniam, S.

- (1986). Two chemically distinct groups of *Calophyllum* species from Sri Lanka. *Phytochemistry* **25**(2): 425-428.
- Bandara, B.M.R., Fernando, I.H.S., Hewage, C.M., Karunaratne, V., Adikaram, N.K.B. and Wijesundara, D.S.A. (1989). Antifungal activity of some medicinal plants of Sri Lanka. J. National Science Council 17(1): 1-13.
- Bandara, B. M. R., Jayasinghe, L., Karunaratne, V., Wannigama, G. P., M. Bokel, M., Kraus, W. and Sotheeswaran, S. (1989). Ecdysterone from Stem of *Diploclisia glaucescens*, *Phytochemistry* **28**: 1073-1075.
- Bandara, C.J., Karunaratne, D.N., Wickramasinghe, A., Wijesundara, D.S.A., Bandara, B.M.R. and Karunaratne, V. (2015). Total polyphenol content and antioxidant and cytotoxic activities of the Sri Lankan endemic plant genus Schumacheria. International Journal of Pharmacy & Pharmaceutical Science 7(3):465-467.
- Bandaranayake, W. M. and Sultanbawa, M. U. S. (1969). List of endemic plants of Ceylon. University of Ceylon, Peradeniya.
- Bandaranayake, W. M., Gunasekera, S. P., Karunanayake, S. Sotheeswaran, S. and Sultanbawa, M. U. S. (1975). Terpenes of Dipterocarpus and Doona species. *Phytochemistry* 14: 2043-2048.
- Biswas, S. (2008). Did biotic impoverishment facilitate phenomenal diversification in Sri Lanka. *Current Science* **95**(8): 1021-1025.

- Brunnbauer, W. (1984-1986). *Die Flechten von Sri Lanka in der Literatur*. Botanische Abteilung, Naturehistorisches Museums Wien, (in 14 teilen, als Kopien verteilt).
- Butler, M. S., Blaskovich, M. A. and Cooper, M. A. (2013). Antibiotics in the clinical pipeline. *Journal of Antibiotics* **66**: 571-591.
- Carr, G., Ratnayake, R., Bandara, R., Wijesundara, S., Williams, D.E., Tarling T., Balgi, A.D., Roberge, M., Karunaratne, V. and Andersen, R.J. (2012). Hydrazulenones from the genus *Hortonia. Journal of Natural Products* **75**(6): 1189-1191.
- Cai, J. E. (1992). The brief history of the usage of European medicinal plants. *Chinese Pharmacy Journal* 27: 493-497.
- Caldecott, J.O., Jenkins, M.D., Johnson, T. and Groombridge, B. (1994). *Priorities for Conserving Global Species Richness and Endemism*. In World Conservation Monitoring Center, Biodiversity Series No. 3 (Collins, N.M. ed.). World Conservation Press, Cambridge, UK. 17
- Carter, G. T. (2011). Natural products and pharma: strategic changes spur new opportunities. *Natural Products Reports* **28**: 1783-1789.
- Castiglioni A. (1985). A History of Medicine. New York, NY, USA: Jason Aronson.
- Chandrasena, J.P.C. (1955). The Chemistry and Pharmacology of Ceylon and Indian Plants. H & C Press, Colombo.
- Cragg, G. M., Katz, F., Newman, D. J. and Rosenthal, J. (2012). The impact of the United Nations Convention on Biological Diversity on natural products research. *Natural Product Reports* 29: 1407-1423.
- Cragg, G. M. and Newman, D. J. (2013). Natural products: a continuing source of novel drug leads. *Biochimica et. Biophysica Acta* **1830** (6): 3670-3695.
- Craig, J. W., Chang, F. Y., Kim, J. H., Obiajulu, S. C. and Brady, S. F. (2010). Expanding smallmolecule metagenomics through parallel screening of broad-host-range cosmid environmental DNA libraries in diverse proteobacteria. Applied Environmental Microbiology 76: 1633-1641.
- Harvey, A. L. (2008). Natural products in drug discovery. *Drug Discovery Today* **13**: 894-901.
- Harvey, A. L. and Gericke, N. (2011). In *Biodiversity* Ch. 15, Intech, (ed. Pavlinov, I. Y.), Pp 323-338.
- Dassanayake, M.D. and Fosberg, F.R. (1980-2000). *A Revised Handbook to the flora of Ceylon*, Amerind Publishers, New Delhi, Vol. 1-14.
- Dhanabalasingham, B., Karunaratne, V., Gunatilaka, A.A.L., Tezuka, Y. and Kikuchi, T. (1996). Biogenetically important quinonemethides and other constituents of *Salacia reticulata*. *Phytochemistry* **42**:1377-1385.

- Dias, D. A., Urban, S. and Roessner, U. A. (2012). Historical overview of natural products in drug discovery. *Metabolites* 2: 303-333.
- Drewry, D. H. and Macarron, R. (2010). Enhancements of screening collections to address areas of unmet medical need: an industry perspective. *Current Opinion in Chemical Biology* **14** (3): 289–298.
- Gunasekera, S. P. and Sultanbawa, M. U. S. (1973). Four new friedelane carboxylic acids from the bark of *Trichadenia zeylanica* Thw. (Flacourtiaceae). *Tetrahedron Letters* **14**(30): 2837-2840.
- Gunaherath, G. M. K. B. and Gunatilaka, A. A. L. (1983). Studies on terpenoids and steroids. Part
  3. Structure and synthesis of a new phenolic D: A-friedo-24-noroleanane triterpenoid, zeylasterone, from kokoona zeylanica. Journal of Chemical Society Perkin Transactions 1: 2845-2850.
- Gunasekera, S. P., Sotheeswaran, S. and Sultanbawa, M. U. S. (1981). Two new xanthones, calozeyloxanthone and zeyloxanthonone, from *Calophyllum zeylanicum* (Guttiferae). *Journal of Chemical Society Perkin Transactions* 1: 1831-1835.
- Gunatilaka, A. A. L., Nanayakkara, N. P. D. and Sultanbawa, M. U. S. (1983). Studies on terpenoids and steroids. Part 1. Structures of six novel 27-hydroxy and 6β-hydroxy di- and trioxygenated D: A-friedo-oleanane triterpenes from Kokoona zeylanica. Journal of Chemical Society Perkin Transactions 1: 2459-2469.
- Gunatilaka A. A. L. (1999). The Alkaloids: Chemistry and Biology. Academic press, New York, USA, Pp 1 101.
- Gunatilaka, A. A. L., Nanayakkara, N. P. D. (1984). Studies on terpenoids and steroids-2: Structures of two new tri- and tetra-oxygenated D:A-friedo-oleanan triterpenes from kokoona zeylanica. *Tetrahedron* **40** (4): 805-809.
- Harvey, A. L. (2008). Natural products in drug discovery. *Drug Discovery Today* **13**: 894-901.
- Harvey, A. L. and Gericke, N. (2011). In Biodiversity Ch. 15, Intech, (ed. Pavlinov, I. Y.) Pp 323-338.
- Hert, J., Irwin, J. J., Laggner, C., Keiser, M. J. and Shoichet, B. K. (2009). Quantifying biogenic bias in screening libraries. *Nature Chemical Biology* **5**: 479-483.
- Hewage, C.M., Bandara, K.A.N.P., Karunaratne, V., Bandara, B.M.R. and Wijesundara, D.S.A. 1997. Insecticidal activity of some medicinal plants of Sri Lanka. *Journal of National Science Council* **25**(3):141-150.
- Hewage, C.M., Bandara, B.M.R., Karunaratne, V., Wannigama, G.P., Pinto, M.R.M. and Wijesundara, D.S.A. 1998. Antibacterial activity of some medicinal plants of Sri Lanka. *J. National Science Council* **26**(1): 27-34.

- Jayalal, U., Wolseley, P., Wijesundra, S., Karunaratne, V. (2008). Macrolichen diversity as an indicator of environmental changes in montane forest of Horton Plains National Park, Sri Lanka. The 6<sup>th</sup> IAL symposium and annual ABLS meetings, California, USA. Pp 140.
- Jayalal, R.G.U., Wolseley, P.A., Gueidan, C., Aptroot, A., Wijesundara D.S.A. and Karunaratne, V. (2012). *Anzia mahaeliyensis* and *Anzia flavotenuis*, two new species from Sri Lanka. *The Lichenologist* **44** (3): 381-389.
- Jayaweera, D.M.A. (1980-82). Medicinal Plants used in Ceylon, Parts 1-5. University Press, Moratuwa, Sri Lanka.
- Karunanayake, E. H., Welihinda, J., Sirimanne, S. R. and Adorai, G. S. (1984). Oral hypoglycaemic activity of some medicinal plants of Sri Lanka. *Journal of Ethnopharmacology* **11**(2): 223-231.
- Karunaratne, V., Bombuwala, K., kathirgamanathar, S. and Thadani, V. (2005). Lichens: A chemically important biota. *Journal of National Science Foundation Sri Lanka* **33**(3): 169-186.
- Karunaratne, V., Hoveyda, H.R. and Orvig, C. (1992). General method for the Synthesis of Trishydroxamic acids. *Tetrahedron Letters* 33: 1827-1830. Karunaratne, V., Bombuwela, K., Kathirgamanathar, S., Kumar, V., Karunaratne, D.N., Ranawana, K.B., Wijesundara, D.S.A., Weerasooriya, A. and De Silva, E.D. (2002). An association between the butterfly, *Talicada nyseus* and the lichen as evidenced from chemical studies. *Current Science* 83(6): 741-745.
- Kathirgamanathar, S., Ratnasooriya, W.D., Baekstrom, P., Andersen, R.J. and Karunaratne, V. (2006). Chemistry and bioactivity of physciaceae lichens: *Pyxine consocians* and *Heterodermia leucomelos*. *Pharmaceutical Biology* **44**: 217-220.
- Kostermans, A.J.G.H (1992). A Handbook of the Dipterocarpaceae of Sri Lanka, Wildlife Heritage of Sri Lanka, Colombo, Pp 8-18.
- Kumar, V., Karunaratne, V. and Meegalla, M.R.S.K. (1989). 1-[2',4'-Dihydroxy-3',5' Di(3"-Methylbut-2"-Enyl)-6'-Methoxy] Phenylethanone from *Acronychia pedunculata* root bark. *Phytochemistry* **28**: 1278-1279.
- Lange, B. M. and Ahkami, A. (2013). Metabolic engineering of plant monoterpenes, sesquiterpenes and diterpenes current status and future opportunities. *Plant Biotechnology Journal* **11**: 169-196.
- Li, Y., Wang, Y., Su, L.,Li, L. Zang, Y. (2013). Exploring potential chemical markers by metabolomics method for studying the processing mechanism of traditional Chinese medicine using RPLC-Q-TOF/MS: a case study of Radix Aconti. *Chemistry Central Journal* 7: 36-45.
- Long, D. G. and Rubasinghe, S.C.K. (2014). Liverworts and Hortnworts of Sri Lanka:a revised

- checklist. Ceylon Journal of Science (Bio. Sci.) **43**(1): 1-36.
- Mao, Q., Yang, J., Cui, X. M., Li, J. J., Qi, Y. T., Zhang, P. H. and Wang, Q. (2012). Taget separation of a new anti-tumour sapoin and metabolic profiling of leaves of Panax notoginseng by liquid chromatography with electrospray ionization quadrupole time-of-flight mass spectrometry. *Journal of Pharmaceutical biomedical* Analysis **59**: 67-77.
- Mishra, B. B. and Tiwari, V. K. (2011). Natural products: an evolving role in future drug discovery. *European Journal of Medicinal Chemistry* **46**: 4769-4807.
- MOE (2012). The National Red List 2012 of Sri Lanka; conservation Status of Fauna and Flora. Ministry of Environment, Colombo, Sri Lanka viii + 476 pp.
- Munasinghe J.T.C., Seneviratne C.K., Thabrew M.I. and Abeysekera A.M. (2001). Antiradical and antilipoperoxidative effects of some plant extracts used by Sri Lankan traditional medical practitioners for cardioprotection. *Phytotherapy Research* **15**(6): 519-523.
- Myers, N., Mittermeier, R. A., Mittermeier, C. G., da Fonseca, G. A. B. and Kent, J. (2000). Biodiversity hotspots for conservation priorities. *Nature* **403**: 853-858.
- Newman, D. J., Cragg, G. M. and Snader, K. M. (2000). The influence of natural products upon drug discovery. *Natural Products Reports* 17: 215-234.
- Newman, D. J. and Cragg, G. M. Natural products as sources of new drugs over the 30 years from 1981 to 2010. *Journal of Natural Products* **75**: 311-335 (2012).
- Orange, A., Wolseley, P., Karunaratne, V. and Bombuwela, K. (2001). Two leprarioid lichens new to Sri Lanka. *Bibliotheca Lichenologica* **78**: 327-333.
- Petronelli, A., Pannitteri, G. and Testa U. (2009). Triterpenoids as new promising anticancer drugs. *Anticancer Drugs* **20** (10): 880-892.
- Pinto, M. M., Sousa, M. E. and Nascimento, M. S. (2005). Xanthone derivatives: new insights in biological activities. *Current Medicinal Chemistry* **12** (21): 2517-2538.
- Puvanendran, S., Manoranjan, T., Wickramasinghe, A., Karunaratne, D. N., Kumar, V., Wijesundara, S., Carr, G., Andersen, R. and Karunaratne, V. (2010). Alkaloids from *Xylopia parvifolia* and *Xylopia nigricans* (Annonaceae). *Journal of the National Science Foundation of Sri Lanka* **38** (1), 75-76.
- Quinn, R. J. (2012). In Chemical Genomics (ed. Fu, H.) 87-98 (Cambridge Univ. Press.
- Ratnayake, R., Bandara, R., Wijesundara, S., Carr, G., Andersen, R. J. and Karunaratne, V. (2008). Four new butanolide derivatives from *Hortonia*, a

- genus endemic to Sri Lanka. *Journal of Chemical Research* **3**: 134-136.
- Ratnayake, R., Jayasinghe, S., Bandara, B. M., Andersen, R. and Karunaratne, V. (2009). Complete 2D NMR assignment and antifungal activity of ishwarane isolated from *Hortonia*, a genus endemic to Sri Lanka. *Journal of the National Science Foundation of Sri Lanka* **36**(1): 109-112.
- Rishton, G. M. (2008). Natural products as a robust source of new drugs and drug leads: past successes and present day issues. *American Journal of Cardiology* **101**: 43D-49D.
- Ruklani, N. C. S. and Rubasinghe, S. C. K. (2013). A Preliminary Survey of Bryophytes in the central Province of Sri Lanka. *Ceylon Journal of Science* (*Bio. Sci.*) **42**(1): 67-72.
- Sharma, V. and Sarkar, I. N. (2013). Leveraging biodiversity knowledge for potential phytotherapeutic applications. *Journal of American Medical Informatics Association* **20**: 668-679.
- Siriwardena, A., Wijesundara, D.S.A. and Karunaratne, V. (2015). A review of biologically active compounds isolated from Sri Lankan plants. *Journal of National Science Foundation* **43**(1): 11-33.
- Somesekaram, T., Perera, M.P., de Silva, M.B.G. and Godellawatta, H. (1997). In *Arjuna's Atlas of Sri Lanka*, Arjuna Consulting Co Ltd, Sri Lanka.
- Stevens, D. C., Conway, K. R., Pearce, N., Villegas-Peñaranda, L. R., Garza, A. G. and Boddy, C. N. (2013). Alternative sigma factor over-expression enables heterologous expression of a type II polyketide biosynthetic pathway in Escherichia coli. *PLoS ONE* **8**:e64858.
- Tezuka, Y., Kikuchi, T., Dhanabalasingham, B., Karunaratne, V. and Gunatilaka, A.A.L. (1993). Salacenonal: A novel Nortriterpenoid aldehyde of biogenetic significance from *Salacia reticulata*. *Natural Product Letters* 3(4): 273-276.
- Tezuka, Y., Kikuchi, T., Dhanabalasingham, B., Karunaratne, V. and Gunatilaka, A.A.L. (1994). Studies on Terpenoids and Steroids, Part 25. Complete <sup>1</sup>H and <sup>13</sup>C NMR assignments of Salaciquinone, A new 7-Oxo-Quinonemethide dinortriterpenoid from *Salacia reticulata*. *Journal of Natural Products* 57(2): 270-276. Thadhani,

- V.M., Choudhary, I. and Karunaratne, V. (2012). Antimicrobial activity and cytotoxicity of lichen metabolites. *Journal of National Science Foundation of Sri Lanka* **40**(1): 43-48. Thorne R. F. (2002). How many species of seed plants are there? *Taxon* **51**: 511-522.
- Trimen, H. (1893-1931). *Handbook to the Flora of Ceylon*, Dulau & Co., London.
- Wall, M. E., Wani M. C., Brown, D. M., Fullas, F., Olwald, J. B., Josephson, F. F., Thornton, N. M., Pezzuto, J. M., Beecher, C. W., Farnsworth, N. R., Cordell, G. A. and Kinghorn, A. D. (1996). Effect of tannins on screening of plant extracts for enzyme inhibitory activity and techniques for their removal. *Phytomedicine* 3: 281-285.
- Wang, Y., Chen, S. and Yu, O. (2011). Metabolic engineering of flavonoids in plants and microorganisms. *Applied Microbiological Biotechnology* **91**: 949-956.
- Weerakoon, G., Wijeyaratne, S.C., Wolseley, P. A., Plata, E. R., Lücking, R. H. Lumbsch, T. (2012). Six new species of Graphidaceae from Sri Lanka. *The Bryologist* **115** (1):74–83.
- Weerasinghe, A., Puvenendran, S., Wickramasinghe, A., Karunaratne, D. N., Wijesundara, S. Karunaratne, V. (2013). Potent bioactivities of the endemic Annonaceae heightens its dire conservation status. *Journal of the National Science Foundation of Sri Lanka* **41**(4): 345-350.
- Wermuth, C. G. (2003). The Practice of Medicinal Chemistry. Amsterdam, the Netherlands: Academic.
- Youns, M., Hoheisel, J.D. and Efferth, T. (2010). Toxicogenomics for the prediction of toxicity related to herbs from traditional Chinese medicine. *Planta Medica* **76**: 2019-2025.
- Zhong, G. S. and Wan, F. (1999). An outline on the early pharmaceutical development before Galen. *Chinese Journal of Medical History* **29**: 178-182.