THE CHEMOTAXONOMIC SIGNIFICANCE OF ALKALOIDS IN THE NAUCLEEAE S.L. (RUBIACEAE)

J. DAVID PHILLIPSON

Department of Pharmacognosy, The School of Pharmacy, University of London 29–39, Brunswick Square, London, WC1N 1AX, U.K.

SARAH R. HEMINGWAY[1]

Department of Pharmacognosy, The University of Manchester, Manchester, M13 9PL, U.K.

COLIN E. RIDSDALE

B. A. Krukoff Botanist of Malesian Botany, Rijksherbarium, Schelpenkade 6, Leiden, The Netherlands

ABSTRACT.—The delimitation and subdivision of the tribe Naucleeae s.l. (Rubiaceae) are briefly reviewed and alkaloids isolated from members of the tribe are summarized. Revision of the tribe s.l. has resulted in the recognition of 21 genera placed in three subtribes. *Cephalanthus* has been removed to a separate tribe, Cephalantheae, while *Mitragyna* and *Uncaria* have been transferred to a new subtribe, Mitragyninae, within the tribe Cinchoneae. The results of alkaloid screening on some 121 small samples, mainly leaves, of herbarium material, representing 18 genera of the Naucleeae s.s., *Cephalanthus* and *Mitragyna*, are presented. The majority of genera screened from the subtribes Adininae and Naucleinae were either negative or contained pyridino-indoloquinolizidinones and/or harmane, as indicated by thin layer chromatography. Heteroyohimbine and oxindole alkaloids were rare in genera of the Naucleeae s.s. but were widespread in genera of the Cephalantheae and Mitragyninae. Twenty alkaloids were identified from *Cephalanthus* species and eighteen alkaloids from *Mitragyna* species. The chemotaxonomic significance of these results is discussed.

TAXONOMIC ASPECTS

Most of the Rubiaceae with flowers borne in globose heads and with ovaries containing numerous ovules per locule were placed initially in the heterogeneous genus '*Nauclea*'. Gradually, several genera became recognized and they were placed in the tribe Naucleeae of the subfamily Cinchonoideae. Successive authors have contributed to a clarification of the delimitation and subdivision of these genera and the considerable taxonomic problems associated with many of the published generic names have been reviewed by Bakhuizen f. (1).

The condensed inflorescence structure, sometimes coupled with partially or totally connate ovaries or calyces, results in few characters being available for taxonomic classification (2). The most important characters are the fused or free nature of the ovaries, the form of stigma, the form of the calyx (quite complex within the Naucleeae), the placentation, and the form of the seeds. Different authors have placed various weightings on these characters. Schumann, 1891 (3), and Haviland, 1897 (4), in their revisions, recognized 11 genera including *Cephalanthus, Mitragyna* and *Uncaria*. Both of these revisions included the Madagascan genus *Paracephaelis*, which has since been transferred to the Gardenieae. The Pacific genus *Sarcopygme*, which was discovered after the above revision, has since been transferred to the Morindeae.

Haviland's revision (4) differed slightly from that of Schumann (3), particularly in recognizing *Mitragyna* and *Uncaria* as composing two separate subtribes. Both authors considered *Cephalanthus* to be closely related to *Neonauclea*. Schumann split the Naucleeae into two groups, depending upon whether the ovaries were free or fused, whereas Haviland's classification placed more emphasis on the nature of the stigma. A schematic representation of the classifications

[1]Present address: Fisons Ltd., Pharmaceutical Division, Loughborough, Leicestershire, U.K.

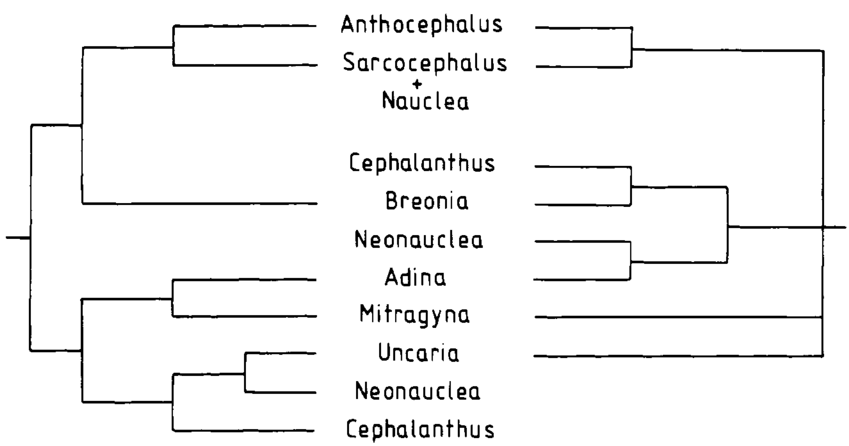
of Haviland and of Schumann is given in figure 1. Subsequent authors considered the tribe to be natural (5, 6) and it has even been raised to family level.

Bremekamp (7), however, questioned the homogeneity of the tribe and restricted it to *Nauclea* and *Sarcocephalus*, transferring the other genera to the neighbouring tribe Cinchoneae. He was uncertain regarding the position of *Cephalanthus* and was even doubtful as to whether the genus could be retained in the subfamily Cinchonoideae. *Cephalanthus* has now been removed from the Naucleeae and has been placed in a separate tribe, Cephalantheae (8).

Ridsdale (9) revised the genera *Mitragyna* and *Uncaria* and has transferred them from the Naucleeae to the Cinchoneae but has placed them in a separate subtribe, Mitragyninae, and a relationship has been suggested between these two genera and *Corynanthe*, *Pansinystalia* and possibly *Hymenodictyon*. However, it is difficult to evaluate relationships with other members of the Cinchoneae due to the absence of any monographic revision of the group.

FIGURE 1

Schematic representation of relationships between the genera of the Naucleeae



SCHUMANN, K. 1891 (3) HAVILAND, G. D. 1897 (4)

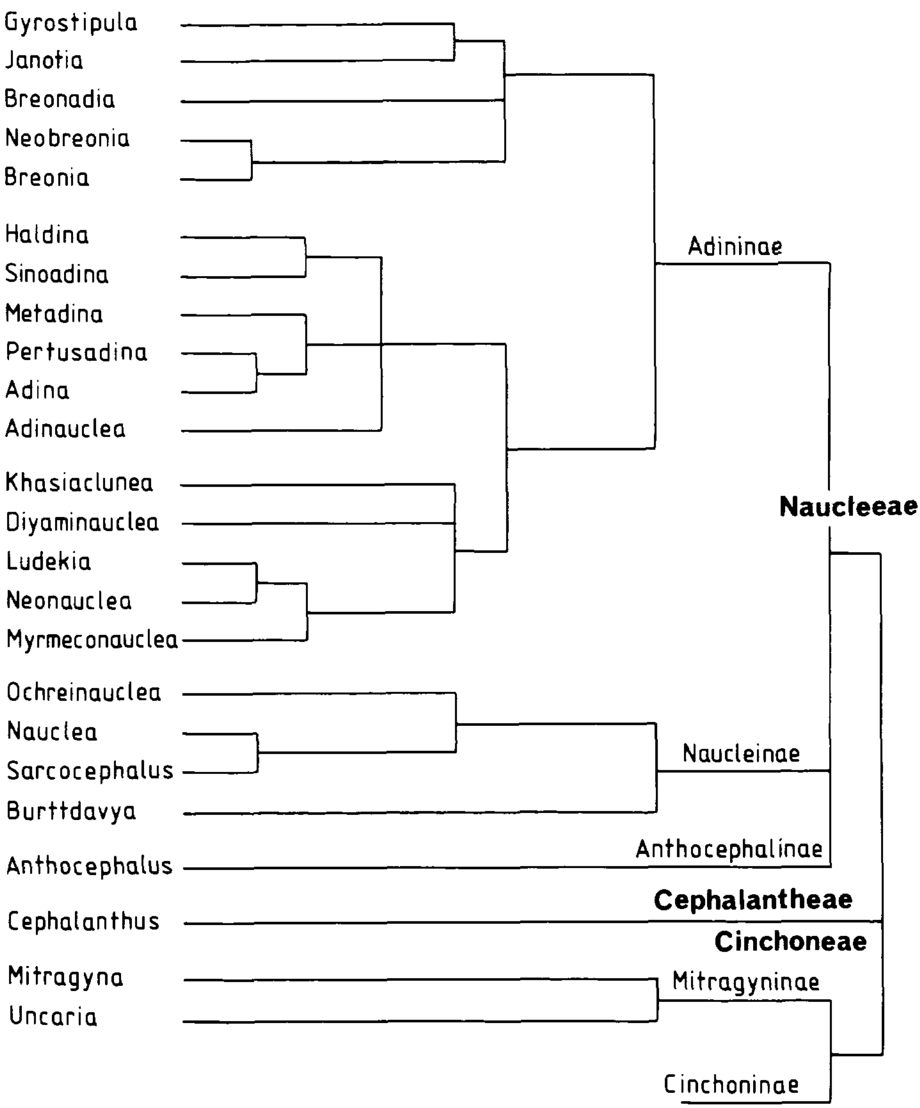
The remaining genera within the Naucleeae s.s. have been revised during the compilation of Flora Malesiana (2, 10). The Madagascan *Gyrostipula*, *Janotia* and *Neobreonia* and the African *Burttdavya* were discovered after 1900 and hence did not feature in the early revisions. New genera have been created in order to accommodate species which were previously included in a heterogeneous '*Adina*' and also segregates from *Neonauclea* and *Nauclea*. In all, some 21 genera have been placed in three subtribes which have only a low level of relationship to each other. The relationships between the genera in these three subtribes Adininae (16 genera, seven being new), Naucleinae (4 genera, one being new) and Anthocephalinae (1 genus), which comprise the Naucleeae s.s. (2), together with *Cephalanthus*, *Mitragyna* and *Uncaria*, which comprise the Naucleeae s.l., are shown in figure 2.

ALKALOIDS OF THE NAUCLEEAE S.L.

Alkaloids have been obtained from a number of genera in the Rubiaceae and the present knowledge has been reviewed recently (11). The Naucleeae s.l. include several alkaloid-yielding genera, viz. *Adina, Anthocephalus, Nauclea, Sarcocephalus, Cephalanthus, Mitragyna* and *Uncaria*. Therefore, it was considered possible that alkaloid content might prove to be a useful character for

FIGURE 2

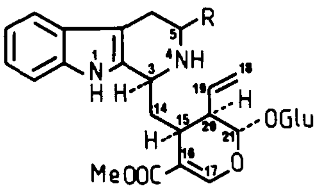
Schematic representation of relationships between the genera of the Naucleeae



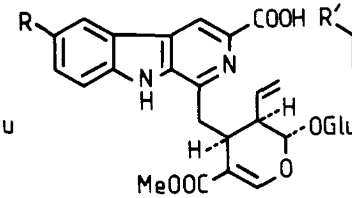
RISDALE, C.E. 1978 (2)

consideration by taxonomists attempting to resolve the classification of members of the Naucleeae and related genera (12). Apart from a few simple pyridine derivatives isolated from *Nauclea* and β-carbolines from *Nauclea* and *Uncaria* species, the majority of alkaloids are apparently derived from condensation of either tryptamine or tryptophan with the monoterpene glucoside secologanin via intermediates such as strictosidine (**1**, R=H, C–3 H α) or presumably 5-carboxystrictosidine (**1**, R=COOH, C–3 H α) (11).

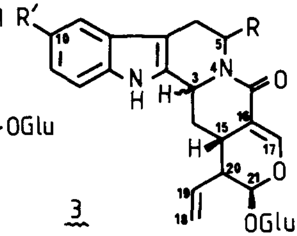
Only three species of the subtribe Adininae (Naucleeae s.s.) have been reported to contain alkaloids, viz. *Pertusadina euryncha* (Miq.) Ridsd. (syn. *Adina rubescens* Hemsl.), *Haldina cordifolia* (Roxb.) Ridsd. (syn. *Adina cordifolia* Hook.), and *Neonauclea lanceolata* (Bl.) Merr. (syn. *Neonauclea schlechteri* (Val.) Merr. and Perry). The alkaloids isolated from *Pertusadina euryncha* include the glycosidic



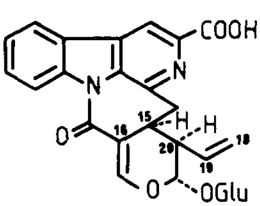
1



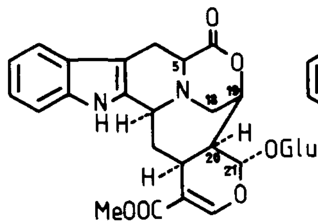
2



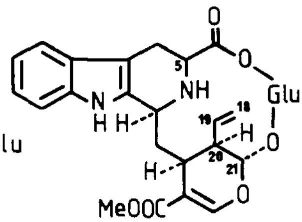
3



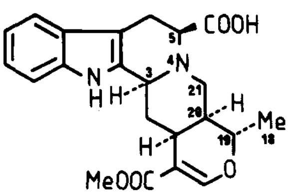
4



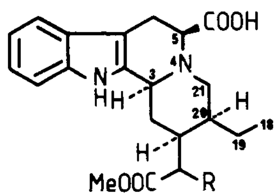
5



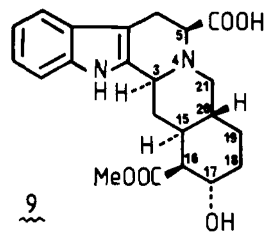
6



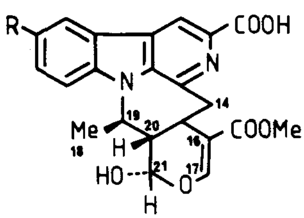
7



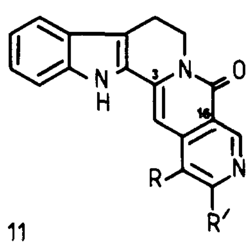
8



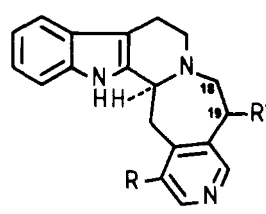
9



10



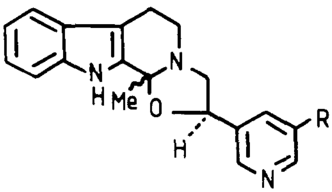
11



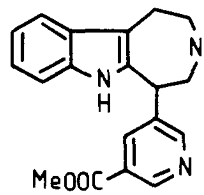
12

alkaloids 5-oxostrictosidine (**1**, R=0, C-3 H α) (13), desoxycordifoline (**2**, R=H) (14), vincoside lactam (**3**, R=R[1]=H), rubescine (caffeic acid ester of **3**), 10-β-glucosyloxyvincoside lactam (**3**, R=H, R[1]=glucosyloxy-) (15, 16, 17), 3α- and 3β-carboxyvincoside lactam (**3**, R=COOH, R[1]=H) (18), desoxycordifoline lactam (**4**) (17), rubenine (**5**) (19), macrolidine (**6**) (20) and the non-glycosidic alkaloids 5-β-carboxytetrahydroalstonine (**7**) (21), adirubine (**8**, R=CH_2OH) (22), anhydro-adirubine (**8**, R=CH_2) (**23**) and 5 β-carboxycorynanthine (**9**) (20, 24). *Haldina cordifolia* contains alkaloids either identical or very similar to *Pertusadina euryncha*; cordifoline (**2**, R=OH) (25, 26), 10-desoxycordifoline (**2**, R=H) (25, 26), 3α- and 3 β-tetrahydrodesoxycordifoline lactam (**3**, R[1]=H, R=COOH) (27), adifoline (**10**, R=OH) and 10-desoxyadifoline (**10**, R=H) (26, 28) have been obtained. The isolation of gambirine (i.e. 9-hydroxydihydrocoryantheine, **22**, R=OH, R[1]=ethyl, C-3 H α, C-20 H β) from *Neonauclea lanceolata* has been reported (29).

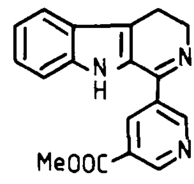
In the subtribe Naucleinae (Naucleeae s.s.), alkaloids have been reported



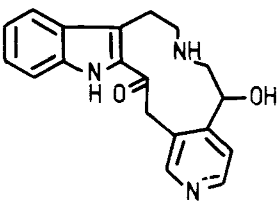
13



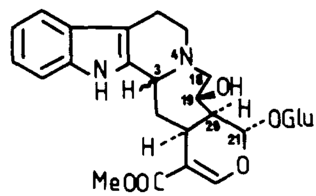
14



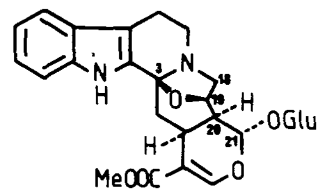
15



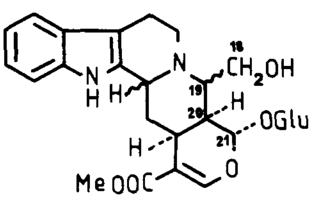
16



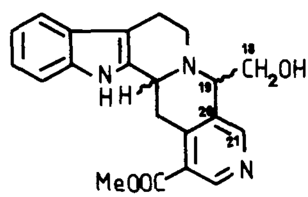
17



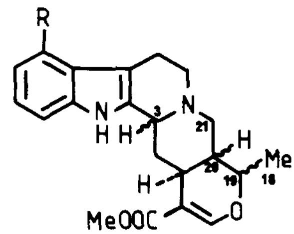
18



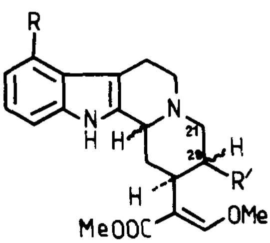
19



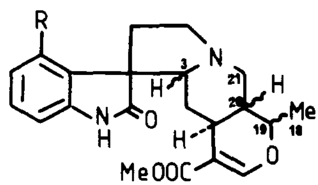
20



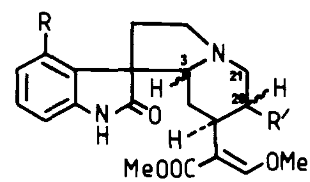
21



22



23



24

from *Sarcocephalus latifolius* (Smith) Bruce (syn. *Nauclea latifolia* (Smith) and from three species of *Nauclea*. Strictosidine lactam (**3**, $R=R^1=H$, C–3 H α) (30, 31), angustine (**11**, $R=CH=CH_2$, $R^1=H$) (32), angustoline (**11**, $R=CHOH$, R^1-H) (32), nauclefine (**11**, $R=R^1=H$) (32), naucletine (**11**, $R=COMe$, $R^1=H$) (32), descarbomethoxy-nauclechine (**12**, $R=H$, $R^1=OH$) (33) and naufoline (**12**, $R=R^1=H$, Δ 18) have been isolated from *Sarcocephalus latifolius*. *Nauclea diderrichi* has yielded a number of pyridine-indole alkaloids including 3 α- and 3 β-naucleonine (**13**, $R=H$), 3 α- and 3β-naucleonidine (**13**, $R=COOMe$), dimeric alkaloid ND 363 B (2 units of **13**), nauclederine (**14**), nauclechine (**12**, $R=COOMe$, $R^1=H$), naucledine (**15**), nauclexine (**16**), 3 α-dihydrocadambine (**17**, C–3 H α), and ND–370 (a nonglycosidic alkaloid structurally similar to cadambine (**18**) (34–36). Nauclefine (=parvine) (**11**, $R=R^1=H$) has been isolated from *Nauclea parva* Merr. (37) and angustine (**11**, $R=CH=CH_2$, $R^1=H$) from *Nauclea orientalis* L. (syn. *N. coadunata* Roxb. ex J. E. Smith) (38).

One species, *Anthocephalus chinensis* (Lamk.) A. Rich. ex Walp. (syn. *A. cadamba* Miq.), from the subtribe Anthocephalinae (Naucleeae s.s.) has yielded cadambine (**18**) (39), 3α- and 3β-dihydrocadambine (**17**) (39), 3α- and 3β-dihydroisocadambine (**19**) (40, 41), cadambine and isocadamine (**20**) (42).

In the Naucleeae s.l., alkaloids have been reported from *Cephalanthus* (43), *Mitragyna* (44) and *Uncaria* (45). The major alkaloids from these genera are of the heteroyohimbine-(**21**, **22**) and oxindole-types (**23**, **24**), although other structural types such as pyridino-indoloquinolizidinones (**11**) are also known.

EXPERIMENTAL

PLANT MATERIAL.—Some 121 small samples of mainly leaf material, but also including some bark, flower, fruit, stem, twig and wood samples, obtained from herbarium specimens representing genera of the Naucleeae s.l., were available for chemical study. The samples extracted are listed in table 1, which includes species name, collector's or herbarium number, geographical origin and date of collection.

EXTRACTION OF ALKALOIDS, CHROMATOGRAPHIC AND SPECTROSCOPIC IDENTIFICATIONS.—The extraction method was the same as that described previously (45). Methods of alkaloid identification by a combination of chromatographic and spectroscopic techniques were identical to those previously published (46).

RESULTS

The results of the alkaloid screening are listed in table 1 together with the details of the samples extracted. Table 1 is arranged in order of Ridsdale's revision of the Naucleeae (figure 2) (2). The weights of plant material available ranged from 120 mg to 11.6 g (only 9 samples were in excess of 7.0 g). In general the alkaloid tests on the Naucleeae s.s. gave either negative or slightly positive reactions to Dragendorff's reagent, whereas the Cephalantheae and Mitragyninae gave stronger reactions. The results are summarized in table 2.

DISCUSSION

One hundred twenty one small samples of either leaf, stem wood or bark, flower, fruit, or twig herbarium material have been examined for non-quaternary non-glycosidic indole alkaloids. Species representing 14 of the 16 genera of the Naucleeae-Adininae were screened, but samples of *Janotia* and *Adinauclea* were not available. The majority of the Adininae which were extracted contained either small amounts of unidentified Ehrlich-positive compounds, harmane and/or pyridino-indoloquinolizidinones (**11**), as indicated by tlc, or were negative in their reaction to alkaloid tests. The failure to detect glycosidic alkaloids related to strictosidine (**1**, R=H, C-3 H α), e.g. types **1–6**, **10**, **17**, **18**, can be attributed, in part, to the extraction method which was used for the isolation of non-glycosidic non-quaternary alkaloids, e.g., the heteroyohimbine- (**21**, **22**) and oxindole-types (**22**, **24**). The isolation of pyridino-indoloquinolizidinone-type alkaloids (**11**), such an angustine (**11**, R=CH=CH$_2$, R^1=H), may be due to the use of ammonia in the extraction procedure and probably indicates the presence of strictosidine-type alkaloids (**1**) or the lactams (**3**) in the plant material (38). Pyridino-indoloquinolizidinone alkaloids (**11**) and/or harmane were detected in *Gyrostipula* (1 species), *Breonadia* (1 species), *Breonia* (2 species), *Sinoadina*[1] (1 species), *Metadina* (1 species), *Pertusadina*[1] (2 species), *Adina* (1 species), *Khasiaclunea*[1] (1 species), *Ludekia*[1] (1 species), *Neonauclea* (26 samples representing 18 species) and *Myrmeconauclea* (1 species) (tables 1 and 2). *Neonauclea lanceolata* (syn. *Neonauclea schlechteri*) (TGH 10512) contained gambirine (**22**, R=OH, R^1= ethyl, C-3 H α, C-20 H β). This finding supports the previous isolation of this alkaloid in 0.02% yield from the leaves of this species. Unidentified alkaloids were detected in 21 of the 38 samples of *Neonauclea*, e.g. *N. lanceolata* ($M^{+\cdot}$, *m/z* 404), *N. gordoniana* (NGF 33405), *N. paracyrtopoides* (NBFD 10425) and *N. philippinensis* (Bur. Sci. 1526) (tables 1 and 2).

[1]New genera (2).

TABLE 1. The alkaloids of species of the Naucleeae s.l.: sample data and alkaloid identifications.

Genera and species[a]	Collector's number[b]	Geographical origin	Date of collection	Alkaloids identified[c]
NAUCLEEAE DC. ex Miq.				
ADININAE Ridsd.				
Gyrostipula foveolata (Capuron) Leroy.... (*Neonauclea foveolata* Capuron)	Humbert and Capon 25383	Madagascar	1950	ag (T), al (T)
Breonadia microcephala (Del.) Ridsd......	SF 4587	Madagascar	2/1952	ag (T), al (T), ha (T), Ehr
B. microcephala (*Adina lasiantha* K. Schum.)........	Stolz 408	Malawi	11/1910	ha (T), Ehr
B. microcephala (*Adina comorensis*).......	d'Alleizette 3004	Comor Is.	—	Ehr
B. microcephala (*Cephalanthus spathelliferus* Baker)........	Lam and Meeuse 6133	Madagascar	12/1938	ha (T), Ehr
Neobreonia decaryana Homolle (Ridsd.)... (*Breonia kiliravina* Homolle)	SF 11063	Madagascar	10/1934	- ve
N. decaryana (*Breonia decaryana*).........	d'Alleizette 3000	Madagascar	—	- ve
Breonia boivinii Havil..........	RN 6234	Madagascar	2/1954	- ve; tw, - ve
B. perrieri Homolle..........	HLB 137440	Madagascar	2/1953	ag (T), al (T), unident (T)
B. sphaerantha (Baill.) Homolle ex Ridsd..........	Hilderbrandt 3309	Madagascar	1880	ag (T), al (T), ad (T), ha (T), 2 unident. (T)
Breonia sp..........	SF 27049	Madagascar	11/1966	- ve
? *Breonia* sp..........	SF 10098	Madagascar	5/1954	2 unident (T)
Haldina cordifolia (Roxb.) Ridsd.......... (*Adina cordifolia* Hook. f. and Thoms)	—	India	—	Ehr
H. cordifolia (*A. cordifolia*)..........	Chand 2986	India	3/1950	- ve
H. coridfolia (*A. cordifolia*)..........	Pierre 1707	Indo-China	3/1877	3 unident. (T)
H. cordifolia (*A. cordifolia*)..........	—	Bogor, W. Java	1973	1 unident. (T)
Sinoadina racemosa (Sieb. and Zucc.) Ridsd.......... (*Adina racemosa* Miq.)	HLB 908.210,529	Japan	—	ag (T), al (T), ha (T), Ehr
Metadina trichotama (Zoll. and Merr.) Bakh. f..........	Pierre 1226	Indo-China	3/1866	ag (T), al (T), ad (T), ha (T), unident. (T); st, ag (T), al (T)

Pertusadina euryncha (Miq.) Ridsd. (*Adina rubescens* Hemsl.)	Kostermans 7046	Borneo	5/1952	ag (T), al (T), ad (T), ha (T); tw, unident. (T); stw, unident. (T); ba, unident. (T)
P. euryncha	Kostermans S 97	Sumatra	2/1957	ag (T), al (T), ad (T)
P. multifolia (Havil.) Ridsd. (*Metadina multifolia* Ridsd.)	Van Royen 5291	New Guinea	1/1955	ag (T), al (T), ad (T), ha (T)
Adina pilulifera (Lamk.) Franchet ex Drake (*A. globiflora* Salisb.)	Lan 20171	China	7/1932	ag (T), al (T), ad (T), ha (T), Ehr
A. rubella Hance	Fan and Li 120	China	7/1935	unident. (T)
Khasiaclunea oligocephala (Havil.) Ridsd. (*Adina oligocephala* Hav.)	Griffith 2751	India	—	ag (T), al (T), ha (T), 2 unident. (T)
Diyaminauclea zeylanica (Hook. f.) Ridsd. (*Neonauclea zeylanica* Merr.)	—	Sri Lanka	—	- ve
Ludekia bernardoi (Merr.) Ridsd. (*Neonauclea bernardoi* Merr.)	Kostermans 6976	Borneo	5/1952	ag (T), al (T), ad (T), ha (T); st ba, unident.; st w, unident.
Neonauclea acuminata Ridsd.	NGF 9104	New Guinea	5/1962	ag (T), al (T), ad (T), 2 unident. (T), ha (T)
N. angustifolia (Havil.) Merr.	Hose 316	Sabah	—	ag (T), al (T), ad (T), Ehr (T)
N. bartlingii (DC.) Merr.	Bur. Sci. 49079	Philippines	4/1927	ag (T), al (T), ad (T), ha (T), Ehr (T)
N. brasii S. Moore	Hoogland 3446	New Guinea	7/1953	ag (T), al (T), ad (T), ha (T); fr, unident. (T), tw, ag (T), al (T), ad (T), 3 unident. (T)
N. calycina (Bartl. ex DC.) Merr.	Achmad 801	Sumatra	12/1918	ag (T), al (T), ad (T), ha (T), Ehr (T); fr, unident. (T), tw, unident. (T)
N. calycina	—	Bogor, W. Java	1973	al (T)
N. chalmersii (F. V. Muell.) Merr.	NGF 14265	New Guinea	7/1962	al (T); tw, ag (T), al (T)
N. chalmersii	NGF 31727	New Guinea	5/1967	Ehr (T)
N. clemensii Merr. and Perry	Clemens 990	New Guinea	1935	ag (T), ad (T), al (T), ha (T), 2 unident (T); tw, unident. (T)
N. clemensii	NGF 22500	New Guinea	10/1965	ha (T), unident. (T)
N. cyclophylla (Miq.) Merr.	Kostermans 871	Moluccas	5/1949	ha (T), unident. (T)
N. excelsa (Bl.) Merr.	Kostermans, BB 34663	Borneo	6/1951	al (T), ha (T), unident. (T)
N. excelsa	Fl. Malaya 2724	Malaya	—	- ve; st ba, - ve
N. formicaria (Elm.) Merr.	PNH 21798	Philippines	3/1954	ag (T, M), al (T), ha (T, M); tw, ag (T, M), al (T)

TABLE 1. Continued.

Genera and species[a]	Collector's number[b]	Geographical origin	Date of collection	Alkaloids identified[c]
N. aff. *formicaria*	PNH 38109	Philippines	1/1958	ag (T), al (T), ad (T), ha (T)
N. gordoniana (F. M. Bailey) Ridsd.	Cowley 92 D	Australia	—	ag (T), al (T), ad (T), ha (T); w. unident. (T); ba, unident. (T)
N. gordoniana	Pullen 6627	New Guinea	4/1967	ag (T), al (T), ad (T), ha (T)
N. gordoniana	Schodde 2501	New Guinea	—	ag (T), al (T), ad (T)
N. gordoniana	Schodde 2592	New Guinea	—	ag (T), al (T), ad (T), ha (T)
N. gordoniana	NGF 33405	New Guinea	7/1967	ag (T), al (T), ad (T), ha (T, M), 2 unident. (T)
N. gracilis (Vidal) Merr.	Elmer 17119	Philippines	—	– ve
N. aff. *griffithii* (Hook. f.) Merr.	Koetz 27579	India	4/1951	– ve
N. hagenii (Laut. and K. Schum.) Merr.	Van Leeuwen 10077	New Guinea	1926	ag (T), al (T); tw, ag (T), al (T), ad (T), ha (T), 2 unident. (T)
N. hagenii	NGF 22281	New Guinea	8/1965	fl, ha (T), unident. (T)
N. lanceolata (Bl.) Merr. (*N. schlechteri* (Val.) Merr and Perry)	Schodde 2184	New Guinea	—	al (T), unident. (T)
N. lanceolata (*N. schlechteri*)	TGH 10512	New Guinea	7/1962	al (T), gamb (T, M), unident. (T)
N. lanceolata	Junghuhn s.n.	Java	—	4 unident. (T)
N. longipedunculata Merr.	NBFD 10425	Borneo	7/1939	unident. (T)
N. media (Hav.) Merr.	Elmer 13454	Philippines	8/1912	al (T), ha (T), unident. (T)
N. obtusa (Bl.) Merr.	Djamhari 341	Java	5/1948	ag (T), al (T), ad (T)
N. obtusa	Junghuhn s.n.	Java	1835–1865	ag (T), al (T), ad (T), unident. (T); tw, unident. (T)
N. observifolia (Val.) Merr. and Perry, rel. aff	NGF 32644	New Britain	12/1967	ag (T), al (T), ad (T), ha (T), unident. (T)
N. pallida (Reinw. ex Havil.) Bakh. f.	Koorders 40854	Java	6/1912	– ve
N. philippinensis Merr.	Bur. Sci. 1526	Philippines	1913	unident. (T)
N. reticulata (Havil.) Merr.	For. Bur. 25992	Philippines	4/1916	al (T)
N. sessifolia (Roxb.) Merr.	Pierre 3162	Indo-China	12/1876	ag (T), 2 unident. (T)
Neonauclea sp.	BW 15304	New Guinea	3/1962	al (T), ad (T), ha (T), unident. (T)
Neonauclea sp.	RSNB 79	Borneo	6/1961	ha (T), Ehr (T)
Myrmeconauclea strigosa (Korth.) Merr. (*Neonauclea strigosa* Korth.)	Hallier 3103	Borneo	1893	ag (T, M), al (T, M), ad (T, M), ha (T,M), unident. (T)
M. strigosa (*N. strigosa*)	Hallier 1531	Borneo	1893/4	ag (T), al (T), ad (T), ha (T)

NAUCLEINAE DC.				
Ochreinauclea maingayii (Hook. f.) Ridsd.	BB 26086	Borneo	10/1935	ag (T), al (T), ad (T), ha (T), naucl (T), unident. (T); tw, unident.
O. maingayii	SAN 560791	Sabah	—	ha (T), unident. (T); tw, al (T), ha (T), unident. (T); fl, al (T), unident. (T)
O. maingayii	SFN 32183	Malaya	10/1936	ad (T), ha (T), 5 unident. (T)
O. maingayii	Kostermans 5825	Borneo	7/1951	ha (T); st ba, ha (T), ag (T), al (T), naucl (T), 2 unident. (T)
O. maingayii	SFN 9165	Malaya	10/1922	st ba, ad (T), al (T), ha (T), naucl (T), unident. (T)
Nauclea diderrichii (De Willd.) Merr.	Le Testu 8294	Gabon	8/1930	ag (T), al (T), ad (T), ha (T), unident. (T); tw, ag (T), al (T), ha (T)
N. diderrichii (*N. trillesii* (Pierre) Merr.)	d'Alleizette s.n.	Gabon	1/1913	ha (T), unident. (T)
N. officinalis (Pierre ex Pitard) Merr. and Chun.	BB 10991	Borneo	3/1927	ag (T, M), al (T, M), ad (T, M), ha (T, M), unident. (M^+ 359), 3 unident. (T)
N. officinalis	BB 15277	Borneo	4/1931	ag (T), al (T), ad (T), ha (T), 4 unident. (T) (ident. with BB 10991)
N. officinalis	BB 14672	Borneo	12/1930	ag (T), al (T), ad (T), ha (T), 4 unident. (T) (ident. with BB 10991)
N. officinalis	BB 34620	Borneo	2/1951	ag (T), al (T), ad (T), ha (T), 3 unident. (T)
N. orientalis (L.) L. (*Sarcocephalus undulatus* Miq.)	—	Bogor, W. Java	1973	ag (T), al (T), ad (T), ha (T)
N. orientalis (*N. coadunata* Roxb.)	van Royen 4841	New Guinea	9/1954	ad (T), al (T), 3 unident. (T); w, ag (T), al (T), ad (T), ha (T), 3 unident. (T)
N. orientalis (*N. coadunata*)	BW 1997	New Guinea	3/1956	ag (T), al (T), ad (T), 3 unident. (T)
N. orientalis (*N. coadunata*)	NGF 35415	New Guinea	3/1968	ag (T), al (T), ad (T)
N. robinsonii Merr.	PNH 14477	Philippines	4/1951	unident. (T); tw, ag (T), al (T), ad (T), ha (T), 2 unident. (T)
N. subdita (Korth.) Steud.	BB 34656	Borneo	6/1951	ag (T), al (T), ad (T), ha (T), 3 unident. (T); tw, unident.
N. subdita (*N. mitragyna* Merr.)	Lam 2655	Taulaud Is.	4/1926	ag (T), al (T), ad (T)

TABLE 1. Continued.

Genera and species[a]	Collector's number[b]	Geographical origin	Date of collection	Alkaloids identified[c]
N. tenuiflora (Havil.) Merr.	BW 6725	New Guinea	10/1957	ag (T), al (T), ad (T), ha (T), 3 unident. (T); tw, unident.
Nauclea sp.	Jacobs 5249	Borneo	8/1958	ag (T), al (T), ad (T), ha (T), 3 unident. (T); st ba unident.
Nauclea sp.	Kostermans 5625	Borneo	7/1951	ag (T), al (T), ad (T), 3 unident. (T); ba, ag (T), al (T), ad (T), ha (T), 3 unident. (T), fr. unident.
Nauclea sp. nov.	Kostermans 8007	Borneo	7/1953	ag (T), al (T)
Sarcocephalus latifolius (Smith) Bruce (*Nauclea esculenta* (Afz.) Merr.)	Zenker 1282	Cameroons	—	al (T), ha (T)
S. latifolius (*Nauclea latifolia* Smith)	Badre 70	Africa	5/1958	ag (T), al (T), ad (T), unident. (T)
S. pobeguinii Pob. ex Pell. (*Nauclea pobeguinii* Merr.)	R. Dubois 32	Gabon	1939	ag (T), al (T), ad (T), ha (T), 3 unident. (T); st ba, st w, unident.
S. pobeguinii (*N. pobeguinii*)	Corbisier-Baland s.n.	Congo	—	ag (T), al (T), ad (T), ha (T), 4 unident. (T)
ANTHOCEPHALINAE Ridsd.				
Anthocephalus chinensis (Lamk.) A. Rich. ex Walp.	Korthals s.n.	Sumatra	—	al (T), ad (T), 2 unident. (T)
A. chinensis	Wind 23	Java	7/1919	ag (T), al (T), ha (T), unident. (T); tw. -ve
A. chinensis	BW 7003	New Guinea	10/1957	ag (T), al (T), ad (T), ha (T), 5 unident. (T)
A. chinensis	BW 33608	New Guinea	9/1948	ag (T), al (T), ad (T), ha (T), 5 unident. (T) (ident with BW 7003); fl, unident., plus isomit (TG), mit (TG)
A. chinensis	NGF 21809	New Guinea	3/1965	ag (T), al (T), ad (T), unident. (T)
A. chinensis	Pullen 6726	New Guinea	4/1967	Ident. with BW 7003
A. chinensis	NGF 17345	New Guinea	12/1963	Ident. with BW 7003, plus 2 pentacyclic oxindoles (M^+ 368), unident. (M^+ 363), unident. (M^+ 382 $C_{21}H_{22}N_2O_5$)

A. macrophyllus (Roxb.) Havil.	BB 5865	Celebes	8/1923	3 unident. (T)
A. macrophyllus	BB Cel/V/166	Celebes	9/1932	– ve
A. macrophyllus (*Nauclea macrophylla* Roxb.)	—	Bogor, W. Java	1973	ag (T), al (T)
CEPHALANTHEAE H.B.K.				
Cephalanthus glabratus (Spreng.) K. Schum.	Hassler 14468	Paraguay	1913	isopter (TG), pter (TG), isomit (TG), mit (TG)
C. glabratus	Pederson 6607	Argentina	10/1962	isopter (TGM), pter (TGM), unc F (TGM), spec (TGM), isomit (TGM), mit (TGM), ak (TGM), isoaj (TG)
C. glabratus	—	La Plate	—	unident. oxindole and heteroyohimbine (T)
C. natalensis Oliver	J.J. Bos 1301	Transvaal	2/1954	– ve; st ba, ag (T), al (T)
C. natalensis	Lotsy and Goddijn s.n.	S. Africa	11/1925	ag (T), al (T), ad (T), ha (T)
C. occidentalis L.	McNeil 598	Texas	—	ak (TGM), tha (TGM), isopter (TGM), pter (TGM), spec (TGM), aj (T)
C. occidentalis L.	—	Wageningen, Netherlands	1974	isorhyn (TGMUN) and N-ox (TGMU), rhyn (TGMU) and N-ox (TU), dhc (TGMU), hir (TGMU) (43)
C. salicifolius Humb. and Bonpl.	Pringle 8474	Mexico	6/1901	– ve
C. salicifolius	Smithsonian Inst. No. 13993	Mexico	—	al (T), unident. (T)
C. salicifolius	Hinton 920	—	—	unident. (T)
C. tetandra Ridsd. and Bakh. f.	Jenkins s.n.	Assam	—	isopter (TGM), pter (TGM), spec (TGM), unc F (TGM), isomit (TGM), mit (TGM), unident. heteroyohimbine (M^+ 368)
C. tetrandra	Tanaku and Shimada 13600	Taiwan	6/1933	isopter (TG), pter (TG), unc F (TG), spec (TG), mit (TG), isomit (TG), unident. (T)
CINCHONEAE DC.				
MITRAGYNINAE Havil.				
Mitragyna hirsuta Havil. (*Paradina hirsuta* Pitard)	SN 386	Thailand	6/1967	isomit (TG), mit (TG), isopter (TG), pter (TG), spec (TG), unc F (TG), ha (T), al (T); st, isomit (TG), mit (TG), ha (T)
M. hirsuta (*Paradina hirsuta*)	Pierre 1230	Indo-China	3/1877	isomit (TGM), mit (TGM), mitrajavine (TGM), rhyn (TGM), 2 unident. (T)

TABLE 1. Continued.

Genera and species[a]	Collector's number[b]	Geographical origin	Date of collection	Alkaloids identified[c]
M. hirsuta (*Paradina hirsuta*)	Pierre s.n.	Indo-China	1835	isorhyn (TGM), rhyn (TGM), cxe A (TGM), cxe B (TGM), cil (TM), specionox (TM), isopay (TM)
M. rubrostipulata (K. Schum.) Havil. (*Adina rubrostipulata* K. Schum.)	Schlieben 16444	E. Africa	—	isorhyn (TG), rhyn (TG), mit (TG), ag (T), al (T)
M. ledermannii (K. Krause) Ridsd. (*M. ciliata* Aubr. and Pellegr., *Adina macrophylla*)	Zenker 2649	Cameroons	1903	isorhyn (TG), rhyn (TG), hir (T); ba, isorhyn (TG), rhyn (TG)
M. ledermannii (*M. ciliata*, *A. macrophylla*)	Zenker 3389	Cameroons	1907	isorhyn (TGMU), rhyn (TGMU)
M. ledermannii	Zenker 1619	—	1902	isorhyn (TG), rhyn (TG)

[a]The genera are arranged in order of Figure 2. The names in brackets refer to the identification on the label.

[b]The collector's name and number is given but where this is not known the institutional series number is given.

Key to abbreviations:

Abbreviations used for institutional series: Bur. Sci., Bureau of Science, Manila; PNH Philippine National Herbarium; BB, bosschenbuitengewesten, Borneo; BW, Boswezen = Forestry Services, Forest Herbarium, Section of Forest Botany, Forest Division, Manokwari, W. Irian, New Guinea; For. Bur., Forestry Bureau, Philippines; HLB, Herb. Lugd. Bat., refer to sheet numbers at the Rijksherbarium, Leiden; NBFD, North Borneo Forest Department, Sandakan; NGF, New Guinea Forces, later New Guinea Forests, Division of Botany, Lae, N.E. New Guinea; PNH Philippines National Herbarium, Manila; RN, Reserves Naturelles, Madagascar; RSNB, Royal Society Expedition North Borneo; S., Sarawak Museum, Kuching; SAN, North Borneo Forest Department, Sandakan; SF, Service Forestier de Madagascar; SFN, Singapore Field Number, Herbarium of the Botanic Garden, Singapore.

[c]Alkaloid abbreviations: ad = angustidine, ag = angustine, aj = ajmalicine, ak = akuammigine, al = angustoline, cil = ciliaphylline, cxe = corynoxeine, dhc = dihydrocorynantheine, Ehr = Ehrlich+ve streaks of many components, epi-aj = 19-*epi*-ajmalicine, gamb = gambirine, ha = harmane, hir = hirsutine, isoaj = 3-*iso*-ajmalicine, isomit = isomitraphylline, isopay = isopaynantheine, isopter = isopteropodine, isorhyn = isorhynchophylline, mit = mitraphylline, naucl. = naucledine, pter = pteropodine, rhyn = rhynchophylline, spec = speciophylline, specionox = specionoxeine, tha = tetrahydroalstonine, unc F = uncarine F.

Plant parts: Unless otherwise stated, all results refer to leaf extracted samples. Plant part abbreviations: ba = bark, fl = flower, fr = fruit, st = stem, tw = twig, w = wood.

Identification technique abbreviations: G = gas chromatography, M = mass spectrometry, N = ^{1}H nuclear magnetic resonance spectroscopy, T = thin-layer chromatography, U = ultra-violet spectroscopy.

TABLE 2. Summary of the alkaloid distribution within the 121 samples of Naucleeae s.l. screened.

TRIBE, SUBTRIBE, *genus*	No. of samples (species)	No. of samples containing					
		P.I.Q. (**11**)	Harmane	Ehr	Het/Ox **21–24**	Unidentified	Alk. - ve
NAUCLEEAE							
ADININAE							
Gyrostipula	1 (1)	1	0	0	0	0	0
Breonadia	4 (1)	1	3	4	0	0	0
Neobreonia	2 (1)	0	0	0	0	0	2
Breonia	5 (5)	2	1	0	0	3	2
Haldina	4 (1)	0	0	1	0	2	1
Sinoadina	1 (1)	1	1	1	0	0	0
Metadina	1 (1)	1	1	0	0	1	0
Pertusadina	3 (2)	3	2	0	0	1	0
Adina	2 (2)	1	1	1	0	1	0
Khasiaclunea	1 (1)	1	1	0	0	1	0
Diyaminauclea	1 (1)	0	0	0	0	0	1
Ludekia	1 (1)	1	1	0	0	1	0
Neonauclea	38 (25)	26	20	5	1[a]	21	4
Myrmeconauclea	2 (1)	2	2	0	0	1	0
NAUCLEINAE							
Ochreinauclea	5 (1)	5[b]	5	0	0	5	0
Nauclea	17 (9)	16	13	0	0	13	0
Sarcocephalus	4 (2)	4	3	0	0	3	0
ANTHOCEPHALINAE							
Anthocephalus	10 (2)	8	5	0	2	8[c]	1
CEPHALANTHEAE							
Cephalanthus	12 (5)	3	1	0	7	3	2
CINCHONEAE							
MITRAGYNINAE							
Mitragyna	7 (3)	2	1	0	7	1	0

[a]The rare alkaloid gambirine (9-hydroxydihydrocorynantheine, **22**, R=OH, R^1=ethyl, C-3 H α, C-20 H β) was isolated from one sample of *Neonauclea lanceolata* (syn. *N. schlechteri*). Heteroyohimbine and oxindole alkaloids (**21–24**) were not detected in any of the other 37 samples of *Neonauclea* investigated.

[b]The pyridine-indole alkaloid naucledine (**15**) was detected in two samples.

[c]The presence of unidentified alkaloids with strong yellow fluorescences in uv light and which gave intense purple colors when sprayed with ferric chloride/perchloric acid reagent was noted in four samples.

From the Naucleeae-Naucleinae, *Ochreinauclea*[1], *Nauclea* and *Sarcocephalus* species were screened, but no sample of *Burrtdavya* was available. The results are similar to those obtained from the Adininae. Pyridino-indoloquinolizidinone alkaloids (**11**) and/or harmane were detected from one species of *Ochreinauclea*[1] (which also contained naucledine **15**), from *Nauclea* (16 samples representing 9 species), and *Sarcocephalus* (2 species). The presence of unidentified alkaloids was also indicated from this subtribe (see tables 1 and 2), but again there was generally a very low level of non-quaternary alkaloids present.

Anthocephalus, the sole genus of the subtribe Anthocephalinae, contains two species, both of which appear variable in their alkaloid content. Several examples of *A. chinensis* contained pyridino-indoloquinolizidine alkaloids (**11**) and harmane as indicated by tlc. In addition, pentacyclic oxindoles (**23**) were detected in two samples, and an unidentified yellow alkaloid (purple color with ferric chloride/perchloric acid spray agent, $M^{+\cdot}$ *m/z* 382, $C_{21}H_{22}N_2O_5$) was present in four others (table 1).

In contrast to the generally weak alkaloid extracts from the Naucleeae s.s., most samples of *Cephalanthus* and *Mitragyna* yielded greater quantities of non-quaternary alkaloids. Twenty alkaloids were identified from 12 samples, representing five species of *Cephalanthus* (table 1). Seven of the twelve samples yielded heteroyohimbines (**21**, **22**) and oxindoles (**23**, **24**) as major alkaloids, with pyridino-indoloquinolizidinones (**11**) detected in three samples. Seven samples representing three of the ten species of *Mitragyna* were examined, and all samples yielded heteroyohimbine- (**21**, **22**) and oxindole- (**23**, **24**) type alkaloids (tables 1 and 2). In all, eighteen alkaloids were identified from the seven *Mitragyna* samples (table 1).

CHEMOTAXONOMY

The postulated biosynthetic relationships between the major alkaloids of the Naucleeae s.l. are set out in figure 3. The results, presented in table 1 and summarized in table 2, clearly demonstrate that the majority of genera within the Naucleeae s.s. do not contain significant quantities of non-quaternary non-glycosidic alkaloids of the heteroyohimbine- (**21**, **22**) and oxindole- (**23**, **24**) types. Such alkaloids, however, are prevalent in species of *Cephalanthus*, *Mitragyna* (tables 1 and 2) and *Uncaria* (43–45). *Cephalanthus* is now segregated from the Naucleeae s.s. and placed in a separate tribe. Cephalantheae (8) has alkaloids of the same type as *Uncaria* (i.e. **21–24**, R = H) (table 3), and this finding supports the view that *Cephalanthus* is distinct from the other genera in the Naucleeae s.s. *Mitragyna* and *Uncaria* have also been removed from the Naucleeae s.s. and placed in a separate subtribe, Mitragyninae, of the tribe Cinchoneae (9). The major alkaloids of *Mitragyna* and *Uncaria* species are of types **21–24** and thus are similar to or identical with alkaloids found in *Pausinystalia* and *Corynanthe*, also of the Cinchoneae (11). Although the major alkaloids of *Mitragyna* and *Uncaria* are mainly of the same types, there are some differences which are summarized in table 3.

TABLE 3. Comparison of alkaloids from *Mitragyna* and *Uncaria* (subtribe Mitragyninae of the Cinchoneae).

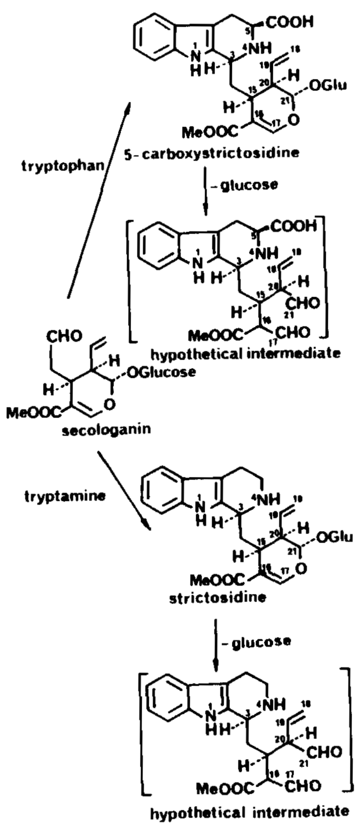
	Mitragyna (10 species)	*Uncaria* (34 species)
No. of species containing alkaloids.	10	21
Heteroyohimbines (**21**, **22**)........	common	common
Oxindoles (**23**, **24**)................	common	common
9-Methoxy substitution (**21–24**)...	common	rare
9-Hydroxy substitution (**21–24**)...	common	infrequent
C-19 Methyl β-configuration (**21**, **23**)......................	not found	infrequent
Gambirtannines (benzenoid E ring pentacyclics)............	not found	rare
Roxburghines (2 tryptamine units+secologanin)...........	not found	rare

In the present study, the major types of alkaloid identified from genera of the Naucleeae s.s. were of the pyridino-indoloquinolizidinone type (**11**). The genera from which these alkaloids were obtained are listed in table 4. Although it has been demonstrated that these alkaloids can be isolated by extraction techniques which avoid the use of ammonia (38), it has to be assumed that the presence of these alkaloids may be indicative of glycosidic alkaloids (e.g. strictosidine lactam or vincoside lactam, **3**, $R = R^1 = H$), which have been converted into pyridine derivatives by the action of ammonia (see figure 3).

The majority of alkaloids which have been reported from *Pertusadina euryncha* and *Haldina cordifolia* of the subtribe Adininae, contain a C-5 carboxyl substituent (structures **1–9**) and presumably they have been derived from secologanin and tryptophan (instead of tryptamine), unless the carboxyl is introduced into strictosidine (**1**, R = H, C-3 H α). This chemical characteristic of a C-5 carboxyl substituent, appears to be restricted to Adininae and has not been found in the Naucleinae or Anthocephalinae (figure 3). A second major characteristic of the Adininae alkaloids is the retention of glucose from the strictosidine-type precur-

FIGURE 3 Postulated biosynthetic relationships between the major alkaloids of the Naucleeae s.l.

PRECURSORS



Reaction	ALKALOID-TYPE (EXAMPLES)	GENUS	SUBTRIBE	TRIBE
-4H	2 (cordifoline, desoxycordifoline)	Haldina, Pertusadina	Adininae	Naucleeae
C-16 CO to N-4	3 (5-β-carboxyvincoside lactam)	Pertusadina	Adininae	Naucleeae
C-16 CO to N-1, -4H	4 (desoxycordifoline lactam)	Pertusadina	Adininae	Naucleeae
C-19 to C-5 carboxyl	5 (rubenine)	Pertusadina	Adininae	Naucleeae
Glucose to C-5 carboxyl	6 (macrolidine)	Pertusadina	Adininae	Naucleeae
C-21 to N-4, C-19 to C-17	7 (5-β-carboxytetrahydro-alstonine)	Pertusadina	Adininae	Naucleeae
C-21 to N-4	8 (adirubine, anhydroadirubine)	Pertusadina	Adininae	Naucleeae
C-21 to N-4, C-17 to C-18	9 (5-β-carboxycorynanthine)	Pertusadina	Adininae	Naucleeae
C-19 to N-1, -4H	10 (adifoline, 10-desoxyadifoline)	Haldina	Adininae	Naucleeae
C-16 CO to N-4	3 (strictosidine lactam, vincoside lactam, rubesine)	Pertusadina, Sarcocephalus	Adininae, Naucleinae	Naucleeae
C-18 to N-4	17 (dihydrocadambine), 18 (cadambine)	Nauclea, Anthocephalus	Naucleinae, Anthocephalinae	Naucleeae
C-19 to N-4	19 (dihydroisocadambine)	Anthocephalus	Anthocephalinae	Naucleeae
C-16 CO to N-4, +N	11 (angustine and other pyridino-indolo-quinolizidinones)	Gyrostipula and ten other genera; Nauclea, Sarcocephalus; Anthocephalus; Cephalanthus; Mitragyna, Uncaria	Adininae; Naucleinae; Anthocephalinae; ——; Mitragyninae	Naucleeae; Cephalantheae; Cinchoneae
C-18 to N-4, +N	12 (nauclechine, naufoline)	Nauclea, Sarcocephalus	Naucleinae	Naucleeae
C-19 to N-4, +N	20 (cadamines)	Anthocephalus	Anthocephalinae	Naucleeae
C-21 to N-4, C-17 to C-19	21 (ajmalicine and other pentacyclic heteroyohimbines) → 23 (mitraphylline and other pentacyclic oxindoles)	Anthocephalus; Cephalanthus; Mitragyna, Uncaria	Anthocephalinae; ——; Mitragyninae	Naucleeae; Cephalantheae; Cinchoneae
C-21 to N-4	22 (dihydrocorynantheine and other tetracyclic heteroyohimbines) → 24 (rhynchophylline and other pentacyclic oxindoles)	Neonauclea (rare); Cephalanthus; Mitragyna Uncaria	Adininae; ——; Mitragninae	Naucleeae; Cephalantheae; Cinchoneae

TABLE 4. Genera of the Naucleeae s.s. containing pyridino-indoloquinolizidinones (**11**).

Subtribe	Genus
Adininae	*Gyrostipula, Breonia, Sinoadina*[a], *Metadina, Pertusadina*[a], *Adina, Khasiaclunea*[a], *Ludekia*[a], *Neonauclea, Myrmeconauclea* (11 of the 16 genera)
Naucleinae	*Ochreinauclea*[a], *Nauclea, Sarcocephalus* (3 of the 4 genera)
Anthocephalinae	*Anthocephalus* (sole genus)

[a]New genera (2).

sor(s) since 15 of the 20 known alkaloids are glucosides. Further biosynthetic pathways are involved after the initial condensation with secologanin and, amongst others, include aromatization of ring C (e.g. desoxycordifoline **2**, R = H), hydrolysis of the C–16 ester and subsequent lactamization with either N–1 (e.g. desoxycordifoline lactam, **4**) or N–4 (e.g. vincoside lactam, **3**, $R = R^1 = H$, C–3 H β), fusion of N–4 with C–18 and lactone formation between C–19 and the C–5 carboxyl (e.g. rubenine, **5**), and fusion of C–19 with N–1 (e.g. adifoline, **10**, R = H) (figure 3). The "odd man out" in the subtribe is *Neonauclea lanceolata* (syn. *N. schlechteri*), which contains small amounts of gambirine (**22**, R = OH, R^1 = ethyl, C–3 H α, C–20 H β) (table 1 and reference 29). This alkaloid is of a type which is more characteristic of Mitragyninae genera. The present work does, however, indicate that hitherto unreported glycosidic alkaloids may be present due to the isolation of pyridino-indoloquinolizidinone alkaloids (**11**) (tables 1 and 2).

The alkaloids isolated to date from the Naucleinae are mainly indolo-pyridine alkaloids (**11–16**); again, although these may be true natural products, the possibility cannot be ignored that these are artifacts formed via ammonia and, hence, are indicative of glycosidic alkaloids. The isolation of strictosidine lactam (**3**, $R = R^1 = H$, C–3 H α) from the Naucleinae shows relationship to the Adininae, whereas the presence of 3 α-dihydrocadambine (**17**, C–3 H α) and ND–370 shows similarities with the Anthocephalinae.

Glycosidic alkaloids also feature in the Anthocephalinae, in which C–18 fusion with N–4 occurs together with either a C–3 to C–19 ether bridge (e.g. cadambine, **18**) or with C–19 hydroxylation (e.g. dihydrocadambine, **17**). An alternative pathway in which C–19 fusion with N–4 occurs is observed in the dihydroisocadambines (**19**), and it is possible that these react with ammonia to form the cadamines (**20**). The presence of pentacyclic oxindoles (**23**) found in two samples of *Anthocephalus chinensis* during the present investigation (tables 1 and 2) not only supports the botanical assessments that the genus is distinct from other members of the tribe, but is also indicative of affinity with genera of the Cephalantheae and Mitragyninae.

CONCLUSIONS

The recent taxonomic revisions of the Naucleeae with the removal of *Cephalanthus* into a separate tribe Cephalantheae and the removal of *Mitragyna* and *Uncaria* into the subtribe Mitragyninae of the tribe Cinchoneae affords an opportunity to assess the relationships between the alkaloidal constituents and the botanical affinities (see figure 3). Knowledge of the distribution of glycosidic alkaloids is still very limited, and it is probable that more will be isolated from members of the Naucleeae s.s. Hence suitable extraction techniques for the isolation of glycosidic indole alkaloids should be applied to the various genera of the Naucleeae s.s. in order to ascertain the actual alkaloids present and to see whether the pyridine-containing alkaloids (**11–16**) are natural products or artifacts. The present findings demonstrate that alkaloids are useful characters for assessing some of the relationships within this group of plants which have been the subject of considerable taxonomic discussion.

Received 25 June 1981

LITERATURE CITED

1. R. C. Bakhuizen van den Brink Jr., *Taxon*, **19**, 468 (1970).
2. C. E. Ridsdale, *Blumea*, **24**, 307 (1978).
3. K. Schumann in A. Engler and K. Prantl 'Die Natürlichen Pflanzenfamilien', Wilhelm Engelmann, Leipzig, 1891, vol. IV, Part 4, p. 1 'Rubiaceae'.
4. G. D. Haviland, *J. Linn. Soc. Bot.*, **33**, 1 (1897).
5. B. Verdcourt, *Bull. du Jard. Bot. de l'Etat Bruxelles*, **28**, 209 (1958).
6. H. K. Airy Shaw in J. C. Willis 'A Dictionary of Flowering Plants and Ferns', 8th Edition, Cambridge University Press (1973).
7. C. E. B. Bremekamp, *Acta Bot. Neerl.*, **15**, 1 (1966).
8. C. E. Ridsdale, *Blumea*, **23**, 177 (1976).
9. C. E. Ridsdale, *Blumea*, **24**, 43 (1978).
10. C. E. Ridsdale, *Blumea*, **22**, 541 (1975).
11. S. R. Hemingway and J. D. Phillipson, 'Alkaloids of the Rubiaceae' in 'Indole and Biogenetically Related Alkaloids', editors J. D. Phillipson and M. H. Zenk, Academic Press, London (1980), p. 63.
12. J. D. Phillipson, S. R. Hemingway and C. E. Ridsdale, *J. Pharm. Pharmac.*, **26**, 113 P (1974).
13. R. T. Brown and A. A. Charalambides, *Experientia*, **31**, 505 (1975).
14. R. T. Brown and B. F. M. Warambwa, *Phytochemistry*, **17**, 1686 (1978).
15. W. P. Blackstock and R. T. Brown, *Tetrahedron Letts.*, 3727 (1971).
16. W. P. Blackstock, R. T. Brown and G. K. Lee, *J. C. S. Chem. Commun.*, 910 (1971).
17. R. T. Brown and W. P. Blackstock, *Tetrahedron Letts.*, 3063 (1972).
18. R. T. Brown and S. B. Fraser, *Tetrahedron Letts.*, 841 (1973).
19. R. T. Brown and A. A. Charalambides, *J.C.S. Chem. Commun.*, 765 (1973).
20. R. T. Brown and A. A. Charalambides, *J.C.S. Chem. Commun.*, 553 (1974).
21. R. T. Brown and A. A. Charalambides, *Tetrahedron Letts.*, 1649 (1974).
22. R. T. Brown, C. L. Chapple and G. K. Lee, *J.C.S. Chem. Commun.*, 1007 (1972).
23. R. T. Brown and A. A. Charalambides, *Phytochemistry*, **14**, 2527 (1975).
24. R. T. Brown and A. A. Charalambides, *Tetrahedron Letts.*, 3429 (1974).
25. R. T. Brown and L. R. Row, *J.C.S. Chem. Commun.*, 453 (1967).
26. L. Merlini and G. Nasini, *Gazz. Chim. Ital.*, **98**, 974 (1968).
27. W. P. Blackstock, R. T. Brown, C. L. Chapple and S. B. Fraser, *J.C.S. Chem Commun.*, 1006 (1972).
28. R. T. Brown, K. V. J. Rao, P. V. S. Rao and L. R. Row, *J.C.S. Chem. Commun.*, 350 (1968).
29. S. R. Johns, J. A. Lamberton and A. A. Sioumis, *Australian J. Chem.*, **23**, 1285 (1970).
30. R. T. Brown, C. L. Chapple and A. G. Lashford, *Phytochemistry*, **16**, 1619 (1977).
31. F. Hotellier, P. Delaveau and J. L. Pousset, *Plantes Medicinales et Phytotherapie*, **11**, 106 (1977).
32. F. Hotellier, P. Delaveau and J. L. Pousset, *Phytochemistry*, **14**, 1407 (1975).
33. F. Hotellier, P. Delaveau, R. Besselièvre and J. L. Pousset, *C.R. Acad. Sci. Paris*, Series C, **282**, 595 (1976).
34. S. McLean and D. G. Murray, *Canad. J. Chem.*, **48**, 867 (1970).
35. S. McLean and D. G. Murray, *Canad. J. Chem.*, **50**, 1478 (1972).
36. G. I. Dmitrienko, A. Szakolcai and S. McLean, *Tetrahedron Letts.*, 2599 (1974).
37. M. Sainsbury and B. Webb, *Phytochemistry*, **14**, 2691 (1975).
38. J. D. Phillipson, S. R. Hemingway, N. G. Bisset, P. J. Houghton and E. J. Shellard, *Phytochemistry*, **13**, 973 (1974).
39. R. T. Brown and S. B. Fraser, *Tetrahedron Letts.*, 1957 (1974).
40. R. T. Brown, S. B. Fraser, J. Banerji, *Tetrahedron Letts.*, 3335 (1974).
41. R. T. Brown and C. L. Chapple, *Tetrahedron Letts.*, 2723 (1976).
42. R. T. Brown and C. L. Chapple, *Tetrahedron Letts.*, 1629 (1976).
43. J. D. Phillipson and S. R. Hemingway, *Phytochemistry*, **13**, 2621 (1974).
44. E. J. Shellard, *Pharm. Weekblad.*, **106**, 224 (1971).
45. J. D. Phillipson, S. R. Hemingway and C. E. Ridsdale, *Lloydia*, **41**, 503 (1978).
46. J. D. Phillipson and S. R. Hemingway, *J. Chromatog.*, **105**, 163 (1975).