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Alkaloids of Some Plants of Sri Lanka—Chemistry and Pharmacology*

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Abstract : Studies on alkaloids in some plants of Sri Lanka are reviewed with special reference to chemical and biosynthetic aspects. Plant species investigated are grouped into families, a short description of the alkaloid types encountered in a family is given followed by a brief botanical description of the plant(s) studied. Where uses of these plants in indigenous and/or western medicine have been noted an attempt is made to relate these uses to the known pharmacology of their constituent alkaloids.

CONTENTS

*Based on a lecture delivered at a Workshop on Phytochemical, Pharmacological and Microbiological screening of local plants held as a prelude to the 3rd Asian Symposium on Medicinal Plants and Spices, Sri Lanka, Jan.—Feb. 1977.

1. General Introduction

Thanks to its geographical situation and climatic conditions, Sri Lanka has an abundant flora. From a total of 3368 flowering plant species, 830 are reported to be endemic to the country[1,2,3,4,11,164] and of this total around 750 species are claimed to have uses in the indigenous system of medicine.[2,3] A good number of local plants are also used as sources of drugs in Western medical practice. Distribution of these medicinal and/or drug-producing plants of Sri Lanka among the pteridophytes, gymnosperms and angiosperms has been presented by Abeywickrema[3] and is summarised in Table 1. Some of these plants owe their medicinal activity to the alkaloids contained in them.

TABLE 1. Distribution of Medicinal and/or Drug-producing Plants among Pteridophytes, Gymnosperms and Angiosperms in Sri Lanka.

		No. of species used as medicinal drugs			
		Total	Indigenous	Introduced	Endemic
Pteridophytes		5	5	0	0
Gymnosperms		1	1	0	0
Angiosperms	Monocots	125	100	22	3
	Dicots	619	564	44	11
TOTAL :		750	670	66	14

Amongst the natural products, alkaloids comprise the largest single class of secondary plant metabolites. Up-to-date, a total of about 6,500 alkaloids are known and a new alkaloid is discovered at the rate of about one per day. Since they display dramatic physiological activities, alkaloids find wide applications in medicine; some alkaloids are toxic to man and animals. There is no completely satisfactory definition of the term alkaloid. However, according to Harbourne,[77] alkaloids generally include "those basic substances which contain one or more nitrogen atoms, usually in combination as part of a cyclic system".

Alkaloids are widely distributed in the plant kingdom. Hegnauer's estimate of 15 to 20% for the distribution of alkaloids in vascular plants[79] seems to be somewhat high. Recent phytochemical screening programmes have however, suggested 10% to be a more logical estimate representing alkaloid-yielding plant species.[45] Alkaloids occur mostly in higher plants belonging to angiosperm families and are absent or infrequent in the gymnosperms, ferns, mosses and lower plants. However, even in the angiosperm families, alkaloid distribution is very uneven and certain families are characteristically devoid of them. Angiosperm families of Sri Lanka which are particularly rich in alkaloids are presented in Table 2, which also shows the number of genera and species of each of these families found here in Sri Lanka.

In addition, Table 2 gives the number of these species endemic to the country and the number employed in indigenous medicine.[3] Distribution of the endemic plant species in various districts of Sri Lanka has been listed by Sultanbawa and Weerasekara.[156]

TABLE 2. Important alkaloid bearing and medicinally useful plant families of Sri Lanka.

Family	No. reported from Sri Lanka			No. of species used in medicine	
	Genera	Species	Endemic	Non-endemic	Endemic
Amaryllidaceae*,†	4	10	—	5	—
Annonaceae†	17	45	18	2	—
Apocynaceae†	23	31	8	13	2
Compositae	60	115	20	21	1
Convolvulaceae	16	57	3	17	1
Cucurbitaceae	18	33	2	22	—
Euphorbiaceae	46	149	47	39	—
Flacourtiaceae	10	16	10	1	3‡
Graminae*	122	295	21	35	—
Lauraceae†	10	33	23	6	—
Leguminosae	85	283	12	88	—
Liliaceae*	14	18	2	5	—
Loganiaceae†	5	18	10	3	1
Malvaceae	13	44	2	21	—
Menispermaceae†	11	13	—	12	—
Moraceae	11	34	5	20	—
Rubiaceae†	50	158	74	23	1
Rutaceae†	18	40	4	14	—
Solanaceae†	9	29	—	11	—
Verbenaceae	16	36	3	14	—
Zingiberaceae*	12	38	17	13	—

*Monocotyledons †Major alkaloid bearing families

‡According to Attygalle[67] one endemic species, *viz*, *Litsea longifolia* (Nees) Alston is used in native medicine.

Research work carried out on the plants of Sri Lanka in the field of alkaloids, their chemistry and pharmacology are found scattered in the literature. The purpose of this review article is, therefore, to attempt to bring these together and provide relevant information to the researcher exploring into these fields. The information presented here is limited only to the work on those plant species collected from Sri Lanka. The alkaloids occurring in the plant species found in Sri Lanka (not necessarily collected from Sri Lanka) and their pharmacology would, however, be the subject of a future presentation.

In this article, the plant species investigated for alkaloids are grouped under their families and their applications in indigenous medicine, their chemistry, pharmacology and where relevant, biosynthesis, have been considered. An attempt has also been made to relate the known pharmacology of these alkaloid bearing plants and/or their contained alkaloids to the use of these plants or the drugs derived from them in indigenous and/or western medical practices.

2. Surveys for Alkaloids

2.1. Introduction

Prior to undertaking any detailed investigations on a particular class of compounds, it is logical for the natural products investigator to make his selection of plants with the help of preliminary screening or survey programmes. Survey of plants for the occurrence of alkaloids has been made easy as tests for this class of compounds in plant extracts are simple and could be conducted rapidly by reasonably reliable methods.[50]

Two systematic surveys of Sri Lanka plants for alkaloids have been reported.

2.2. A Survey of the Endemic Annonaceae for Alkaloids

In 1973, Sultanbawa, Wannigama and their co-workers reported a general survey of the endemic Annonaceae for alkaloids.[99] In this study, crude basic fractions from leaves and twigs were subjected to Mayer's test[119] and *TLC* examination. The endemic species investigated included *Alphonsea coriacea* (Thwaites) Finet and Gagnep, *Desmos elegans* (Thwaites) Safford, *Enicosanthum acuminatum* (Thwaites) Airy-Shaw, *Sageraea thwaitesii* Hook f. and Thoms., *Xylopia championii* Hook f. and Thoms., and *X. nigricans* Hook f. and Thoms. The following non-endemic species were also tested ; *Cyathocalyx zeylanicum* Champ. ex Hook f. and Thoms., *Miliusa indica* Leschen ex A.DC. and *Uvaria semecarpifolia* Hook. f. and Thoms. All these 9 species had shown the presence of alkaloids and authors have undertaken a fuller investigation into the alkaloids present in the endemic Annonaceae.[99]

2.3. A Screening of 464 Sri Lanka Plants for Alkaloids

An extensive survey of Sri Lanka plants for the occurrence of alkaloids has recently been reported.[157,158] In this study, 464 plant species including 170 endemic species have been investigated. Extracts obtained by 3 different procedures were tested for the presence of alkaloids by Mayer's reagent[119] and the approximate number of alkaloids in each extract determined by *TLC* analyses. The results obtained in this survey are summarised in Table 3. In this study, 128 new plant species including 59 endemics (distributed in 25 families) containing alkaloids have been uncovered.

TABLE 3. Summary of test results from the screening of 464 Sri Lanka plant species for alkaloids.

BOTANICAL COLLECTIONS			TEST RESULTS		
No. of families	Total	96	Meyer's test	No. tested	464
	Tropical	49		No. positive	91
No. of genera		314	Dragendorff (*TLC* method)	No. tested	417
				No. positive*	137
No. of species	Total	464	Iodoplatinate (*TLC* method)	No. tested	214
	Endemics	170		No. positive*	89
			No. positive†	Total	201
				Endemics	59
				New spp.	128

*Excludes doubtfully positive species

†By either Meyer's, Dragendorff or Iodoplatinate tests.

3. Alkaloids of Ancistrocladaceae

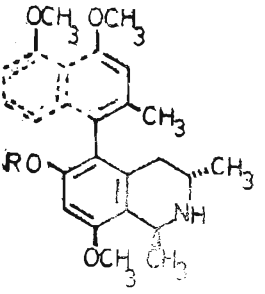
3.1. Introduction

The genus *Ancistrocladus* of the family Ancistrocladaceae has been recently investigated for alkaloids, and some unique isoquinoline alkaloids have been reported.[62,63,64,65,66] Almost all the alkaloids isolated contained a 1,2,3,4-tetrahydroisoquinoline moiety coupled to an oxygenated naphthalene at varying positions of the aromatic ring of the former. Unlike other isoquinoline alkaloids, *Ancistrocladus* alkaloids have a polyketide biogenesis.[63]

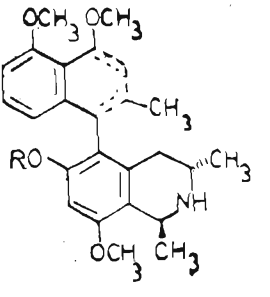
In Sri Lanka, the family Ancistrocladaceae is represented by a single genus containing only one species, *Ancistrocladus hamatus* (Cahl) Gilg.[1], which is endemic to the country.[11] It is a very strong creeper and in rural areas it is used to tie cattle, hence the Sinhala name, gona-wal.[12]

3.2. Alkaloids of *Ancistrocladus hamatus*

Govindachari's group in the course of their studies on isoquinoline alkaloids in plants belonging to the genus *Ancistrocladus*,[62,63,64,65,66] have investigated roots of *A. hamatus* obtained from Sri Lanka.[66] In addition to ancistrocladine (I) which has already been isolated from several members of this genus, a new alkaloid named hamatine (III) was also isolated from the Sri Lankan species. The two alkaloids were present to the extent of 0.50 and 0.06% respectively. It has been shown that the product derived from *O*-methylhamatine (IV) by dehydrogenation is enantiomeric with the isoquinoline made from *O*-methylancistrocladine (II) by the same process. This finding coupled with the *NMR* and *CD* (Circular Dichroism) data suggested ancistrocladine and hamatine to be isomeric with each other, the only difference being the relative orientation of the substituted naphthalene ring.



(I) : R = H
(II) ; R = CH_3

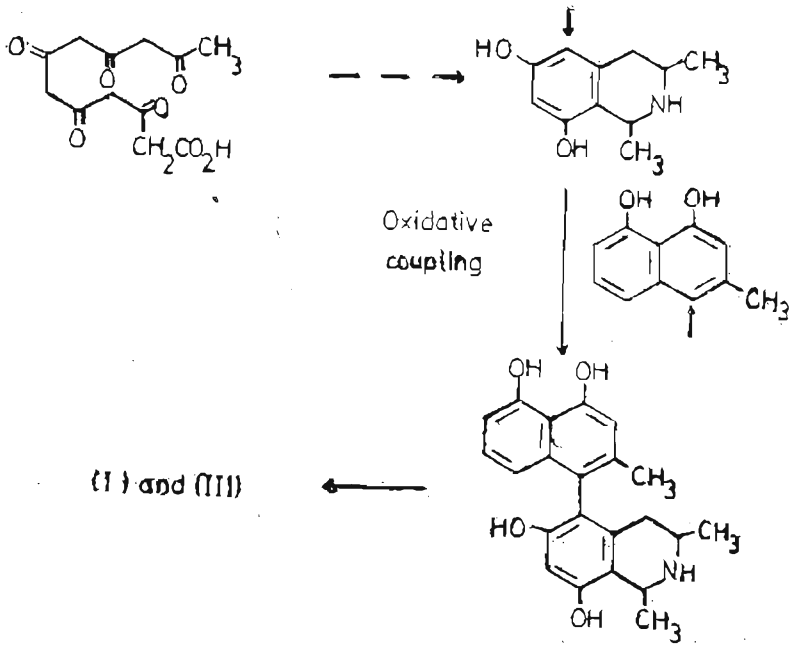


(III) ; R = H
(IV) ; R = CH_3

Although the 2 alkaloids from *A. hamatus* have not been subjected to any pharmacological evaluation, a related alkaloid ancistrocladidine from the Indian species *A. heyneanus* Wall. had shown spasmolytic activity on the isolated guinea pig ileum at a concentration of 5μg/ml, comparable with that of papaverine.

3.3. Biosynthesis of Hamatine and Ancistrocladine

Isoquinoline alkaloids are biogenetically derived from aromatic amino acids such as phenylalanine or tyrosine.[13] However, the rare oxygenation pattern in *Ancistrocladus* alkaloids suggested that the tetrahydroisoquinoline moiety in these has a polyketide origin.[63] Subsequent oxidative coupling of the tetrahydroisoquinoline with an oxygenated naphthalene accounts for the formation of all known *Ancistrocladus* alkaloids. Biogenetic origin of these alkaloids is given in Scheme 1. This polyketide biogenetic hypothesis is supported by the isolation of alkaloids coupled at other positions of the benzene ring in the tetrahydroisoquinoline moiety.[65]



Scheme 1. Biosynthetic origin of Hamatine and Ancistrocladine.

4. Alkaloids of Apocynaceae

4.1. Introduction

Botanically, the Apocynaceae or the dog-bane family is divided into 3 sub-families: Cerberoideae, Echitoideae (Apocynoideae) and Plumericideae. The plants of this family contain well over 250 alkaloids, majority having an isoprenoid origin. For example, the first two sub-families produce steroidal alkaloids, whereas the sub-family Plumerioideae contains indole alkaloids derived from the amino-acid tryptophan and a terpenoid moiety. The steroidal alkaloids are of the types aminosteroids and aminoglycosteroids. However, the genus *Holarrhena* in the sub-family Plumerioideae is an exception as the plants of this genus bear only steroidal alkaloids and as they do not contain indole alkaloids of this sub-family.[167]

The family Apocynaceae is well known for skynanthine-type monoterpene alkaloids, pregnane-type steroidal alkaloids and complex indole alkaloids. A number of these alkaloids bear pharmacological activity and have become indispensable drugs in western medicine ; e.g. complex indole alkaloids of *Rauwolfia* have anti-hypertensive action[139] and the *bis*-indole alkaloids of *Catharanthus roseus* are unique in their antileukemic activity[118] (see below).

4.2. *Holarrhena* Alkaloids

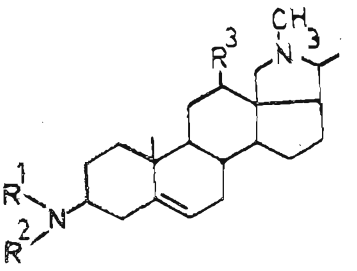
The genus *Holarrhena* in Sri Lanka contains a single species *H. mitis* (Vahl) R. Br. ex Roen and Schult. (*Sinh.*— Kiriwalla, Kirimawaran ; *Tam.*- Vellupalai) which is endemic to this country.[1,11] The bark juice of this plant under the name of Kalindu is reputed in native medicine as a remedy for dysentery and fevers.[95] Alkaloids of *H. mitis* had been the subject of a series of papers by Wannigama, Goutarel and their co-workers.[8,19,27,89,101,102] Alkaloids isolated from various parts of this plant by these workers are presented in Table 4. In addition to the isolation of conessine (V) from the bark of *H. mitis* during their very early investigations, Wannigama and Bhavanandan obtained evidence for the occurrence of *N*-demethylated conessines.[19] Further investigations had confirmed the occurrence of a large number of steroidal alkaloids in the bark extracts of this plant. The seeds of *H. mitis* have been shown to be devoid of mitiphylline (XV). Isolation of triacanthine (XIV) from these seeds marks the first occurrence of this base in any seed. The alkaloidal extract of the fruit pericarp was shown to constitute only of triacanthine.

TABLE 4. Alkaloids of *H. mitis*.

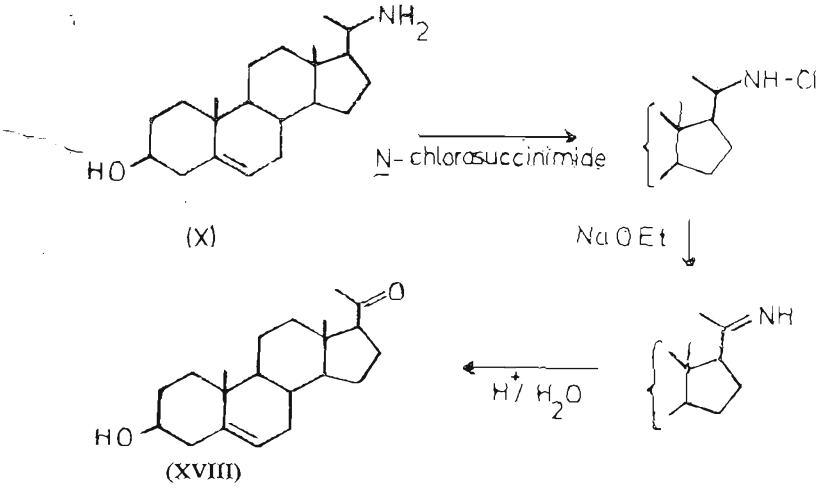
Plant part	Alkaloid(s) isolated	Yield (%)	Ref.
Bark	conessine (V)	—	19
Bark	conessine (V)	0.098	27
	iso-conessimine (VI)	0.098	27
	holadienmine (IX)	0.013	27
	conkurchine (XIII)	0.020	27
	holarrhenine (VII)	0.026	27
	holafebrine (X)	0.098	27
	holarrhimine (XI)	0.098	27
	N-3-methyl-holarrhimine (XII)	0.098	
Leaves	mitiphylline (XV)	[40(65]*†	89, 102
	N-desmethylmitiphylline (XVI)	[9(10)*†	89, 102
	triacanthine (XIV)	[45(20)*†	89, 102
Seeds	triacanthine (XIV)	0.080	101
	conamine (VIII)	0.360	101
	conessine (V)	0.160	101
	iso-conessimine (VI)	0.016	101
Fruits (pericarp)	triacanthine (XIV)	0.400	101

*Ref. 89.
†Represented as percentage of the total bases.

TABLE 5. Some pregnane type steroidal alkaloids of *H. mitis*.

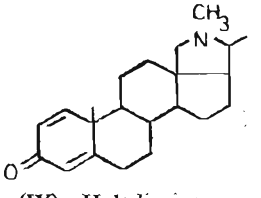


		R^1	R^2	R^3
Conessine	(V)	CH_3	CH_3	H
Iso-conessimine	(VI)	CH_3	H	H
Holarrhenine	(VII)	CH_3	CH_3	OH
Conamine	(VIII)	H	H	H

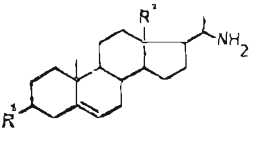


(X) (XVIII)

Scheme 2. Chemical transformation of Holafebrine to Pregnenolone.

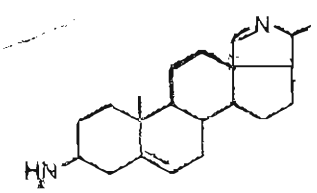


(IX) Holadienine

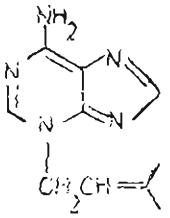


		R^1	R^2
(X)	Holafebrine	OH	CH_3
(XI)	Holarrhimine	NH_2	CH_2OH
(XII)	*N*-3-Methyl-holarrhimine	$NHCH_3$	CH_2OH

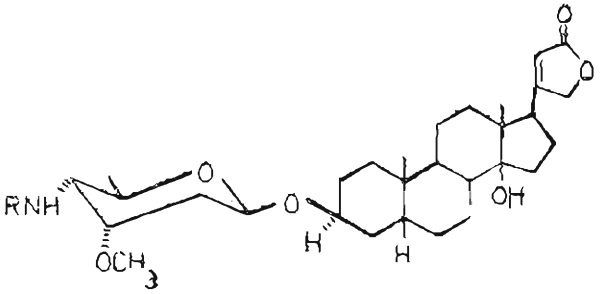
Much attention has been focussed on the steroidal alkaloids of *Holarrhena* spp. with the intention of economic exploitation of these in the synthesis of valuable steroidal hormones.[61] Conversion of holarfebrine (X), an alkaloid of Sri Lankan *H. mitis*, to pregnenolone (XVIII) which involves a series of simple chemical transformations is depicted in Scheme 2.



(XIII) Conkurchine



(XIV) Triacanthine



Mitiphylline	(XV)	R = CH_3
N-Demethylmitiphylline	(XVI)	R = H
N-Demethyl-*N*-acetylmitiphylline	(XVII)	R = $COCH_3$

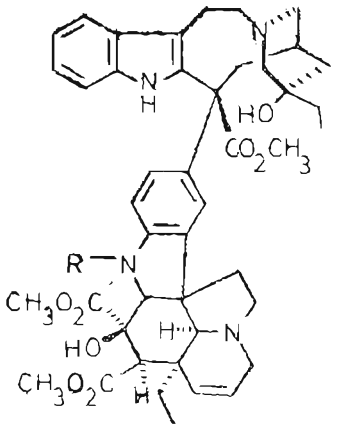
4.3. *Catharanthus* Alkaloids

The genus *Catharanthus* is known to produce some 72 alkaloids,[162] most of which are of complex indole type. A few of these are pharmacologically active and have medicinal applications. Of the pharmaceutically important alkaloids, vincaleukoblastine (VLB) also called vinblastine (XIX) and leurocristine (LCR) also known as vincristine (XX) have been employed in the treatment of leukaemia in children.[161] Ajmalicine (AJM) (XXI) and vincamine (VIC) (XXII) are two other useful alkaloids reported from *Catharanthus* species.[46]

In Sri Lanka, the genus *Catharanthus* has two species, *C. roseus* (L.) G. Don and *C. pusillus* (Murr.) G. Don.[1] *C. roseus* (*Sinh.*—Mini-mal; *Tam.*— Patti-poo, *Eng.*— Madagascar Periwinkle) incorrectly called *Vinca rosea* or *Lochnera rosea* is a perennial herb or subshrub and is found commonly as a weed in the dry and in the wet zones at low elevations, especially on sandy soil and in the coastal habitats. Three different forms of *C. roseus* have been reported.[85] *C. pusillus* is an annual herb indigenous to Sri Lanka and India. In Sri Lanka, it is a rather rare weed on cultivated land and has been recorded exclusively from Batticaloa and Jaffna districts.[107]

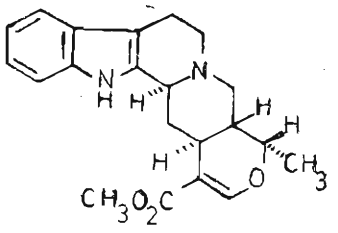
C. roseus, in the form of a tea, is used in folk medicine as a remedy for diabetes and an infusion of leaves under the name of Vincalin is sold in the U.K. as a cure for the same ailment.[35] However, pharmacological studies have not confirmed this alleged hypoglycaemic activity.[47,162] The leaf-juice is also reported to be used as an application for wasp stings.[35]

The two pharmaceutically important alkaloids VLB and VCR have been obtained from *C. roseus*. Although the synthesis of both these alkaloids[130] and the chemical transformation of the more abundant VLB to more potent antileukaemic alkaloid VCR is known, *C. roseus* still remains to be the main source of this valuable alkaloid.[46] Therefore, this plant is at present uprooted and exported by local agents to drug manufacturers in Europe for the extraction of these alkaloids.[9] Realisation of the disadvantages of this practice had prompted investigation into the feasibility of extracting these alkaloids from *C. roseus* (and *C. pusillus*) with locally available solvents and facilities with the hope of obtaining better returns to the country from this non-traditional export.[70,152] This work has led to 2 important findings, *viz.* the possibility of harvesting the leaves for extraction at periodic intervals and the reduction in cost of freight by exporting the crude alkaloidal extract instead of the dried plant material. This study has also shown that the processing of crude alkaloidal mixture from *C. pusillus* for VLB and VCR would prove to be less difficult than that from *C. roseus*.

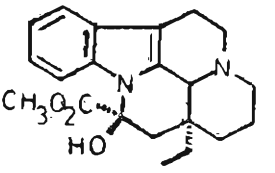


(XIX) Vincaleukoblastine (VLB) R = CH_3

(XX) Leurocristine (LCR)[1] R = CHO



(XXI) Ajmalicine (AJM)



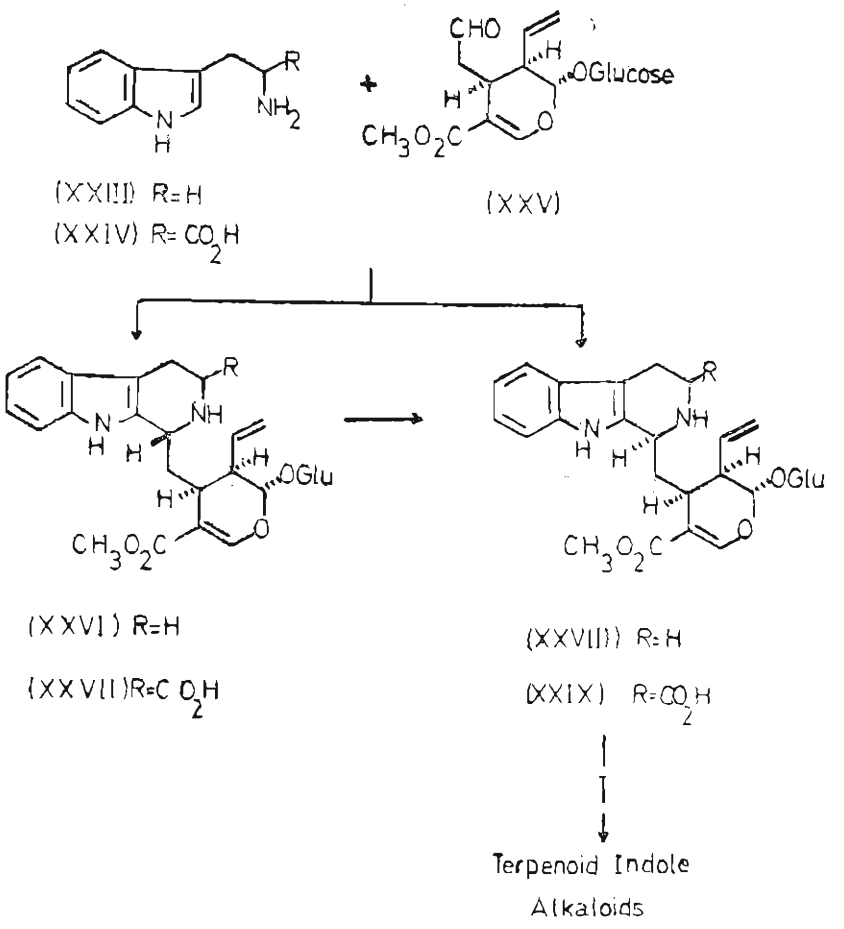
(XXII) Vincamine (VIC)

4.4. Pharmacology of *C. roseus* Alkaloids

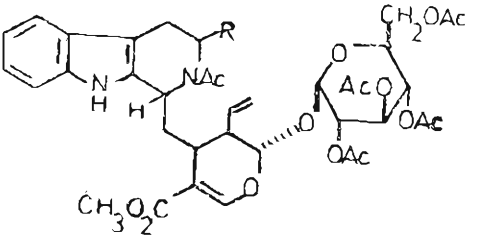
Two important drugs, Oncovin and Velban, produced by Eli-Lilly Co. in the U.S. contain the sulphates of VCR and VLB respectively.[114] Oncovin arrests mitosis in metaphase and is known to be effective in the treatment of leukaemia in children, lymphosarcoma, reticulum sarcoma, neuroblastena, Wilm's tumour and tumours of the breast, brain and lungs. Velban is a cytotoxic drug arresting cell growth in the metaphase and is effective in the treatment of Hodgkin's disease and other lymphomas and choriocarcinomas.

4.5. Screening for Biosynthetic Intermediates

The first step in the biosynthesis of terpenoid indole alkaloids, the major group of alkaloids in Apocynaceae (and Rubiaceae) involves condensation of tryptophan (XXIV) or its decarboxylation product, tryptamine (XXIII) with secologanin (XXV) having monoterpene origin (Scheme 3). Although a satisfactory biogenetic theory for terpenoid indole alkaloids has emerged from the results of extensive radioactive labelling experiments, de Silva and his co-workers had felt that a number of important questions in this theory had to be answered.[37] As a result they have approached the problem in order to (*a*) decide on chemical, structural and biosynthetic grounds, the compounds that can be probable intermediates, synthesise them and test them as precursors of the alkaloids, and (*b*) isolate the probable intermediates and test them as precursors. Thus, these workers have carried out a screening of indole alkaloid producing plants for the occurrence of the first nitrogenous monoterpenoid precursor.[36] In this survey, *Rauwolfia serpentina* (*Sinh.* - Ekaweriya, *Tam.*— Sorannamilbori), *Strychnos nux-vomica* (*Sinh.*—Kaduru ; *Tam.*—Yetti, Yettie-kottai) and a number of *Mitragyna* and *Vinca* species all of Apocynaceae and *Cinchona ledgeriana* of Rubiaceae have been tested for the presence of vincoside (XXIV) and 5α-carboxy-vincoside (XXVII). Although these two bio-intermediates have not been detected, macro-isolation techniques had revealed the presence of 5α-carboxystrictosidine (XXIX), an isomer of (XXVII), in all the plants tested and strictosidine (XXVIII), an isomer of (XXVI), only in *Rauwolfia*, *Vinca* and *Strychnos* species. Strictosidine (XXVIII) and its 5α-carboxy derivative (XXIX) have been isolated from *R. serpentina* and *S. nux-vomica* and were characterised as the pentaacetate (XXX) and the methoxycarbonyl pentaacetate (XXXI) respectively.



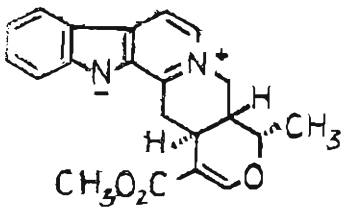
Scheme 3. Early stages in the Biosynthesis of Terpenoid Indole Alkaloids.



(XXX) R = H
(XXXI) R = CO_2CH_3

4.6. Screening for Ajmalicine

Ajmalicine (AJM, raubasine, δ-yohimbine) (XXI) is a medicinally important alkaloid occurring chiefly in *Rauwolfia* and *Catharanthus* species of plants. It has vasodilator, hypotensive and tranquillising properties.[24,35] The economic importance of AJM is evident from its demand in Europe which is *ca.* 5000 to 6000 kg per year and the price paid for it in the U.K. in the year 1973 which is £ 1.00 per g.[21] Although AJM is obtained in practice by chemical or catalytic reduction of serpentine (XXXII) which is the principal alkaloid in the above species, looking for natural sources for its extraction appeared attractive. Thus, a *TLC* survey of some local plants of Apocynaceae for AJM has been carried out.[7] The results had indicated absence of this alkaloid in *Alstonia macrophylla* (leaves), *Bassia acuminata* (leaves), *Cerbera manghas* (fruits), *Ochrosia bobornica* (twigs and fruits) and *Pajiantha dichotoma* (leaves), and occurrence of trace quantities of it in *Kopsia fruticosa* (leaves), *O. bobornica* (leaves) and *P. dichotoma* (twigs).



(XXXII)

4.7. Miscellaneous Studies

Wannigama and his co-workers in their studies on the plants of Apocynaceae have investigated fruits, leaves and twigs of the endemic species *Petchia ceylanica* (Wight) Livera of the sub-family Plumerioideae and found to contain indole alkaloids which were sensitive towards both light and air.[73]

5. Alkaloids of Asclepiadaceae

5.1. Introduction

In Sri Lanka, the family Asclepiadaceae is represented by 42 species belonging to 24 genera,[1] of which 6 species contained in 3 genera are reported to be endemic to the country.[1] The genera *Ceropegia, Gymnema* and *Tylophora* each contains two endemic species.* Several species of the genus *Tylophora* have folk-medicinal reputation. *T. asthmatica* Wight et. Arn. (Syn. *T. indica* (Burm.) Merr.), known as Indian Ipecacuanha is used in indigenous medicine as an emetic, expectorant and anti-dysenteric.[112,133]

*However, according to a recent revision[86], Sri Lanka has 37 species in 21 genera of which 3 species are endemic.

The genus *Tylophora* comprises some 50 species and phenanthrene-indolizidine alkaloids have been isolated from several species. *Tylophora* alkaloids have been the subject of a number of recent investigations as several of them have been reported to possess activity against l-1210 Leukaemia,[40,54,132] the position of the methoxy group been decisive for the anti-tumour potency.[141]

5.2. *Tylophora* alkaloids

Alkaloid screening on various parts of *T. asthmatica*, *T. cordifolia* Thwaites and *T. flava* Trim. (endemic species) collected in different localities of Sri Lanka has been reported by Phillipson *et al.*[126] In this study, the alkaloid contents were assessed in terms of percentage total crude alkaloid and by comparison of the colour intensities produced by Dragendorff reagent with the extracts and with known amounts of tylophorinine (XXXIV). Their results are summarised in Table 6. *T. cordifolia* and *T. flava* have not been examined previously for alkaloids.

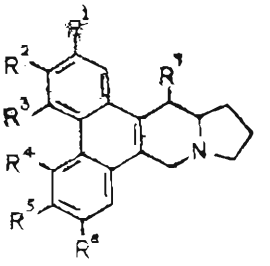
TABLE 6. Alkaloids of *T. cordifolia* and *T. flava* collected at Matara.

Species	Plant part	Alkaloids	
		%	*TLC* indication
T. cordifolia	leaves	0.17	tylophorinine + 1*
	stem	0.10	tylophorinine + 2*
	roots	0.16	tylophorinine + 3*
T. flava	leaves	0.15	tylophorinine (major) + tylophorine
	stem	0.12	tylophorinine + 4*
	roots	0.15	tylophorinine + 4*

*Number of unidentified alkaloids.

Eight samples of *T. asthmatica* collected from different localities were also screened by the same group of workers for the content of alkaloids.[126] *TLC* has indicated that in most samples the major alkaloid was tylophorinine (XXXIV) in at least one part of the plant, although in one leaf and two stem samples tylophorine (XXXIII) predominated. Their results contrasted with those previously reported for Indian plants[67,133] and implied that either there were some variations in alkaloid content from season to season or that different strains of *T. asthmatica* existed. However, these authors have suggested that further investigations would be required to verify these points. One similarity which did exist between the Indian and Sri Lankan materials was the very low yield of the antileukaemic alkaloid tylophorinine (XXXIV).[116]

TABLE 7. Alkaloids of *Tylophora* species.



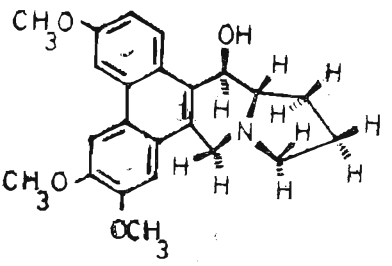
		R^1	R^2	R^3	R^4	R^5	R^6	R^7
Tylophorine	(XXXIII)	OCH_3	OCH_3	H	H	OCH_3	OCH_3	H
Tylophorinine	(XXXIV)	H	OCH_3	H	H	OCH_3	OCH_3	OH
Tylophorinidine	(XXXV)	H	OCH_3	H	H	OH	OCH_3	OH
Tylocrebine	(XXXVI)	OCH_3	OCH_3	H	OCH_3	OCH_3	H	H
Isotylocrebine	(XXXVII)	H	OCH_3	OCH_3	H	OCH_3	OCH_3	H

A detailed isolation work of a large batch of *T. asthmatica* was also carried out by Phillipson's group. Their results are given in Table 8 along with the alkaloids isolated from the Indian species by previous workers. A detailed analysis of the *NMR* spectrum of tylophorinine (XXXIV) has aided in the postulation of the preferred conformation of this alkaloid as given in (XXXVIII).

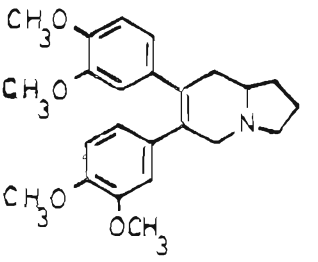
TABLE 8. Alkaloids of *T. asthmatica* from India and Sri Lanka.

Origin	Alkaloids isolated	Ref.
India	tylophorine (XXXIII), tylophorinine (XXXIV), tylophorinidine (XXXV), isotylocrebine (XXXVII), septicine (XXXIX), alkaloids A*, B* and C*	67, 68, 138
Sri Lanka	tylophorine (XXXIII), tylophorinine (XXXIV), tylophorinidine (XXXV)	126

*Unidentified alkaloids.



(XXXVIII)



(XXXIX)

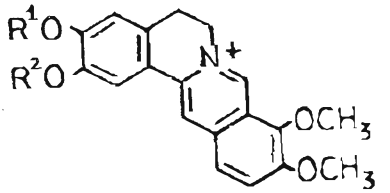
5.3. Pharmacology of *Tylophora* species

In addition to the above mentioned uses, *T. asthmatica* has been employed widely in folk medicine to cure asthma, one leaf per day being taken during a period of 6 days. Recent clinical trials by Shivpuri's group while proving the validity of its use in treating asthma has also shown it to be active against allergic rhinitis.[151] Preliminary clinical studies have also indicated that tylophorine (XXXIII) could be the active constituent in this plant.

6. Alkaloids of Berberidaceae

6.1. Introduction

The family Berberidaceae has yielded a total of more than 50 alkaloids, many of which are from the genera *Berberis, Leontice* and *Nandina*.[129] These alkaloids are of the types : aporphine, bisbenzylisoquinoline, oxoaporphine, protoberberinium and tetrahydroisoquinoline. The pharmacologically important protoberberinium alkaloid, berberine (XL) and its close relatives palmatine (XLI) and jatrorrhizine (XLII) are known to occur in *Berberis, Mahonia* and *Mandina* species.[129] These three alkaloids have a wide distribution in the plant kingdom and have been reported from Annonaceae (1 genus), Menispermaceae (8 genera), Ranunculaceae (5 genera), Papaveraceae (8 genera) and Rutaceae (3 genera).[80]



		R^1	R^2
Berberine	(XL)	$-CH_2-$	
Palmatine	(XLI)	CH_3	CH_3
Jatrorrhizine	(XLII)	H	CH_3

In Sri Lanka, the family Berberidaceae is represented by a single genus *Berberis* which has three species,[1] *B. tinctoria* Leschen, *B. wightiana* Schneider and *B. ceylanica* Schneider of which none is endemic. Several varieties of *Berberis* are known to yield a drug sold in Sri Lanka by the name of Rasadun (*Sanskrit*-Daruharidra).[10] Dried stem of *B. aristata* and dried rhizome and roots of other *Berberis* species are used both in native and modern medicine as febrifuge, carminative, bitter tonic and externally as dressing for indolent ulcers.[113] Rasadun is also used in indigenous medicine as a prophylactic for tetanus and is replaced nowadays by readily available *Coscinium fenestratum* (*Sinh.*—Veniwal, *Tam.*—Mara-manjal) of the family Menispermaceae.[10] Native medical practitioners, however, had a good reason though they may not have been aware of it, for using *C. fenestratum* as a substitute for *B. aristata* since the chemical analysis had revealed the presence of berberine (XL)[163] which is known to be the active principle in both species.

6.2. Alkaloids of *Berberis tinctoria*

B. tinctoria collected from Nuwara Eliya has recently been analysed by Shamma and his co-workers at the Pennsylvania State University. Their work has shown the presence of 12 alkaloids in the basic fraction of which two were new.[144] The alkaloids identified included simple tetrahydroisoquinolines, aporphines, oxoaporphines, protoberberinium salts and bisbenzylisoquinolines. A new protoberberinium having an unusual substitution pattern has been isolated and named lankamine.

6.3. Pharmacology of Berberine and *Berberis* species

The known pharmacology of *Berberis* species could be related to the presence of berberine in them. Berberine (XL) has been used internally as an anti-malarial, febrifuge, carminative and externally as dressing for indolent ulcers.[113] Pharmacological evaluation of several *Berberis* species, berberine and other plants known to contain this alkaloid and related alkaloids have been reported and an extensive review on alkaloids of the genus *Berberis* and their pharmacological action has recently appeared.[42] In addition to the above, some other properties are also observed with either *Berberis* species or berberine and a summary of these are presented in Table 9.

TABLE 9. Pharmacological action of *Berberis* spp. and berberine.

Sample tested	Pharmacological action	Ref.
B. amurensis roots	depression effects in cats and vasoconstriction in isolated rabbit ears	41
Berberis spp. and berberine	inhibition of respiration of dysentery bacteria	120
Berberine, palmatine and jatrorrhizine and extracts of *Coptis japonica* (Ranunculaceae).	effective against *Staphylococcus aureus*	75
B. lysinum roots	depressant action on isolated rabbit heart, acute fall in blood pressure	128
Berberine sulphate from *B. vulgaris* rhizome cortex	bactericidal on *Staphylococci*	98

7. Lauraceae Alkaloids

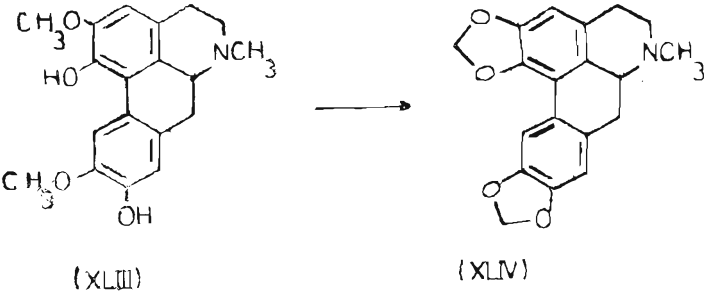
7.1. Introduction

This family of plants produces 5 basic types of alkaloids,[129] of which aporphines and their biogenetic progenitors, tetrahydrobenzylisoquinolines occupy a chief place. The dimeric alkaloids, bisaporphines and bisbenzylisoquinolines are also not uncommon in the plants of Lauraceae.

Lauraceae is one of the major alkaloid bearing families of Sri Lanka which has 23 endemic species out of the total of 33 species available.[11] In addition to 6 medicinally useful plants, this family contains the economically important cinnamon (*Cinnamomum zeylanicum* Bl.) plant.[170]

7.2. Alkaloids of *Neolitsea fuscata*

The genus *Neolitsea* of the family Lauraceae has 2 species in Sri Lanka,[1] *N. fuscata* (Thwaites) Alston and *N. Cassia* (L) Kosterman (= *N. involucrata* Alston) of which the former is endemic to the country.[11] Although *N. fuscata* has no reported medicinal uses, some other species of this genus have reputed medicinal activity.[96] A number of aporphine alkaloids have been isolated from plants of the genus *Neolitsea*.[87,117] Investigation of *N. fuscata* stem bark collected at Hakgala has shown the presence of aporphine base, isoboldine (XLIII) as the major alkaloid,[72] which represented the first report of its occurrence in this genus. Presence of isoboldine in this genus is significant since it could be regarded as the biosynthetic precursor[14] of neolitsine (XLIV), an aporphine base isolated from *N. pulchella*[87] (see Scheme 4).



(XLIII) (XLIV)

Scheme 4. Biosynthesis of Neolitsine from Isoboldine.

8 Alkaloids of Leguminosae

8.1. Introduction

Leguminosae, one of the largest plant families of Sri Lanka contains 283 species distributed in 85 genera,[1] of which 12 species are endemic to the island,[11] and 88 of these species find applications in indigenous medicine.[3] Although Leguminosae has no alkaloids characteristic of the family *Crotalaria* and *Erythrina*, two of the

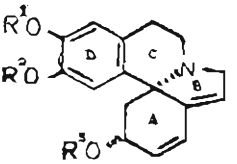
genera found in Sri Lanka contain alkaloids characteristic of these genera. The former genus bears alkaloids of pyrrolizidine type and the latter a spiroamine type (see below). The indole base, hypaphorine (LX) is recorded from a number of *Erythrina* and *Acacia* species.

8.2. *Erythrina* alkaloids

Four species of *Erythrina*, *viz. E. variegata* (= *E. indica*), *E. fusca*, *E. lithosperma* (= *E. subumbrans*), and *E. suberosa* have been reported from Sri Lanka.[164] Of these, various parts of *E. variegata* L. (*Sinh.*—era-badu, era-mudu ; *Tam.*—mullu murukku) are known to have an array of medicinal applications; the bark is used as an astringent and a febrifuge, in liver trouble and in epilepsy, as a nervine sedative an anti-asthmatic and as a collyrium in ophthalmia ; the leaves are used as a stomachic and diuretic and for relieving pain in joints[10] the juice is applied to syphilitic buboes. *E. variegata* is also used both as a lactogogue and an emmenagogue and is an ingredient in many decoctions.[10]

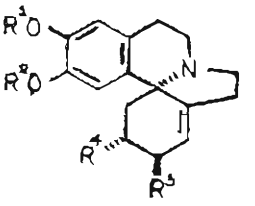
Up-to-date over 30 *Erythrina* alkaloids are known.[78] These are conveniently classified into 2 main structural types, those containing a conjugated diene in the A and B rings (Table 10) and those containing a $\Delta^{1,6}$ double bond in the ring A (Table11). A third group of alkaloids (LIV to LX) with various structural features includes α—and β—erythroidines and erythroculine (LIX), an *Erythrina* alkaloid isolated from *Coculus laurifolious* of the family Menispermaceae.[88] A number of other alkaloids not belonging to the *Erythrina* group have also been isolated from various *Erythrina* species. These are mainly the tetrahydrobenzyl-isoquinoline type (Table 12) and the indole type (eg. hypaphorine). Hypaphorine (LX) has been reported to be present in almost every *Erythrina* species studied and is probably ubiquitous.[78]

TABLE 10. Some *Erythrina* alkaloids of the dienoid type.



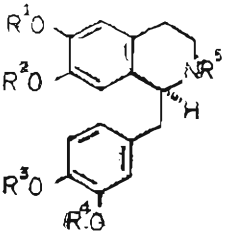
		R^1	R^2	R^3
Erysopine	(XLV)	H	H	CH_3
Erythraline	(XLVI)	—CH_2—		CH_3
Erysodine	(XLVII)	H	CH_3	CH_3
Erysotrine	(XLVIII)	CH_3	CH_3	CH_3
Erysonine	(XLIX)	H	CH_3	H

TABLE 11. Some *Erythrina* alkaloids of the alkenoid type.

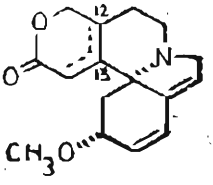


		R^1	R^2	R^3	R^4
Erythratinone	(L)	CH_3	CH_3	=O	OCH_3
3-Demethoxyerythratidinone	(LI)	CH_3	CH_3	=O	H
Erythratine	(LII)	—CH_2—		OH	OCH_3
Erythramine	(LIII)	—CH_2—		H	OCH_3

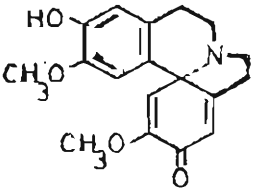
TABLE 12. Some tetrahydrobenzylisoquinoline alkaloids of *Erythrina* species.



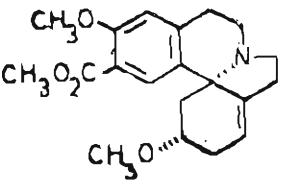
		R^1	R^2	R^3	R^4	R^5
N-Norprotosinomenine	(LIV)	H	CH_3	CH_3	H	H
Protosinomenine	(LV)	H	CH_3	CH_3	H	CH_3
N-Nororientaline		CH_3	H	H	CH_3	H
Orientaline		CH_3	H	H	CH_3	CH_3



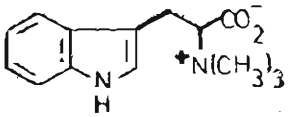
(LVI) Δ^{12}
(LVII) Δ^{13}



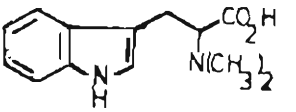
(LVIII)



(LIX)



(LX)



(LXI)

The pods of the Indian variety of *E. lithosperma* Blume has yielded 12 alkaloids[56] belonging to 3 classes, benzylisoquinoline, *Erythrina* and indole (see Table 13) including 2 biogenetically significant alkaloids (+) *N*-norprotosinomenine (LIV) and erysodienone (LVIII). Alkaloids present in other parts of the Indian plant are summarised in Table 14.[53,60] Investigation of the leaves of *E. lithosperma* Blume (smooth variety, a thorny variety is also available) collected in Sri Lanka has revealed the absence of the latter 2 alkaloids.[15,16] However, from the local species 2 new alkaloids structurally related to erysodienone, *viz.* erythratidinone (L) and 3-demethoxyerythratidinone (LI) have been isolated. Among the other alkaloids present were erythratine (XLVI) and erysotrine (XLVIII) (see Table 13).

Chemical analysis of the leaves of *E. fusca* Lour. from Sri Lanka has revealed the presence of only erysotrine (XLVIII) in isolable quantities.[15]

TABLE 13. Alkaloids of Indian and Sri Lankan varieties of *E. lithosperma* Blume.

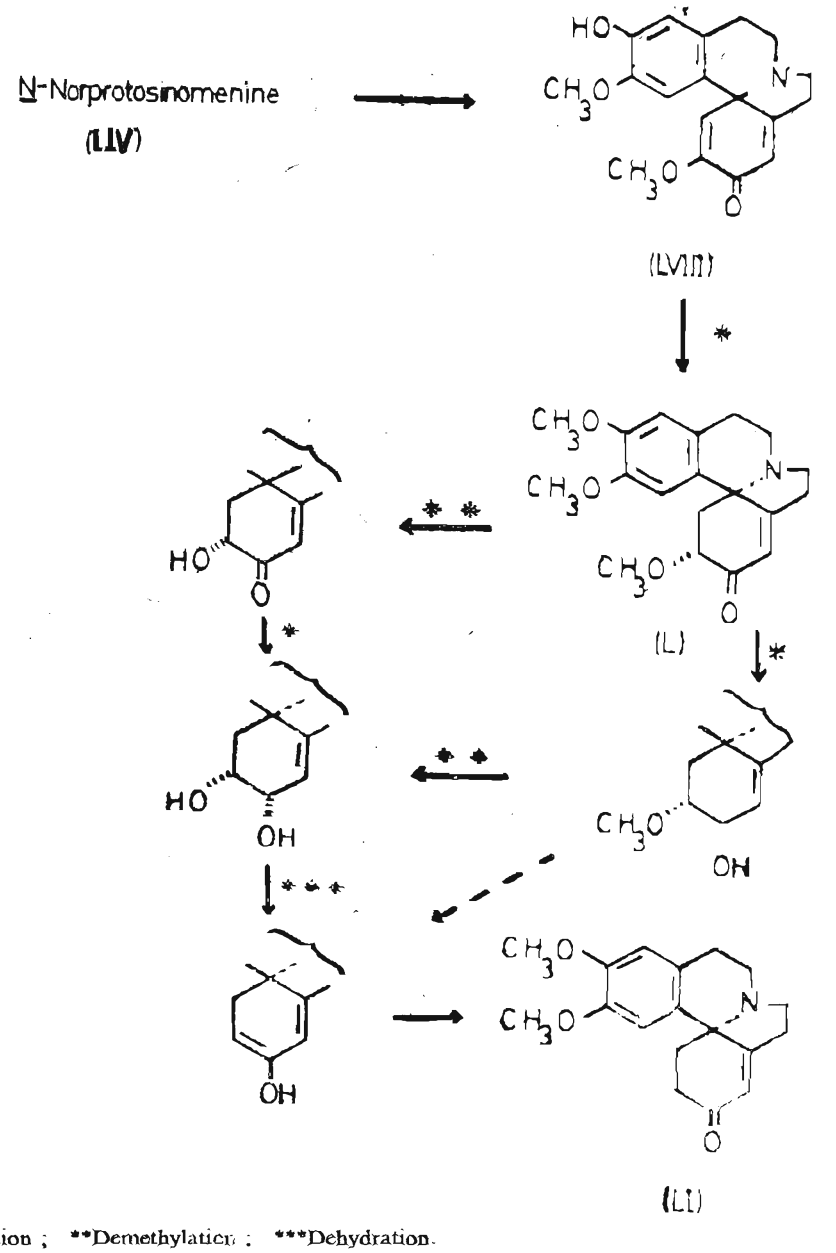
Alkaloid			Pods of Indian variety ($\times 10^{-5}$%)	leaves of Sri Lankan variety ($\times 10^{-2}$%)
Class	Identity			
Benzylisoquinoline	*N*-Norprotosinomenine	(LIV)	6.7	—
	Protosinomenine	(LV)	2.8	—
Erythrina	Erysodienone	(LVIII)	1.8	—
[Rearranged benzyl soquinoline or spiroamine]	Erythratidinone	(L)	—	12.0
	3-Demethoxyerythratidinone	(LI)	—	1.6
	Erysopine	(XLV)	4.8	—
	Erythraline	(XLVI)	5.8	Trace
	Erysodine	(XLVII)	7.6	—
	Erysotrine	(XLVIII)	5.2	22.0
	Erythratine	(LII)	1.6	—
	Erythramine	(LIII)	1.4	—
	β-Erythroidine	(LVI)	2.7	—
Indole	*N, N*-Dimethyltryptophan	(LXI)	3.7	—
	Hypaphorine	(LX)	1.9	—

TABLE 14. Alkaloids of various parts of the Indian *E. lithosperma*.

Plant part	Alkaloids present
Seeds	Erysodine (XLVII), Erysopine (XLV) Erysonine (XLIX)
Leaves	Erysopine (XLV)
Bark	Erysotrine (XLVIII), Erysodine (XLVII), Erythramine (LIII), Erythratine (LII)

8.3. Biosynthesis of 3-Demethoxyerythratidinone

3-Demethoxyerythratidinone (LI) is unique in the Sri Lankan variety of *E. lithosperma* in its lack of 3-methoxy group. This implies a late stage modification of the normal biosynthetic pathway.[15] Some plausible routes to (LI) from *N*-norprotosinomenine (LIV) *via* erysodienone (LVIII) is depicted in Scheme 5.



*Reduction ; **Demethylation ; ***Dehydration.

Scheme 5. Biosynthetic routes to 3-Demethoxyerythratidinone in Sri Lankan *Erythrina lithosperma*

8.4. Pharmacology of *Erythrina* Alkaloids

The curare-like action of extracts of the seeds of *E. americana* was recognised as far back as 1877,[39] and was confirmed later by several workers.[49,131] However, first isolation of a crystalline biologically active *Erythrina* alkaloid, named erythroidine from seeds of the same species was reported in 1937 by Folkers and Major.[49] Further analysis of erythroidine had shown that it was a mixture of 2 isomeric alkaloids which were named α—and β—erythroidines. β—erythroidine (LVI) and its more potent derivative dihydro-β—erythroidine have been used clinically as muscle relaxants, but have now been replaced by other drugs.[78] Following the discovery of erythroidines, intensive studies were initiated on *Erythrina* species and these resulted in the isolation of a number of physiologically active alkaloids, most of which showed some curariform activity.

The total alkaloids of *E. variegata* had shown several characteristic pharmacological effects :[55] neuromuscular blocking effect of the antidepolarizing type, smooth muscle relaxant effect, and also hydrocholeretic, CNS depressant, and anticonvulsant effects. The reported uses of the extracts of this plant in indigenous system of medicine as a remedy for biliousness, in liver troubles, in epilepsy, and as a nervine sedative could be correlated with the above pharmacological effects observed. The other uses of *E. variegata* and related plants, such as laxative, diuretic and antiasthmatic uses would seem to be due to the intermediate alkaloids (*N*-norprotosinomenine and equivalents) to the spiroamines. Occurrence of *N*-norprotosinomenine in the Indian variety of *E. lithosperma*[56] is significant from the latter point of view. The emmenagogue activity of *E. variegata*[10] could be related to the presence of erysotrine (XLVIII) as erysotrine in *Cassia absus* (Leguminosae) has been shown to stimulate uterine tissue.[48,127]

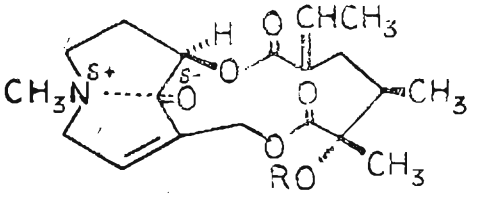
8.5. *Crotalaria* Alkaloids

The genus *Crotalaria* contains at least 40 different alkaloids,[129] many of which belong to the pyrrolizidine type. Pyrrolizidine alkaloids also occur in a large number of plants including the genera, *Senecio* and *Erechtites* (Compositae) *Echium, Heliotropium Trachelanthus* and *Trichodesma* (Boraginaceae).[106] Of the 29 species of *Crotalaria* recorded from Sri Lanka,[1] *C. multiflora* (Arn.) Benth. and *C. walkeri* Arn. are known to be endemic.[11]

C. verrucosa L. (*Sinh.*— nilandanahiriya ; *Tam.*— kilvenlappa) and *C. juncea* L. (*Sinh.*— Hana ; *Tam.*— shanal imappu) find many applications in the indigenous system of medicine.[10] The leaves and seeds of these plants are said to have a cooling effect and blood-purifying action and hence used in cases of fever and skin diseases. *C. verrucosa* which is used more often in medicine than *C. juncea* is employed also as a bitter and as an expellent of bile. The juice of the tender leaves

is applied both internally and externally for scabies and impetigo. The leaf preparation is also applied to eruptions of the skin so as to clean them before applying curative medicines.

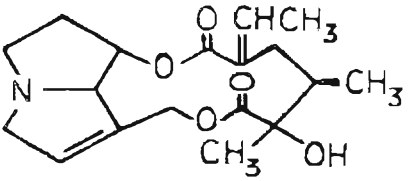
During their chemical studies on the genus *Crotalaria*, Atal and his co-workers have examined,[160] the seeds of *C. walkeri* Arnott for alkaloids. Although this species has been described by Trimen as endemic to Sri Lanka,[164] according to Hooker it is a variety of the Indian species *C. semperflorens*.[160] Quantitative estimation had revealed seeds of *C. walkeri* to contain 0·20% tertiary bases and 0·06% *N*-oxides. The ethanol extract of the powdered dehusked seeds on partition chromatography over buffered celite 525 has afforded a new secopyrrolizidine alkaloid, crotaverrine (LXII) and its derivative, O-acetylcrotaverrine (LXIII). The structures of these tertiary bases have been elucidated by combined chemical and spectral analyses.



(LXII) ; R = H
(LXIII) ; R = $COCH_3$

8.6. Pharmacology and Toxicology of *Crotalaria* Species

Monocrotaline (LXIV), a pyrrolizidine alkaloid from *C. spectabilis* is found to be responsible for the activity of *Crotalaria* extracts against adenocarcinoma-755 in mice.[100] Similar alkaloids have been screened for anti-tumour activity.[34,145] However, as pyrrolizidine alkaloids are known to be hepatotoxic,[84] it is questionable whether they could have applications in chemotherapy of cancer. Besides, presence of these alkaloids in this genus demands a complete evaluation of the medicinally employed *Crotalaria* species (see 8.5) for their hepatotoxicity.*



(LXIV)

*Investigation of these and other plant species used in native medical practice for hepatotoxicity and the occurrence of pyrrolizidine alkaloids has been undertaken by Prof. S. N. Arseculeratne of the Dept. of Microbiology, Peradeniya Campus in collaboration with the author.

Poisoning by the pyrrolizidine alkaloids has recently been reviewed by Bull, who suggests that the condition should be called pyrrolizidine alkaloidosis.[25] The pyrrolizidine alkaloids are not all poisonous. For an alkaloid to be toxic it must have a double bond between C-1 and C-2.[142] The cyclic diesters (e.g. (LXIV)) are twice as toxic as the open diesters, and 4 times as toxic as the open monoesters. Esters of branched-chain acids are toxic while esters of straight chain acids are not.[143] It has been suggested that the alkaloids themselves are not hepatotoxic, but are converted in the liver to toxic pyrrole-like derivatives which react with tissue constituents to form bound pyrroles which either remain in the tissues or are excreted in the urine.[109]

9. Alkaloids of Liliaceae

9.1 Introduction

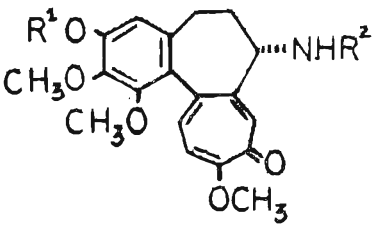
The monocotyledonous family, Liliaceae, produces a number of alkaloidal types of which colchicine and *Veratrum* types are of wide occurrence.[129] Colchicine group of alkaloids have a 1-phenethyl-1,2,3,4-tetrahydroisoquinoline origin and *Veratrum* group is of steroidal type. Alkaloids based on the steroid nucleus are not very widely distributed, being restricted to plants of the *Holarrhena* (Apocynaceae, see 4.2), *Solanum* (Solanaceae) and *Veratrum* species.[18]

Abeywickrema has listed 18 species of Liliaceae[1] belonging to 14 genera containing 2 endemic species, *Urginea rupicola* (Trim.) Trim. ex Hook. f. and *Asparagus zeylanicus* (Baker) Hook. f.[11] The non-endemic *Gloriosa superba* L. (*Sinh.*— Niyagala) grows wild in Sri Lanka. This plant is known to ancient medical writers in Sanskrit as "Gharbha ihatin"— that which causes abortion. Decoctions containing *G. superba* have found considerable use in native medicine particularly as abortifacients.[26,48] The roots are used for snake-bites and scorpion stings and the starch from roots is given internally for gonorrhoea.[29]

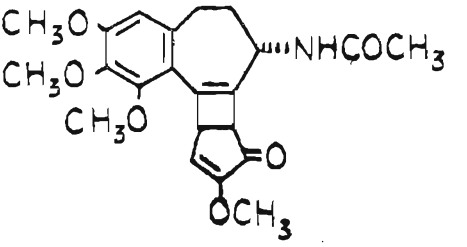
9.2 Alkaloids of *Gloriosa superba*

The tubers of *G. superba* gathered from Sri Lanka were chemically investigated as far back as 1915 by Clewer and his co-workers.[31] During their studies they were able to isolate 2 alkaloids and a few other non-alkaloidal constituents. One of the bases was colchicine (LXV) and the other with m.p. 177° to 178°C and probable molecular formula, $C_{33}H_{38}O_9N_2$ was left unidentified due to the non-availability of sufficient quantities for further studies. In 1968, Dunuwille, Balasubramanium and Bibile reinvestigated the mature and tender tubers, the seeds and the flowers of *G. superba*.[43,44] Their examination of the mature tubers which commonly cause poisoning in the rural areas of Sri Lanka, had revealed colchicine (LXV) to be the major alkaloid (0.025%). However, the colchicine content was remarkably low

compared to that found in the tubers of European (*ca.* 0.20%) and African (0.12%) origin. Colchicine was also found to occur in the tender tubers, seeds and flowers. Three other alkaloids, namely *N*-formyl-*N*-desacetylcolchicine (LXVI) (0.003%) 2-demethylcolchicine (LXVII) and lumicolchicine (LXVIII) were also isolated from the mature tubers. They also found several other unidentified alkaloids to be present in trace amounts.



(LXV) ; $R^1 = CH_3$, $R_2 = COCH_3$
(LXVI) ; $R^3 = CH_3$, $R^2 = CHO$
(LXVII) ; $R^1 = H$, $R^2 = COCH_3$



(LXVIII)

Seeds of *G. superba* obtained from Sri Lanka were also analysed by Santavy *et al.* [110] by paper chromatographic techniques and was shown to contain colchicine (LXV), *N*-formyl-*N*-deacetylcolchicine (LXVI) and 2-demethylcolchicine (LXVII).

9.3 Pharmacology and Toxicology of *G. superba*

Numerous fatalities due to ingestion of *G. superba* in decoctions used as abortifacients are on record.[168] Poisoning has also occurred in Sri Lanka through the tubers being mistaken for those of the yams of sweet potato (*Ipomeoa batatas*).[44,59] Jayatilaka and Balasubramanium have investigated[90] the digestive tract histopathology in rats poisoned by the extracts of *G. superba* tubers and have found that the lesions are similar to those poisoned by colchicine (LXV) which was shown to be an alkaloidal constituent of these tubers (see above).

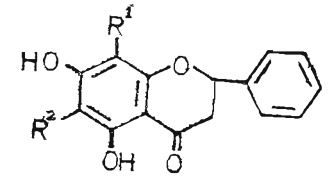
Subbaratnam obtained another alkaloid named gloriosine from *G. superba* during the isolation of colchicine.[154] Amoroso found both colchicine and gloriosine to have an anti-mitotic effect.[6] It has also been demonstrated that gloriosine is more effective than colchicine in polyploid formations. Colchicine has been used in the treatment of gout for many years. It has also been used as a cytotoxic drug in the treatment of inoperable carcinoma.[23] Therefore, in view of its wide use in therapy, experiments have been conducted on mice, rats and sheep with the aim of discovering its action and toxicity. Alopecia (loss of hair) caused by treatment with colchicine[135,136] and due to the ingestion of tubers of *G. superba* is known.[59]

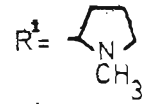
10. Alkaloids of Moraceae

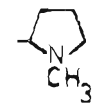
10.1 Introduction

Moraceae in Sri Lanka has 34 species distributed in 11 genera.[164] Of these, 5 species in the genera *Allaeanthus* (more correctly *Broussonetia*[32]), *Artocarpus* and *Ficus* are reported to be endemic. The former two genera contain one each of endemic species and *Ficus* has 3 species which are endemic.[11]

Alkaloids are infrequent in the plant species of Moraceae. From *Ficus* spp. 5 alkaloids have been known, 3 having a phenanthro-indolizidine skeleton, *viz.* tylocrebine (XXXVI), tylophorine (XXXIII) and septicine (XXXIX) (see 5.2. *Tylophora* alkaloids) and two flavonoid-type alkaloids, *viz.* ficine (LXIX) and isoficine (LXX).[129] No alkaloids have been reported from the genera *Artocarpus* and *Broussonetia*.



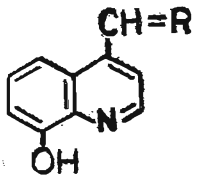
(LXIX) R^1=  , R^2=H

(LXX) R^1=H , R^2= 

10.2 Alkaloids of *Broussonetia zeylanica* (*Allaeanthus zeylanicus*)

The genus *Broussonetia* in Sri Lanka is represented by a single species *B. zeylanica* Thwaites (*Sinh.*— Alandu) which is endemic to the country.[11] This graceful tree, the very tough inner bark-fibres of which were used for string, seems to have become rare as its lowland forest habitat has disappeared.[32]

Although *B. zeylanica* had no claims of medicinal applications, when screened some of its extracts exhibited significant antimicrobial activity against three common pathogenic organisms ; *Candida albicans*, *E. coli* and *Staphylococcus aureus*.[71] Prompted by this, an investigation directed towards the isolation and identification of the active constituent had led to the recognition of a new alkaloid, 8-hydroxy-quinoline-4-carboxaldehyde (LXXI) in 0.25% yield from the dried timber. This alkaloid was found to be active against *C. albicans* and *S. aureus*. This was the first report of a naturally occurring 8-hydroxyquinoline (oxine). However, 8-hydroxy 4-quinolone has been recently reported as a constituent of the ink of giant octopus, *Defleini martimi*.[153]

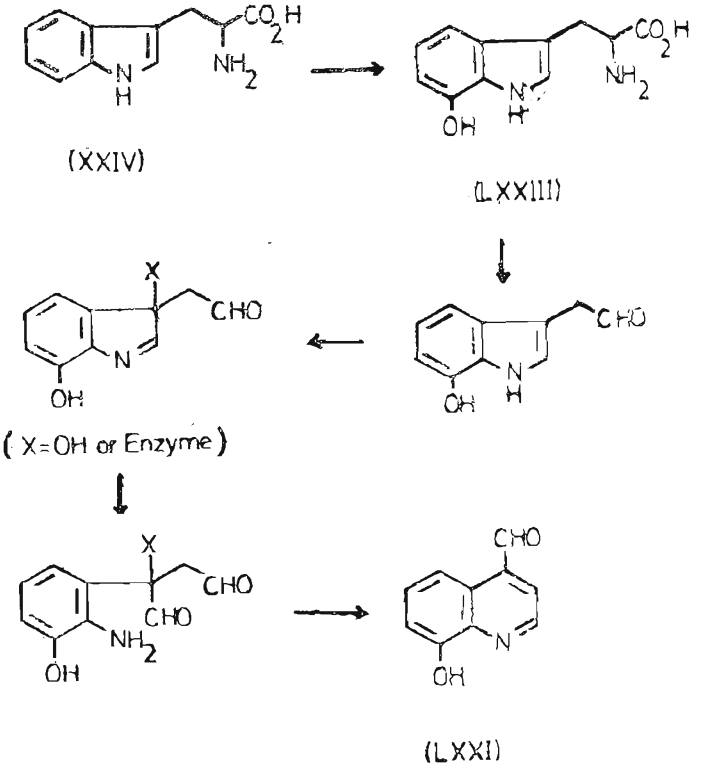


(LXXI) ; R = O

(LXXII) ; R = N—NH—C(=S)—NH_2

10.3 Biosynthesis of 8-Hydroxyquinoline-4-carboxaldehyde

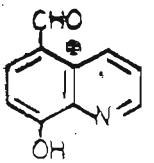
Some naturally occurring quinolines are known to arise from the corresponding indole precursors,[104] an important example being cinchonine which arises biogenetically from cinchonamine (see 11.6). It has been proposed, on similar grounds, that 8-hydroxyquinoline-4-carboxaldehyde (LXXI) could arise from 8-hydroxytryptophan (LXXIII) by a biosynthetic pathway depicted in Scheme 6, for which chemical analogues are known.[165]



Scheme 6. Proposed biosynthetic route to 8-Hydroxyquinoline-4-carboxaldehyde from *Broussonetia zeylanica*.

10.4 Pharmacology of 8-Hydroxyquinolines

8-Hydroxyquinoline and its derivatives are known to have an array of antimicrobial properties and a number of them find uses in western medicine as topical antiseptics and disinfectants.[33] The possible relationship between complex formation property and tuberculostatic activity of this class of compounds had prompted synthesis and testing of a number of 8-hydroxyquinoline carboxaldehydes and their thiosemicarbazones.[24] 8-Hydroxyquinoline-5-carboxaldehyde (LXXIV) was found to be the most effective against human type H-37 Rv strain of *Myobacterium tuberculosi*.[94] However, the effective doses were found to be toxic to mice. Pharmacological evaluation of 8-hydroxyquinoline-4-carboxaldehyde (LXXI) and the thiosemicarbazone (LXXII) has suggested that the introduction of —CHO and —CH=N—NH —$CSNH_2$ groups causes a decrease in tuberculostatic activity.[24]



(LXXIV)

11. Alkaloids of Rubiaceae

11.1 Introduction

Rubiaceae, one of the major alkaloid bearing families of Sri Lanka, is known to contain mainly the alkaloids of oxindole,[57] yohimbine[124] and heteroyohimbine types.[57] Alkaloids have been reported from several genera belonging to this family (see Table 15).

In Sri Lanka, Rubiaceae has 158 species distributed in 50 genera of which 74 species are endemic to the country. Twenty species are reported to have uses in the indigenous system of medicine. Table 15 summarises the medicinally useful and alkaloid containing genera of this family occurring in Sri Lanka. Of these, *Mitragyna parvifolia* (Roxb.) Korth., *Uncaria thwaitesii* (Hook. f.) Alston and *Cinchona ledgeriana* Moens. have been subjected to detailed investigations.

11.2 *Mitragyna* Alkaloids

Mitragyna and *Uncaria* are members of the tribe Naucleae of the family Rubiaceae.[20] Trimen has recorded two species of *Mitragyna*, *viz. M. parvifolia* and *M. tubulosa* (Arn. *ex* Bedd.) Kuntze from Sri Lanka.[164]

TABLE 15. Medicinally used and alkaloid containing genera of Rubiaceae found in Sri Lanka.

Genus	No. of species in Sri Lanka (No. endemic)	No. of species used in indigenous medicine	Presence of Alkaloids*
Anthocarpus	1	1	++
Borreria	3	1	++
Canthium	7 (5)	2	++
Cinchona	0	—	++
Gardenia	3	1	—
Hedyotis	29 (22)	1	++
Ixora	5 (2)	1	++
Knoxia	4 (1)	0	++
Lasianthus	9 (9)	0	++
Morinda	3	3	+
Mitragyna	2	0	++
Mussenda	2	2	—
Nauclea	1	1	—
Neonauclea	1 (1)	0	+
Oldenlandia	7	5	—
Ophiorrhiza	7 (4)	1	++
Pavetta	11 (3)	1	++
Psychotria	13 (9)	0	++
Randia	5	2	+
Rubia	1	1	—
Tarenna	2	1	—
Tricalysia	2 (2)	0	++
Uncaria	1 (1)	0	++
Urophyllum	2 (1)	0	++

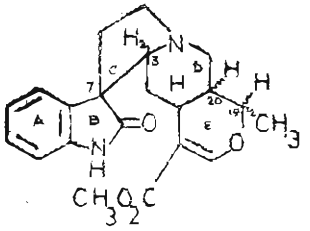
*(++) indicates that alkaloids have been isolated
(+) indicates that alkaloids have been detected (Ref. 157)

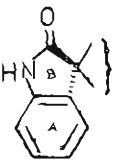
Although *Mitragyna* species find no applications in local medical practice, some Asian and African species have been employed in folk medicine.[137] In Thailand, the leaves of *M. speciosa* Korth. are chewed as a narcotic and the leaves of *M. parvifolia* are reputed as an antidote for opium addiction. The bark of *M. africana* Korth. is used as a febrifuge in Western Africa.

In their series of investigations on *Mitragyna* alkaloids,[147,148,149,150] Shellard and his co-workers have examined the bases present in the leaves of *M. parvifolia* collected in Kekirawa and have reported the presence of 8 tertiary alkaloids and the *N*-oxides of 4 of them.[149] The tertiary alkaloids present were akuammigine (LXXV), tetrahydro-alstonine (LXXVI), Uncarine C [pteropodine (LXXVII)], Uncarine D [speciophylline (LXXVIII)], Uncarine E [isopteropodine (LXXIX)], Uncarine

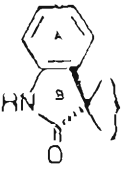
F(LXXX), coryantheidol (LXXXI) and dihydrocorynantheol (LXXXII). The *N*-oxides were characterised from their mass spectra and by sulphurous acid reduction to the corresponding parent tertiary alkaloids which were identified by *TLC* with authentic samples in a number of developer solvent systems. Characterised in this manner were the *N*-oxides of akuammigine, speciophylline, Uncarine F and dihydrocorynantheol (see Table 18).

TABLE 16. Some pentacyclic ring E heteroxindole alkaloids of Sri Lankan Rubiaceae.



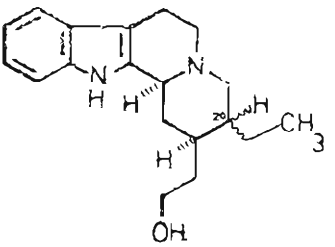


C(7)-R



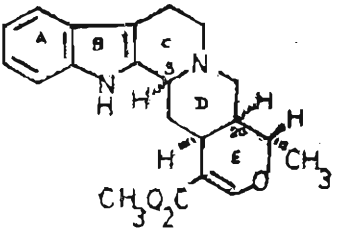
C(7)-S

		C(7)	C(3)-H	C(19)-H	C(20)-H
Uncarine C	(LXXVII)	R	α	β	α
Uncarine D	(LXXVIII)	S	β	β	α
Uncarine E	(LXXIX)	S	α	β	α
Uncarine F	(LXXX)	R	β	β	α
Mitraphylline	(LXXXIV)	R	α	β	β
Isomitraphylline	(LXXXV)	S	α	β	β
Formosanine	(LXXXVIII)	R	α	α	β

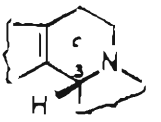


		C(20)—H
Corynantheidol	(LXXXI)	α
Dihydrocorynantheol	(LXXXII)	β

TABLE 17. Some terpenoid indole alkaloids of Sri Lankan Rubiaceae.

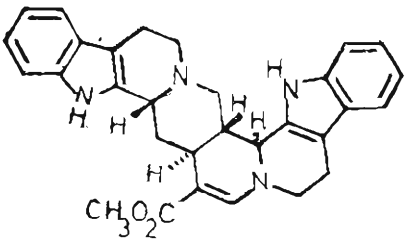


allo, normal



epiallo pseudo

		C(3)-H	C(20)-H
Akuammigine	(LXXV)	β	α
Tetrahydroalstonine	(LXXVI)	α	α
Ajmalicine	(XXI)	α	β
Isoajmalicine	(LXXXIII)	β	β



Roxburghine D (LXXXIX)

TABLE 18 Alkaloidal *N*-oxides of Sri Lankan *M. parvifolia*

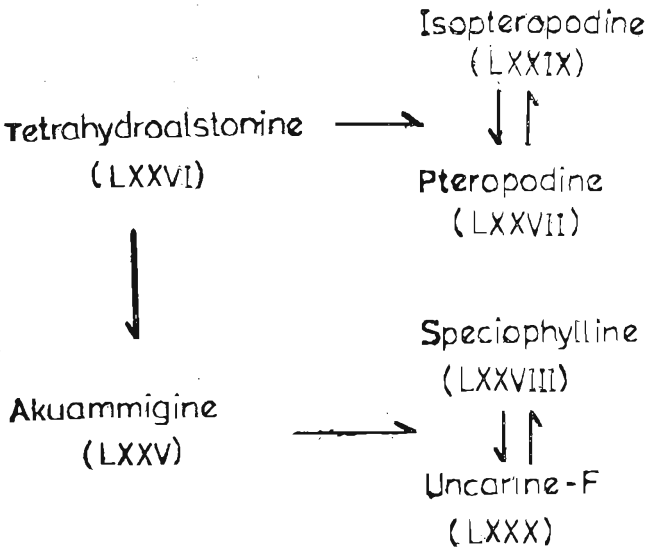
Alkaloid		% yield	*TLC* Rf × 100 *	†
Speciophylline	*N*-oxide	1.33	14	4
Uncarine—F	*N*-oxide	1.33	36	28
Akuammigine	*N*-oxide	1.66	38	46
Dihydrocorynantheol	*N*-oxide	0.67	50	56

*Using Silica gel G/methanol

†Using Silica gel G/chloroform—methanol, 6 : 1

11.3. Biosynthesis of *Mitragyna* Alkaloids

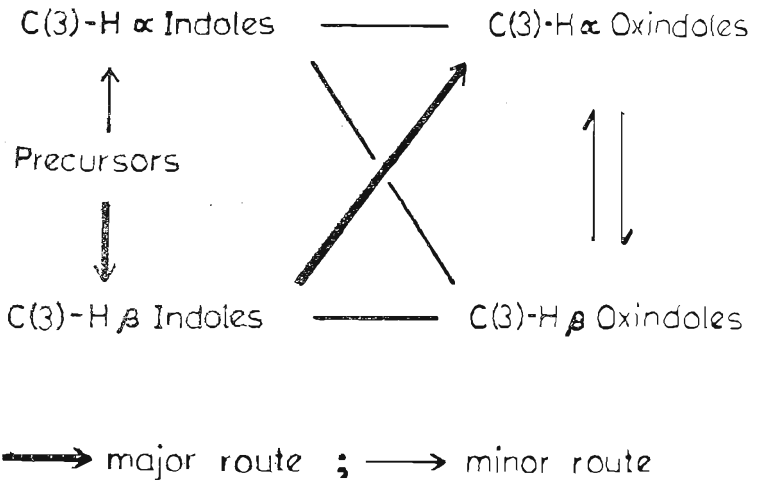
Mitragyna species are known to produce both indole and oxindole groups of alkaloids. In 1969, Shellard, Phillipson and Gupta observed that when both indole and oxindole alkaloids occurred in *Mitragyna* species, the D/E ring systems (as in LXXIV and LXXIII) were identical in both types of alkaloids.[146] Furthermore, with the exception of *M. speciosa*, the major indole alkaloids present are the ones with thermodynamically least stable configurations, *i.e. epiallo* and *pseudo* configurations (see Table 17). This gave rise to the possibility that there was a well defined biogenetic link between the formation of indole and oxindole alkaloids. The hypothesis put forward by Shellard *et. al.*[146] states that : (*a*) the plant synthesised thermodynamically more stable indole alkaloids according to the scheme suggested by Battersby and Hall[17] for the biogenesis of indole alkaloids, (*b*) these alkaloids then isomerised into the corresponding thermodynamically less stable configuration, and (*c*) all the indole alkaloids were then converted to the corresponding oxindole alkaloids. The pattern of alkaloids in *M. parvifolia* obtained from Sri Lanka is shown in Scheme 7, which is different to the alkaloid pattern found in *M. parvifolia* samples from Burma and Uttar Pradesh state of India.



Scheme 7. Alkaloidal pattern in *Mitragyna parvifolia* from Sri Lanka.

During these biosynthetic investigations, Shellard and Houghton fed ajmalicine (XXI) and 3-isoajmalicine (LXXXII) into young plants of Sri Lankan *M. parvifolia* and in both cases obtained mitraphylline (LXXXIV) and isomitraphylline (LXXXV). This and a similar series of biosynthetis experiments led to the modification of the originally postulated hypothesis (see above). Further experiments with labelled precursors supported this modification of the original hypotheses for the biosynthesis of oxindole alkaloids in *Mitragyna* species as indicated in Scheme 8.

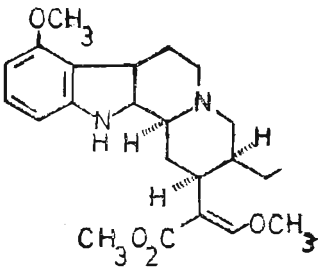
The Chelsea group has also examined the distribution of alkaloids in young plants of *M. parvifolia* grown from the seeds obtained from Sri Lanka.[148] During this study they were able to resolve one of the major problems ; the role of mitraphylline (LXXXIV) in the biosynthesis of *Mitragyna* alkaloids. Mitraphylline was found only in the lower part of the stem (hypocotylar region) and was absent in leaves or roots. The results of these isolation studies and experiments with labelled precursors using the plants grown from the seeds from Sri Lanka were considered with the results obtained using the plants grown from the seeds of Uttar Pradesh and the alkaloid distribution in the mature trees supported the above metabolic pathway indicated in Scheme 8.



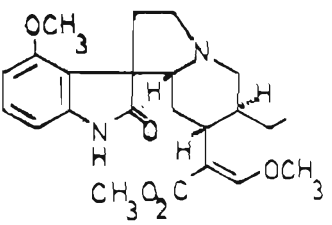
Scheme 8. Biosynthesis of Oxindole alkaloids in *Mitragyna* species.

11.4. Pharmacology of *Mitragyna* Alkaloids

Some *Mitragyna* alkaloids are known to have pharmacological activity. Mitragynine (LXXXVI) is a general protozoal poison but is ineffective against bacteria or pathogenic protozoa. It has a depressant effect in isolated tissues, facilitates the passage of impulses in the autonomic nervous system and increases the excitability in the medulla and probably of motor centres.[69] Mitraphylline (LXXXIV), an alkaloid reported from a number of *Mitragyna* species, resembles mitragynine in its pharmacological activity but is less effective.[108] Mitraphylline is also hypotensive.[121] It is interesting to note that, in connection with the employment of *Mitragyna* extracts as febrifute (see above), rhynchophylline [mitrinermine (LXXXVII)] exhibits a significant antipyretic action.[123,137] Rhynchophylline was also found to be toxic to paramecium.[121]



(LXXXVI) Mitragynine



(LXXXVII) Rhynchophylline

The alkaloids of *M. africana* Korth. and *M. macrophylla* Hiern. produce a reduction of the arterial pressure and a decrease in the volume of the kidney. Like yohimbine, the alkaloids invert the action of adrenaline on arterial blood pressure. After a previous application of the alkaloids, adrenaline produces hypotension. It is supposed that the alkaloids have a paralysing effect on the sympathetic nervous system.[122] It has been suggested that the hypotensive effect of the above extracts are, in part, due to rhynchophylline (LXXXVII).[115]

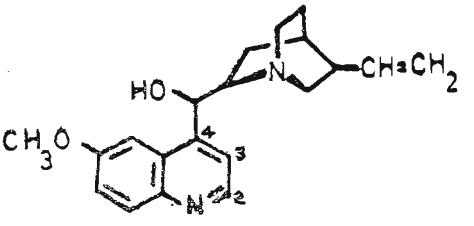
11.5. Alkaloids of *Uncaria thwaitesii*

The members of the genus *Uncaria* are large woody climbers most of which are found in the tropics particularly in the Far East. Not much attention has been directed towards the chemical studies on this genus which was partly due to the confusion that existed in the taxonomy and nomenclature. However, recently the genus *Uncaria* has been revised and 39 species out of a total of 120 have been recognised. A number of alkaloids were isolated and identified from these species by Phillipson and Hemingway by means of sensitive chromatographic and spectroscopic techniques.[125] The distribution of more than 60 alkaloids reported from *Mitragyna* and *Uncaria* species have been recently summarised by Herath.[83]

The only Sri Lankan species of the genus *Uncaria*, *U. thwaitesii* (Hook. f.) Alston which is endemic to the country has been investigated recently for alkaloids.[81,82,83] From the bark basic extract, four indole alkaloids *viz.*, formosamine (LXXXVIII), mitraphylline (LXXXIV), roxburghine D (LXXXIX) and another roxburghine isomer with a m.p. 215°C have been isolated in the yields of 0.009, 0.19, 0.002 and 0.003% respectively. The occurrence of these less polar bases formosamine, mitraphylline and a roxburghine isomer with a m.p. 215°C all in trace amounts has also been demonstrated in the timber extracts of *U. thwaitesii*. Identification of these alkaloids was based on spectral analysis and chemical reactions.

11.6. Studies on *Cinchona* Alkaloids

The four principal *Cinchona* alkaloids, quinine (XC), quinoline, cinchonine and cinchonidine, all contain a quinoline ring linked by a secondary alcohol at its fourth position to a quinuclidine ring. Quinidine is the dextrorotatory optical isomer of quinine (XC) ; cinchonidine is quinine minus the methoxy group and cinchonine is the *D* isomer of cinchonidine. All 4 *Cinchona* alkaloids have schizonticidal activity, but quinine is the only one used in the treatment of malaria because of its high absorption property.



(XC)

Plants belonging to the genus *Cinchona* are not indigenous to this country. However, *C. ledgeriana* Moens. has been introduced to Sri Lanka with the sole intention of exporting the bark[5,91] for the purpose of extracting the antimalarial alkaloid, quinine (XC) and its *D*-isomer, quinidine, an alkaloid active against cardiac arrhythmias.[114] Therefore, Wijesekera and his co-workers had felt the necessity to devise a simple technique to demonstrate the distribution of alkaloids in various specimens of *Cinchona* submitted by exporters.[171] Their method involved a two dimensional *TLC* analysis using silica gel plates and the developer solvent system $CHCl_3$–MeOH–17% NH_3 (24 : 6 : 0.05 v/v) and diethyl ether-diethylamine (17 : 1, v/v). Further, this method may prove useful in the study of varietal and geographical variation of alkaloid content in *Cinchona* samples.

Quinine (XC) is one of the least toxic alkaloids known. Non-fatal cases of poisoning have been caused from its use as an antimalarial,[111] but fatalities were usually due to its use as an abortifacient.[58]

Extracts of *C. ledgeriana* have been screened for the occurrence of biogenetic precursors of indole alkaloids and 5-carboxystrictosidine (XXIX) has been isolated (see 4.5).[36]

12. Alkaloids of Rutaceae

12.1. Introduction

The Rutaceae family of plants produces some 13 basic alkaloid types[129] and the acridan-9-one (acridone) group of alkaloids represents a class specific to this family. Recently, the number of acridone alkaloids known has doubled,[92] but in all cases so far reported, the structures have been represented by modifications on a single acridone ring system.

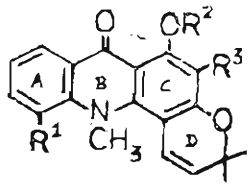
Rutaceae in Sri Lanka has 40 species distributed in 18 genera,[1] of which 4 species are endemic.[11] Fourteen non-endemic species of Rutaceae find applications in the indigenous system of medicine (see Table 2).[3] Further, this family contains such useful plants as lime (*Citrus aurantifolia* L.), lemon (*C. limonium* L.), orange (*C. sinensis*) and curry leaf (*Murraya koenigii*, *Sinh.*—karapincha). *Acronychia* represents an important genus in the family Rutaceae as acronycine (XCI) isolated from different species of this genus has shown the broadest experimental anti-tumour activity of any alkaloid studied.[93] However, no evidence for clinical trials with this alkaloid has yet been found in the literature.[140] It is noteworthy that the bark of *A. laurifolia* (*Sinh.*—ankenda) is used in indigenous system of medicine as an application to sores and ulcers.[10]

12.2. Alkaloids of *Atalantia ceylanica*

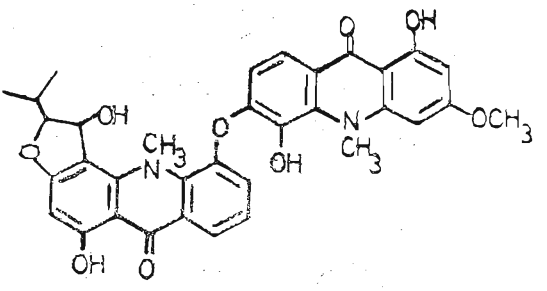
A. ceylanica (Arn.) Oliv. (*Sinh.*—yakinaran ; *Tam.*—peykuruntu) is a much branched bush armed with sharp stout spines and is common in low country and in eastern province. The leaf juice of this plant is used for administration of pills and is an emperical remedy to prevent attacks of ague.[10]

Fraser and Lewis have recently investigated *A. ceylanica* obtained from Sri Lanka.[51,52] From the wood extractives of this plant they isolated 2 major acridone alkaloids, 3,12-dihydro-6,11-dihydroxy-3,3,12-trimethylpyrano (2,3-C) acridine-7one (XCII) and its 5-(3-methylbut-2-enyl) derivative (XCIII) in the yields of 0.04 and 0.003% respectively.[52] The structures of these two alkaloids were established from the analysis of their spectral data. These 2 alkaloids are close relatives of the acridone alkaloid acronycine (XCI) (see above). Occurrence of (XCII) as a plant product is particularly interesting since it has been tentatively reported as one of the metabolites isolated from rat bile after dosage with acronycine.[155]

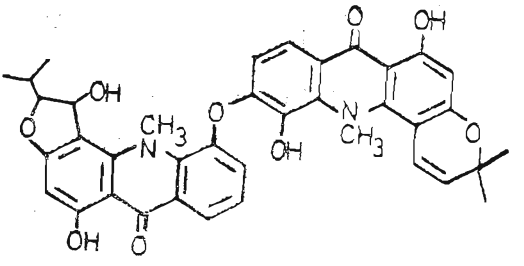
TABLE 19. Some acridone alkaloids from *A. ceylanica*.



	R^1	R^2	R^3
(XCI)	H	CH_3	H
(XCII)	OH	H	H
(XCIII)	OH	H	$-CH_2-CH=C<$



(XCIV)



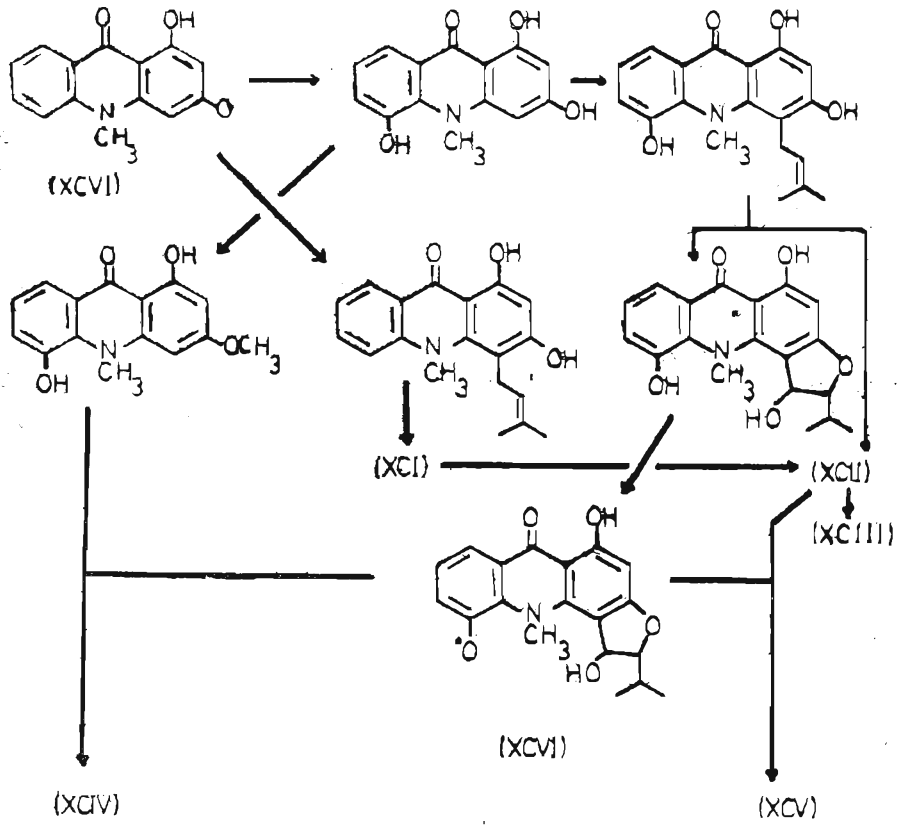
(XCV)

Two novel types of alkaloids where two acridone rings are joined to each other by an ether linkage has also been obtained from *A. ceylanica*.[51] These two bi-acridone alkaloids have been named atalanine (XCIV) and ataline (XCV).

12.3. Biosynthesis of *Atalantia* Alkaloids

1, 3-Dihydroxyacridan-9-one (XCVI) could be regarded as the biogenetic precursor for all the known acridone alkaloids.[76] Possible biosynthetic routes from this precursor to the 4 alkaloids obtained from *A. ceylanica* are given in Scheme 9. Biogenetically, the introduction of the 5-hydroxy function into acronycine (XCI) to obtain (XCII) probably occurs at a later stage, perhaps *via* an arene oxide intermediate.[74]

Biogenetic considerations have aided Fraser and Lewis to locate the ether linkages in the two novel bi-acridone alkaloids, ataline (XCV) and atalanine (XCIV) isolated from *A. ceylanica*.[51] In both alkaloids, the ether linkage was assigned to C-5^1—C-6 since all the acridone alkaloids isolated with hydroxy groups in ring A (see structures XCII and XCIII) have it located at 5 position. In this position, it would enable the radical intermediate (XCVI, Scheme 9) to couple with another acridan-9-one at the C-6 position, *i.e. ortho* to its hydroxy group. However, the authors have stated that alternative sites for the ether linkage cannot be excluded.

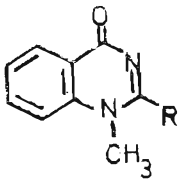


Scheme 9. Possible biosynthetic routes to the alkaloids of *Atalantia ceylanica*.

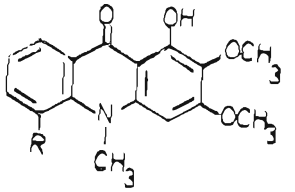
12.4. Alkaloids of *Glycosmis bilocularis*

The genus *Glycosmis* has 2 species in Sri Lanka, *G. bilocularis* Thwaites and *G. pentaphylla* (Retz.) Corr. The former, a very rare shrub found in low country and Mihintale in the North Central province, is endemic to the country and has been recently analysed for its constituent alkaloids.[22] Although this plant has no reported medicinal applications, the non-endemic *G. pentaphylla* (*Sinh.*—dodanpana ; *Tam.*—kulapannai) is used in snake-bites and given in cases of low fever.[28]

From the basic extract of the leaves and stems of *G. bilocularis*, Bowen and Perera,[22] had isolated 7 alkaloids out of which one is a new acridone alkaloid. The known alkaloids isolated were of acridone, quinazolone and furo (2,3-b) quinoline types. The quinazolone alkaloids identified were glycorine (XCVII) and arborine (XCVIII) whereas furo (2,3-b) quinolines included dictamnine (XCIX), skimmianine (C) and kokusaginine (CI). The acridone type which is characteristic of the family Rutaceae included the known alkaloid arborinine (CII) and a new base 5-hydroxyarborinine (CIII). It is important to note that the presence of acridones hydroxylated at C-5 appears to be a characteristic of the Sri Lankan Rutaceae (refer XCII, XCIII XCIV, and XCV).

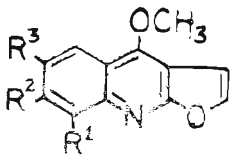


Glycorine (XCVII) ; R = H
Arborine (XCVIII) ; R = CH_2Ph



Arborinine (CII) ; R = H
5-Hydroxyarborinine (CIII) ; R = OH

TABLE 20. Some furo (2, 3—b) quinoline alkaloids of Rutaceae.



		R^1	R^2	R^3
Dictamnine	(XCIX)	H	H	H
Skimmianine	(C)	OCH_3	OCH_3	H
Kokusaginine	(CI)	OCH_3	H	OCH_3

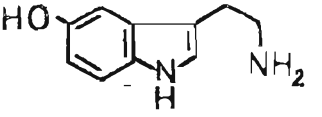
12.5. Alkaloids of *Micromelum ceylanicum*

Micromelum ceylanicum Swingle, the only species of this genus found in Sri Lanka which has been wrongly reported by Trimen[164] as *M. pubescens* (*Sinh.*—wal-karapincha ; *Tam.*—kakaipalai) is a small tree common in low country especially in the dry region. This plant has also been examined by the same authors[22] and they have isolated an alkaloid whose structure is presently under investigation.

13. Miscellaneous Studies

13.1. 5-Hydroxytryptamine in Edible Fruits

5-Hydroxytryptamine (5HT) or serotonin (CIV) which is known to be derived from the amino acid tryptophan (XXIV) is considered to be an important biogenetic amine.[103] Prompted by a report[166] of its occurrence in banana, and clinical consequences, Dharmatilaka and Kottegoda have investigated a number of edible fruits from Sri Lanka[38] for its presence. Their method of analysis involved the preparation of extracts of these fruits by a known procedure[169] and an assay for 5HT by a method developed by Kottegoda[97] on the heart of brackish water molluscs, after identification by paper chromatography. It was found that anamalu plantain, papaw (*Carica papaya*) and Jambola (*Citrus decumana*) contained appreciable amounts of 5HT.



(CIV)

The authors have commented that the presence of 5HT in common edible fruits is of clinical significance as the ingestion of these may produce false positive results when the urine samples of patients with suspected carcinoid tumour are examined.

14. Summary and Conclusions

The plant species of Sri Lanka that have been studied for alkaloids and the alkaloids isolated from these are summarised in Table 21. A total of 22 plant species including 9 endemics have been investigated and from these 68 alkaloids have been isolated and 11 detected by chromatographic techniques. Amongst the alkaloids isolated, 10 were found to be new. Besides 8-hydroxyquinoline-4-carboxaldehyde (LXXI) obtained from the endemic species *Broussonetia zeylanica* (Moraceae), these new bases have not been evaluated for their biological activity.

TABLE 21. Alkaloids found in Sri Lanka Plants

FAMILY Plant species	Alkaloid(s) present Name(s)	Formula(e)	Ref.
ANCISTROCLADACEAE			
Ancistrocladus hamatus[1]	ancistrocladine	(I)	66
	hamatine[3]	(III)	66
APOCYNACEAE			
Holarrhena mitis[1]	conessine	(V)	19, 27, 101
	iso-conessimine	(VI)	27
	holadienine	(IX)	27
	conkurchine	(XIII)	27
	holarrhenine	(VII)	27
	holafebrine	(X)	27
	holarrhimine	(XI)	27
	N-3-methylholarrhimine	(XII)	27
	mitiphylline	(XV)	89, 102
	N-desmethylmitiphylline	(XVI)	89, 102
	triacanthine	(XIV)	89, 101, 102
	conamine	(VIII)	101
Catharanthus roseus	vincaleukoblastine[2,4]	(XIX)	70, 152
and *C. pusillus*	leurocristine[2,4]	(XX)	70, 152
	ajmalicine[2,4]	(XXI)	70, 152
	vincamine[2,4]	(XXII)	70, 152
(*Vinca* spp.)	5α-carboxystrictosidine	(XXIX)	36
	strictosidine	(XXVIII)	36
Rauwolfia serpentina	5α-carboxystrictosidine	(XXIX)	36
	strictodesine	(XXVIII)	36
Kopsia fruticosa	ajmalicine[2,4]	(XXI)	7
ASCLEPIADACEAE			
Tylophora asthmatica	tylophorine	(XXXIII)	126
	tylophorinine	(XXXIV)	126
	tylophorinidine	(XXXV)	126
T. cordifolia	tylophorinine[2]	(XXXIV)	126
T. flava[1]	tylophorine[2,4]	(XXXIII)	126
	tylophorinine[2]	(XXXIV)	126
BERBERIDACEAE			
Berberis tinctoria	berberine[4]	(XL)	144
	lankamine[3] and 11 other alkaloids		144
LAURACEAE			
Neolitsea fuscata[1]	isoboldine	(XLIII)	72

FAMILY Plant species	Alkaloid(s) present Name(s)	Formula(e)	Ref.
LILIACEAE			
Gloriosa superba	colchicine[4]	(LXV)	31, 43, 44, 110
	N-formyl-*N*-deacetyl -colchicine	(LXVI)	44, 110
	2-demethyl colchicine	(LXVII)	44, 110
	lumicolchicine	(LXVIII)	44
LEGUMINOSAE			
Erythrina lithosperma	erythratidinone	(L)	15, 16
	3-demethoxyery-thratidinone	(LI)	15, 16
	erythraline[4]	(XLVI)	15, 16
	erysotrine	(XLVIII)	15, 16
E. fusca	erysotrine	(XLVIII)	15
Crotolaria walkeri[1]	crotaverrine[3]	(LXII)	160
	O-acetylcrotaverrine	(LXIII)	160
MORACEAE			
Broussonetia zeylanica[1] (= *Allaeanthus zeylanicus*)	8-hydroxyquinoline -4-carboxaldehyde[3,4]	(LXXI)	71
RUBIACEAE			
Mitragyna parvifolia	akuammigine	(LXXV)	149
	tetrahydroalstonine	(LXXVI)	149
	Uncarine C	(LXXVII)	149
	Uncarine D	(LXXVIII)	149
	Uncarine E	(LXXIX)	149
	Uncarine F	(LXXX)	149
	corynantheidol	(LXXXI)	149
	dihydrocorynantheol	(LXXXII)	149
	akuammigine *N*-oxide		
	Uncarine D *N*-oxide		
	Uncarine F *N*-oxide		149
	dihydrocorynantheol *N*-oxide		149
Uncaria thwaitesii[1]	Uncarine A	(LXXXVIII)	81-83
	mitraphylline[4]	(LXXXIV)	81-83
	roxburghine D	(LXXXIX)	81-83
Cinchona ledgeriana	quinine[2,4]	(XC)	171
	quinidine[2,4]		171
	5α-carboxystrictosidine	(XXIX)	36
RUTACEAE			
Atalantia ceylanica[1]	acridone alkaloid A[3]	(XCII)	52
	acridone alkaloid B[3]	(XCIII)	52
	atalanine[3]	(XCIV)	51
	ataline[3]	(XCV)	51
Glycosmis bilocularis[1]	glycorine	(XCVII)	22
	arborine	(XCVIII)	22
	dictamnine	(XCIX)	22
	skimmianine	(C)	22
	kokusaginine	(CI)	22
	arborinine	(CII)	22
	5-hydroxyarborinine[3]	(CIII)	22
Citrus decumana	serotonin[2]	(CIV)	38

[1]endemic to Sri Lanka
[2]alkaloids detected but not isolated
[3]new alkaloids
[4]pharmacologically active alkaloids.

Although Sri Lanka has a rich flora and alkaloids are of medicinal significance, it seems surprising that only a little effort had been directed towards the isolation of this important group of metabolites from local plants. Recently, a comprehensive phytochemical study of Sri Lanka plants had been presented.[159] This report contained only 2 alkaloid bearing species out of the 101 plant species that have been investigated. On the other hand, an extensive screening programme had shown that out of the 464 plants tested at least 201 contained alkaloids which is above the average incidence anticipated.[157,158] However, this is not unexpected from the plants of tropical region,[172] especially as the collections have been made mainly from alkaloid rich families.

The importance of research in the field of plant alkaloids with potential medicinal applications need not be overemphasized. Since at least 830 flowering plants are unique to the island, the prospects of obtaining new drugs from this source would appear to be good. It may therefore, seem strange that pharmacologists, unlike botanists and chemists in Sri Lanka have given little attention to native plants.

There is no good reason to believe that if plants are examined at random, the chemicals extracted from them would provide a useful collection of medicinal agents. However, if folkloric claims are used in conjunction with preliminary screening programmes there is a greater chance of obtaining new drugs from local plants.

Acknowledgements

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References

1. Abeywickrema, B. A. (1959). *Cey. J. Sci.* **2** : 120.
2. Abeywickrema, B. A., Dassanayake, M. D. & Fonseka, R. N. de (1964). *Proc. Internat. Symp. Med. Plants*, Kandy, Ceylon, p. 41.
3. Abeywickrema, B. A. (1975). *Proc. Workshop on Natural Products*, Colombo, Sri Lanka, p. 11.
4. Alston, A. H. G. (1931). *Handbook of the Flora of Ceylon*, Supplement 6, Dulau & Co., London.
5. Ameer-Ali, A. C. L. (1974). *Modern Ceylon Studies*, **5** : 93.
6. Amoroso, E. C. (1935). *Nature* (Lond.) **135** : 266.

7. AMUNUGAMA, H., BALASUBRAMANIAM, S., GUNATILAKA, A. A. L., SALAAM, A. S. A. & SOTHEESWARAN, S., Unpublished results.
8. AMUTHASAKARAN, N. & WANNIGAMA, G. P., (1969). *Proc. Cey. Assoc. Advmt. Sci.*, **25** : 94.
9. ANON. (1974). *Markets for Selected Medicinal Plants & their Derivatives*, Internat. Trade Centre UNCTAD/GATT, Geneva.
10. ATTYGALLE, J. (1917). *Sinhalese Materia Medica*, M. D. Gunasena & Co. Ltd., Colombo, Sri Lanka.
11. BANDARANAYAKE, W. M. & SULTANBAWA, M. U. S. (1969). *A list of Endemic Plants of Ceylon*, University of Sri Lanka.
12. BANDARANAYAKE, W. M., SULTANBAWA, M. U. S., WEERASEKARA, S. C. & BALASUBRAMANIAM, S. (1974) *The Sri Lanka Forester, XI* : 67.
13. BARTON, D. H. R. & COHEN, T. (1957). *Festschrift A. Stoll*, Birkmeier (Basel) p. 117.
14. BARTON, D. H. R., KIRBY, G. W. & TAYLOR, J. B. (1962) *Proc. Chem. Soc.*, 340.
15. BARTON, D. H. R., GUNATILAKA, A. A. L., LETCHER, R. M., LOBO, A. M. F.T. & WIDDOWSON, D. A. (1973). *J.C.S. Perkin I*, 874.
16. BARTON, D. H. R., GUNATILAKA, A. A. L. & LOBO, A. M. F. T. (1972). *Congresso National de Biochemica, IV* ; 25.
17. BATTERSBY, A. R., BURNETT, A. R. & PARSONS, P. G. (1969). *J. Chem. Soc. (C)*, 1193 and references cited therein.
18. BENTLEY, K. W., (1965). *The Alkaloids*, Part II, John Wiley & Sons Ltd., Great Britain.
19. BHAVANANDAN, V. P. & WANNIGAMA, G. P. (1960). *J. Chem. Soc.* 2368.
20. BISSET, N. G., HOUGHTON, P. J. & SHELLARD, E. J. (1974). *Phytochemistry*, **13** : 973.
21. BOMBARDELLI, E. (1977). *Proc. 3rd Asian Symp. Medicinal Plants & Spices*, Colombo, Sri Lanka.
22. BOWEN, I. H. & PERERA, K. P. W. C., Unpublished results.
23. BROWN, W. O. & SUD, L. (1945). *Amer. J. Chem. Path.* **15** ; 189.
24. BUCHI, J., AEBI, A., DEFLORIN, A. & HURNI, H. (1956). *Helv. Chim. Acta* 39 : 1676.
25. BUIL, L. B. (1967). *New South Wales Vet. Proc.* 3.
26. CASEY, R. C. D. (1960). *Indian J. Med. Sci.*, 14 : 590.
27. CAVE, A. & WANNIGAMA, G. P. (1972). *Ann. Pharmaceutiques Francaises* 30 : 535.
28. CHANDRASENA, J. P. C. (1935). *The Chemistry and Pharmacology of Ceylon and Indian Medicinal Plants*, H & C Press, Colombo, Ceylon.
29. CHOPRA, R. N., CHOPRA, I. C., HANDA, K. L. & KAPUR, L. D. (1958). *Chopra's Indigenous Drugs of India*, 2nd Ed., U. N. Dhur & Sons Private Ltd., Calcutta, India.
30. CHOPRA, R. N., NAYAR, S. L. & CHOPRA, I. C. (1956). *Glossary of Indian Medicinal Plants*, C.S.I.R., New Delhi, India, p. 111.
31. CLEWER, H. W. B., GREEN, S. J. & TUTIN, F. (1915). *J. Chem. Soc.* 835.
32. CORNER, E. J. H. (1977). *A Revised Handbook to the Flora of Ceylon*, Vol. I, Part II, University of Sri Lanka, p. 116.
33. COURMONT, P., MOREL, A., PERROT, L. & DENARD, F. (1936). *Compt. rend. Soc. Biol.* **122** : 113, 1110.
34. CULVENOR, C. C. J. (1968). *J. Pharm. Sci.* 57 : 1112.
35. DATTA, S. C. (1976). *J. Indian Drugs* (Bombay), Nov. Issue.
36. DE SILVA, K. T. D. & KALUARACHCHI, S. (1972). *Proc. Cey. Assoc. Advmt. Sci.*, **28** : 128.
37. DE SILVA, K. T. D. (1975). *Proc. Workshop on Natural Products*, Colombo, Sri Lanka, p. 138.
38. DHARMATILAKE, R. M. & KOTTEGODA, S. R. (1966). *Proc. Cey. Assoc. Advmt. Sci.* **22** : 8.
39. DOMINGUEZ, R. & ALTAMIRANO, F. (1877). *Gac. Med. Mexico* 12 : 77, through ref. 78.
40. DONALDSON, G. R., ATKINSON, M. R. & MURRAY, A. W. (1968). *Biochem. Biophys. Res. Commun.* **31** : 104.
41. DRAKE, K. N. & KIRYUTINA, N. I. (1954). *Farmakol. i Toksikol.* **17** : 39, through *Chem. Abs.* (1954) **48** : 13985 g.
42. DROST, K., MIROSLAWA, S. & KOWALESKI, Z. (1974). *Herba Pol.* 20 : 310, through *Chem. Abs.* (1975) **83** : 101 x.

43. DUNUWILLE, R., BALASUBRAMANIAM, K. & BIBILE, S. W. (1966). *Proc. Cey. Assoc. Advmt. Sci.* **22** : 7.
44. DUNUWILLE, R., BALASUBRAMANIAM, K. & BIBILE, S. W. (1968). *Cey. J. Med. Sci.*, **22** : 7.
45. FARNSWORTH, N. R. (1966). *J. Pharm. Sci.* **55** : 225.
46. FARNSWORTH, N. R. (1975). *Half-time Report of the Section-D submitted at the Natural Products Workshop*, Colombo, Sri Lanka.
47. FARNSWORTH, N. R. (1961). *Lloydia* **24** : 105.
48. FARNSWORTH, N. R., BINGEL, A. S., CORDELL, G. A., CRANE, F. A. & FONG, H. H. S. (1975). *J. Pharm. Sci.* **64** : 535.
49. FOLKERS, K. & MAJOR, R. T. (1937). *J. Amer. Chem. Soc.* **59** : 1580.
50. FONG, H. H. S., TIN-WA, M. & FARNSWORTH, N. R. *Phytochemical Screening*, Dept. of Pharmacognosy & Pharmacology, University of Illinois, Chicago, U.S.A.
51. FRASER, A. W. & LEWIS, J. R. (1973). *J.C.S. Chem. Comm.* 615.
52. FRASER, A. W. & LEWIS, J. R. (1973). *J.C.S. Perkin I*, 1173.
53. GAMES, D. E., JACKSON, A. H., KHAN, N. A. & MILLINGTON, D. S. (1974). *Lloydia* **37** : 581.
54. GELLERT, E. & RUDZATS, R. (1964). *J. Med. Chem.* **7** : 361.
55. GHOSAL, S., DUTTA, S. K. & BHATTACHARYA, S. K. (1972). *J. Pharm. Sci.* **61** : 1274.
56. GHOSAL, S., MAJUMDAR, S. K. & CHAKRABORTI, A. (1971). *Aust. J. Chem.* **24** : 2733.
57. GILBERT, B., BRISSOLESE, J. A., FINCH, N., TAYLOR, W. I., BUDZIKIEWICZ, H., WILSON, J. M. & DJERASSI, C. (1963). *J. Amer. Chem. Soc.* **85** : 1523.
58. GLICK, L. & MUMFORD, J. (1955). *Brit. Med. J.* **11** : 94.
59. GOONERATNE, B. W. M. (1966). *Brit. Med. J.* 1 : 1023.
60. GOSH, D. K. & MAJUMDAR, D. N. (1972). *Curr. Sci.* **41** : 578.
61. GOUTAREL, R. (1964). *Bull. Soc. Chim. France* 1665.
62. GOVINDACHARI, T. R. & PARTHASARATHY, P. C. (1970). *Ind. J. Chem.* **8** : 567.
63. GOVINDACHARI, T. R., PARTHASARATHY, P. C. & DESAI, H. K. (1971). *Ind. J. Chem.* 9 : 931, 1421.
64. GOVINDACHARI, T. R., PARTHASARATHY, P. C. & DESAI, H. K. (1972). *Ind. J. Chem.* 10 : 1117.
65. GOVINDACHARI, T. R., PARTHASARATHY, P. C. & DESAI, H. K., (1973). *Ind. J. Chem.* 11 : 1190.
66. GOVINDACHARI, T. R., PARTHASARATHY, P. C., RAJAGOPALAN, T. G., DESAI, H. K. & RAMACHANDRAN, K. S. (1975). *Ind. J. Chem.* **13** : 641.
67. GOVINDACHARI, T. R., VISWANATHAN, N., RADHAKRISHNAN, J., PAI, B. R., NATARAJAN, S. & SUBRAMANIAM, P. S. (1973). *Tetrahedron* **29** : 891.
68. GOVINDACHARI, T. R. (1967). *The Alkaloids* (Ed. MANSKE, R. H. F.) Academic Press, New York, **6** : 517 and references therein.
69. GREWAL, K. S. (1932). *J. Pharmacol.* **46** : 251.
70. GUNATILAKA, A. A. L., SIRIWARDENA, H. M. U., SOTHEESWARAN, S., & BALASUBRAMANIAM, S. (1976). *J. Nat. Sci. Coun., Sri Lanka* 4(2) : 163.
71. GUNATILAKA, A. A. L., PERERA, J. H. S. Q., SULTANBAWA, M. U. S., THOMSON, R. H. & BROWN, M. (1977). *Proc. 3rd Asian Symp. Medicinal Plants & Spices*, Colombo, Sri Lanka, Abs. No. 28.
72. GUNATILAKA, A. A. L. *and others*, Unpublished results.
73. GUNAWARDENA, Y. A. G. P., KANDIAH, S., KESAVAMOORTHY, S., SIRISENA, D. M., WIJESUNDERA, R. C. & WANNIGAMA, G. P. (1973). *Proc. Sri Lanka Assoc. Advmt. Sci.* **29** : 151.
74. GUROFF, G., DALY, J. W., JERINA, D., RENSON, J., WITKOP, B. & UDENFRIEND, S. (1967). *Science* **157** : 1524.
75. HAGINIWA, I. & HARADA, M. (1962). *Yakugaku Zasshi* **82** : 726, through *Chem. Abs.* (1962) **57** : 9145 d.
76. HALL, C. R. & PRAGER, R. H. (1969). *Aust. J. Chem.* **22** : 2437, 2627.
77. HARBORNE, J. B. (1973). *Phytochemical Methods*, Chapman & Hall, London.
78. HARGREAVES, R. T., JOHNSON, R. D., MILLINGTON, D. S., MONDAL, M. H., BEAVERS, W., BECKER, L., YOUNG, C. & RINEHART, K. L. (1974). *Lloydia* **37** : 569.

79. HEGNAUER, R. (1963). *Chemical Plant Taxonomy* (Ed. SWAIN, T.) Academic Press Inc. New York, p. 389.
80. HEGNAUER, R. (1966). *Comparative Phytochemistry* (Ed. SWAIN, T.) Academic Press, London, p. 211.
81. HERATH, W. H. M. W., (1975). *Annual Report on the Chemical Investigation of Endemic Plants of Ceylon*, Dept. of Chemistry, University of Sri Lanka, Peradeniya, p. 101.
82. HERATH, W. H. M. W. (1976). *ibid.* p. 43.
83. HERATH, W. H. M. W. (1977). *M.Sc. Thesis*, University of Sri Lanka, Peradeniya Campus.
84. HILL, K. R. (1960). *Proc. Roy. Soc. Med.* **53** : 281.
85. HUBER, H. (1973). *A Revised Handbook of the Flora of Ceylon*, Apothecaries, Colombo, **1** : 1-27.
86. HUBER, H. (1973). *ibid.*, p. 31.
87. HUI, W. H., LOO, S. N. & ARTHUR, H. R. (1965). *J. Chem. Soc.* 2285.
88. INUBUSHI, Y., FURUKAWA, H. & JU-ICHI, M. (1970). *Chem. Pham. Bull.*, **18** (10): 1951.
89. JANOT, M. M., LEBOEUF, M., CAVE, A., WIJESEKERA, R. O. B. & GOUTAREL, R. (1968). *Compt. rend.* **267C** : 1050.
90. JAYATILAKA, A. D. P., BALASUBRAMANIAM, K., DUNUWILLE, R. & BIBILE, S. W. (1967). *Cey. J. Med. Sci.* **16** : 11.
91. JAYAWEERA, D. M. A. (1943). *Trop. Agriculturist* 99 : 91.
92. JOHNE, S. & GROGER, D. (1972). *Die Pharmazie* 4 : 195.
93. JOHNSON, I. S., SVOBODA, G. H., POORE, G. A. & BODER, G. B. (1966). *Proc. Cancer Chemotherapy*, Takeda Int. Conf. Osaka (Publ. 1967) (Ed. Goldin, A.) Merizen Co. Ltd., Tokyo.
94. KIKUI, S. *and others* (1956). *Kitasata Arch. Expt. Med.* **29** : 65, through *Chem. Abs.* (1957) **53** : 19128 d.
95. KIRTIKAR, B. D. & BASU, L. M. (1935). *Indian Medicinal Plants*, (Ed. BASU, L. M.) Vol. II, Allahabad, India, p. 1573.
96. KOO, W-Y (1964). *Proc. Internat. Symp. Medicinal Plants*, Kandy, Sri Lanka, p. 93.
97. KOTTEGODA, S. R. (1959). *Proc. Cey. Assoc. Advmt. Sci.* **15** : 5.
98. KOWALEWSKI, Z., WLODZIMIERZ, K. & ILONA, M. (1972). *Arch. Immunol. Ther. Exp.* **20** : 353, through *Chem. Abs.* (1972). **77** : 135606 n.
99. KUMAR, V., PERERA, L. F., SULTANBAWA, M. U. S. & WANNIGAMA, G. P. (1973). *Proc. Cey. Assoc. Advmt. Sci.* **29** : 138.
100. KUPCHAN, S. M., DOSKOTCH, R. W. & VANEVENHOVEN, P. W. (1964). *J. Pharm. Sci.* **53** : 343.
101. LEBOEUF, M., CAVE, A., GOUTAREL, R. & WANNIGAMA, G. P. (1972). *Ann. Pharmaceutiques Francaises* 837.
102. LEBOEUF, M., CAVE, A., GOUTAREL, R. & WANNIGAMA, G. P., (1972). *Phytochemistry* **11** : 843.
103. LEETE, E. (1963). *Biogenesis of Natural Compounds* (Ed. BERNFELD, P.) Pergamon Press, New York.
104. LEETE, E. & WEMPLE, J. N. (1969). *J. Amer. Chem. Soc.* **91** : 2698.
105. LEHMAN, A. J. (1937). *J. Pharmacol.* **60** : 69.
106. LEONARD, N. J., (1960). *The Alkaloids* (Ed. MANSKE, R. H. F.) Academic Press, New York, **6** : 35.
107. MAC MILLAN, H. F. (1946). *Tropical Planting & Gardening*, Longmans, London.
108. MASSION, L. (1934). *Arch. Internat. Pharmacodyn*, **48** : 217 through *Chem. Abs.* (1935) **29** : 884.
109. MATTOCKS, A. R. (1968). *Nature* (Lond.) **217** : 723.
110. MATUROVA, M., LANG, B., REICHSTEIN, T. & SANTAVY, F. (1959). *Planta Med.* **7** : 298.
111. MCGREGOR, I. S. & LOEWENSTEIN, A. (1944). *Lancet*, **11** : 566.
112. MEHRA, P. N., BHATNAGER, J. K. & HANDA, S. S. (1970). *Res. Bull. Panjab University* (N. S.) **20** : 261.
113. MERCK INDEX (1968). 8th Ed., Merck & Co. Ltd., U.S.A. p. 143.

114. MEYERS, F. H., JAWETZ, E. & GOLDFIEN, A. (1974). *A Review of Medical Pharmacoloyg*, 4th Ed., Lange Medical Publications, California, p. 473.
115. MILLAT, L. (1946). *Ann. Pharm. France*, 4 : 27, through *Chem. Abs.* (1947) **41** : 1228.
116. MULCHANDI, N. B., IYER, S. S. & BADHEKA, L. P. (1971). *Chem. Ind.* 505.
117. NAKASATO, T., ASADA, S. & KOEZUKA, Y. (1966). *Yakagaku Zasshi* **86** : 129, through *Chem. Abs.* (1966) **64** : 19695 f.
118. NOBLE, R. L. (1965). *Pharmacology of Oriental Plants* (Ed. CHEN, K. K., MUKARJI, B. & VOLICER, L.) Pergamon Press, Oxford, p. 61.
119. PAECH, K. & TRACY, M. V. (1955). *Modern Methods of Plant Analysis*, Vol. 4, Springer Verlag, p. 373.
120. PAO, Y-T. (1960). *Chem. Abs.* **54** : 19826 b.
121. PERROT, E., RAYMOND-HAMET & MILLAT, L. (1936). *Bull. Acad. Natl. Med.* 116 : 266, through *Chem. Abs.* (1937) **31** : 5875.
122. PERROT, E., RAYMOND-HAMET & LARRIEU, P. (1930). *Bull. Sci. Pharmacol.* **37** : 401.
123. PERROT, E., RAYMOND-HAMET & MILLAT, L. (1936). *Bull. Sci. Pharmacol.* **43** : 694, through *Chem. Abs.* (1937) **31** : 2290.
124. PHILLIPSON, J. D. & HEMINGWAY, S. R. (1975). *Phytochemistry* **14** : 1855.
125. PHILLIPSON, J. D. & HEMINGWAY, S. R. (1975). *J. Chromatography* 105 : 63.
126. PHILLIPSON, J. D., TEZCAN, I. &. HYLANDS, P. T. (1974). *Planta Medica* **25** : 301.
127. QAYUM, A., KHANUM, K. & MIANA, G. A. (1971). *Pak Med. Forum* **6** : 35.
128. QAYUM, A. (1967). *Pakistan J. Sci. & Ind. Res.* 10 : 34, through *Chem. Abs.* (1968) **68** : 20205 y.
129. RAFFAUF, R. F. (1970). *A Handbook of Alkaloids and Alkaloid Containing Plants*, Wiley-Interscience, New York.
130. RAHAMN, A.-U., BASHA, A. & GHAZALA, M. (1977). *Proc. 3rd Asian Symp. Medicinal Plants & Spices :* Abs. No. 30.
131. RAMIREZ, E. & RIVERO, M. D. (1935). *Annales Inst. Biol.* (Mexico) **6** : 301.
132. RAO, K. V., WILSON, R. A. & CUMMINGS, B. (1971). *J. Pharm. Sci.* 60 : 1725.
133. RATNAGIRISWARAN, A. N. & VENKATACHALAM, K. (1935). *Ind. J. Med. Res.* **22** : 433.
134. RAYMOND-HAMET (1933). *Compt. Rend. Soc. Biol.* 114 : 692.
135. ROOK, A. (1965). *Brit. J. Derm.* **77** : 114.
136. ROOK, A. (1965). *Brit. Med. J.* **1** : 609.
137. SAXTON, J. E. (1965). *The Alkaloids* (Ed. MANSKE, R.H.F.) Academic Press, New York, **8**: 59.
138. SAXTON, J. E. (1972). *The Alkaloids*, Vol. 2, Specialist Periodical Report, The Chemical Society, London, p. 74, and references therein.
139. SCHLITTLER, E. (1965). *The Alkaloids* (Ed. MANSKE, R.H.F.) Academic Press, New York, **8** : 287.
140. SCHLITTLER, E. (1971). *The Alkaloids*, Vol. 1, Specialist Periodical Report, The Chemical Society, London.
141. SCHLITTLER, E. (1971). *ibid.* p. 489.
142. SCHOENTAL, R. (1960). *Proc. Roy. Soc. Med.* 53 : 284.
143. SCHOENTAL, R. & MATTOCKS, A. R. (1960). *Nature* (Lond.) **185** : 842.
144. SHAMMA, M., Personal Communication to Prof. S. BALASUBRAMANIAM.
145. SHARMA, R. K. & HEBBORN, P. (1968). *J. Medicinal Chem.* **11** : 620.
146. SHELLARD, E. J., PHILLIPSON, J. D. & GUPTA, D. (1969). *Planta Medica* 17 : 146.
147. SHELLARD, E. J. & HOUGHTON, P. J. (1972). *Planta Medica* 21 : 16 ; (1973) **22** : 97.
148. SHELLARD, E. J. & HOUGHTON, P. J. (1974). *ibid.* **23** : 80.
149. SHELLARD, E. J. & HOUGHTON, P. J. (1974). *ibid.* **23** : 172.
150. SHELLARD, E. J. & HOUGHTON, P. J. (1975). *ibid.* **24** : 341.
151. SHIVPURI, D. N., MENON, M. P. & PRAKASH, D. (1968). *J. Assoc. Physicians* (India) **16** : 9 ; (1969) *J. Allergy* **43** : 145.
152. SIRIWARDENA, H. M. U., GUNATILAKA, A. A. L., SOTHEESWARAN, S., JAYASURIYA, V. S. C. DE S. & BALASUBRAMANIAM, S. (1975). *Proc. Sri Lanka Assoc. Advmt. Sci.* **31** : 61.

153. SIUDA, J. F. (1974). *Lloydia* **37** : 501.
154. SUBBARATNAM, A. V. (1951). *Chem. Abs.* **45** : 2152 ; (1952). *J. Sci. Ind. Res.* **11B** : 446 ; (1954) *ibid.* **13B** : 67.
155. SULLIVAN, H. R., BILLINGS, R. E., OCCOLOWITZ, J. L., BOAZ, H. E., MARSHALL, P. J. & MCMAHON, R. E. (1970). *J. Medicinal Chem.* **13** : 904.
156. SULTANBAWA, M. U. S. & WEERASEKARA, S. C. (1960). *Distribution of Endemic Plants in Ceylon*, University of Sri Lanka.
157. SULTANBAWA, M. U. S., WANNIGAMA, G. P., BANDARANAYAKE, W. M., KUMAR, V., GUNATILAKA, A. A. L., MARIKAR, F. A., BALASUBRAMANIAM, S. & ARSSECULARATNE, S. N. (1978) *Lloydia*, in press.
158. *idem.* (1976). *Proc. Xth IUPAC Symp. on Chemistry of Natural Products*, New Zealand, Abs. No. D 23.
159. SULTANBAWA, M. U. S. (1977). *Proc. 3rd Asian Symp. on Medicinal Plants & Spices*, Colombo, Sri Lanka.
160. SURI, K. A., SAWHNEY, R. S. & ATAL, C. K. (1976). *Ind. J. Chem.* **14B** : 471.
161. SVOBODA, G. H. (1966). *Antitumoral Effects of Vinca rosea Alkaloids* (Ed. GARATTINI, L. & SPROSTON, E. M.) Internat. Congress Ser. No. 106, Medical Foundation, New York, N.Y. pp. 9-28.
162. TAYLOR, W. I. & FARNSWORTH, N. R. (1973). *The Vinca Alkaloids*, Marcel Dekker Inc., New York.
163. THORNBER, C. W. (1970). *Phytochemistry* **9** : 157.
164. TRIMEN, H. (1893-1900). *A Handbook of Flora of Ceylon*, Vol. I to V, Dalau & Co., London
165. VAN TAMELEN, E. E., HAARSTAD, V. B. & ORVIS, R. L. (1968). *Tetrahedron* **24** : 687.
166. WAALKES, T. P., SJOERDSMA, A., CREVALING, C. R., WEISSBACH, H. & UDENFRIEND, S. (1958). *Science* **127** : 648.
167. WANNIGAMA, G. P., personal communication.
168. WATT, J. M. & BREYER-BRANDWIJK, M. G. (1962). *The Medicinal & Poisonous Plants of Southern and Eastern Africa*, Livingstone, Edinburgh & London.
169. WEISSBACH, H., WAALKES, T. P. & UDENFRIEND, S. (1957). *J. Biol. Chem.* **230** : 865.
170. WIJESEKARA, R. O. B. & FONSEKA, K. H. (1974). *J. Nat. Sci. Coun., Sri Lanka* **2**(1) : 35.
171. WIJESEKARA, R. O. B., RAJAPAKSE, L. S. & CHELVARAJAN, D. W. (1976). *J. Chromatography* **121** : 388.
172. WILLAMAN, J. J. & LI, H. L. (1963). *Economic Botany* **17** : 780.