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NITROGEN-CONTAINING NON-STEROIDAL SECONDARY METABOLITES OF *SOLANUM, CYPHOMANDRA, LYCIANTHES* AND *MARGARANTHUS*

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Key Word Index—*Solanum*; *Cyphomandra*; *Lycianthes*; *Margaranthus*; Solanaceae; cuscohygrine; solamine; amides; amines; chemotaxonomy.

Abstract—Of the 49 species of *Solanum* studied, cuscohygrine has been detected in 25, solamine and related amines in 17 and solamine-derived amides in 16. Five species of *Cyphomandra* examined all contained both amines and amides. From roots of *Margaranthus solanaceus* cuscohygrine has been isolated which probably occurs, too, in roots of *Lycianthes rantonnettii*. The distribution of these compounds throughout the taxa could be of chemotaxonomic value.

INTRODUCTION

Solanum, one of the large genera of the plant kingdom, contains some 1400 species widely distributed throughout the world but chiefly concentrated in tropical regions. It is of considerable economic importance as a source of food, drugs and ornamentals. The several taxonomic treatments of the genus include those of Dunal, 1852 [1]; Bitter 1912–1922 [2]; Seithe, 1962 [3]; Danert, 1967, 1970 [4, 5] and D'Arcy, 1979 [6].

In recent years the genus has been extensively screened for steroidal alkaloids and similar non-nitrogen-containing isoprenoids which have a potential value to the steroid industry. Other nitrogen-containing substances have been reported in isolated species and range from simple betaines to complex alkaloids. Two amides [7], solapalmitine (**1b**) and solapalmitenine (**1c**), of *S. tripartitum* have antitumour activity. Solamine (**1a**), solacaproine (**1d**), tropinone and cuscohygrine (**2**) have been isolated [8] from the related genus *Cyphomandra* (*C. crassifolia* syn. *C. betacea*) and the urethane, solaurethine (**1e**), together with solamine, cuscohygrine and anabasine from *S. carolinense* [9]. These findings prompted us to examine 49 species of *Solanum* and 5 species of *Cyphomandra* for the presence of these compounds to ascertain whether they could be usefully included in any chemotaxonomic treatment of the genus. One species each of the genera *Lycianthes* (200 spp.) and *Margaranthus* (3 spp.) was also included in the survey.

RESULTS AND DISCUSSION

From the preliminary screening of 0.2–0.4 g of dried plant material, the distribution of solamine and related bases, cuscohygrine, amides and other bases in the species under investigation was obtained. Those plants which gave reasonable positive tests, and for which adequate material was available, were then examined in more detail using preparative TLC and standard column chromatography (see ref. [8]) for the isolation of individual components. The results are recorded in Table 1.

Cuscohygrine (**2**), solamine (**1a**) and the amides (**1b**, **1c**, **1d**) considered in this paper are all derived biosynthetically from ornithine or putrescine. Cuscohygrine is formed as an early offshoot of the tropane alkaloid pathway [10] and, not surprisingly, co-occurs (W. C. Evans in ref. [6]) with these alkaloids in many species; its occurrence, independent of tropane alkaloids, is indicated in 29 of the 56 species listed in Table 1 as well as in other solanaceous genera. In contrast, solamine and its various amides have been reported to date only in the species indicated in Table 1, none of which is noted for tropane alkaloid production.

Although the limited number of species of *Solanum*, relative to the whole genus, studied in this paper precludes

$Me_2N \cdot [CH_2]_4 \cdot NR \cdot [CH_2]_4 \cdot NMe_2$

1a R = H
1b R = CO · $[CH_2]_{14}$ · Me
1c R = CO · CH: CH · $[CH_2]_{12}$ · Me
1d R = CO · $[CH_2]_4$ · Me
1e R = CO · OEt

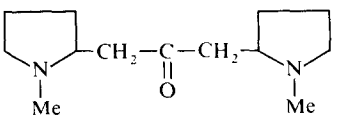

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Table 1. The distribution of nitrogen-containing secondary metabolites in species of *Solanum*, *Cyphomandra*, *Lycianthes* and *Margaranthus*

	Plant source*	Organs investigated	Cuscohygrine	Amines†	Amides‡	Detection of other bases
Genus *SOLANUM*						
Subgenus *Solanum*						
Section *Solanum* (Morella (Dun.) Bitt.)						
Solanum americanum Mill.	B	Roots	—	—	—	+
S. nigrum L.	E	Roots	—	—	—	+
S. nitidibaccatum Bitt.	B	Roots	—	—	—	—
S. scabrum Mill.	B	Roots	—	+[a]	?+[a]	—
S. villosum Mill. ssp. *villosum*	B	Roots	—	—	—	+
S. villosum ssp. *puniceum* (Kirschleger) Edmonds	D	Roots	—	—	—	—
Section *Parasolanum* Child (in ed.)						
S. radicans L.f.	C	Aerial parts	—	+	+	—
S. tripartitum Dun.	D	Aerial parts	—	+	+	—
Section *Pseudocapsicum* (Dun.) Bitt.						
S. diflorum Vellozo (*S. capsicastrum* Link.)	E	Roots	—	—	—	+
S. pseudocapsicum L.	E	Roots	—	—	—	+
S. tucamanense Grisb.	D	Aerial parts	—	?+	?+	+
Section *Holophyllum* Walp.						
S. cervantesii Lagoski	B	Roots	—	—	—	+
S. crispum Ruiz et Pav.	B	Roots	—	—	—	—
S. valdiviense Dun.	B	Roots	—	—	—	—
Section *Brevantherum* Seithe						
S. abutiloides Bitt. et Lillo	E	Roots	?+	—	—	—
S. mauritianum Scop.	A	Roots	—	—	—	—
S. erianthum D. Don. (*S. verbascifolium* sensu auct. non L.)	F	Roots	+	+[b]	—	—
Section *Jasminosolanum* Bitt. ex Seithe						
S. jasminoides Paxt.	E	Roots	?+	—	—	—
S. seaforthianum Andr.	D	Aerial parts	—	—	—	+
Section *Aculeigerum* Seithe						
S. wendlandii Hook. f.	A	Roots	+[c]	+[c]	?+[c]	—
Section *Petota* Dumortier						
S. tuberosum L., cv Sutton Foremost	E	Roots	+[d]	—	—	—
Section *Basarthrum*						
S. caripense H.B. ex Dun.	C	Roots	—	+	+	—

Table 1. (*Continued*)

	Plant source*	Organs investigated	Cuscohygrine	Amines†	Amides‡	Detection of other bases
Subgenus *Archaesolanum* Bitt. ex Marz.						
S. aviculare Forst.	D	Roots	+	—	—	—
S. laciniatum Ait.	G	Roots	+	—	—	—
Subgenus *Leptostemonum* (Dun.) Bitt.						
Section *Melongena* Nees von Esenbek						
S. hermannii Dun. (*S. sodomeum* auct. non L.)	D	Roots	—	—	—	—
S. melongena L.	B	Roots	?+	—	—	—
S. marginatum L.f.	A	Roots	—	—	—	—
S. marcrocarpon L.	D	Roots	—	—	—	—
Section *Oliganthes* (Dun.) Bitt.						
Series *Aethiopica* Bitt.						
S. aethiopicum L.	D	Roots	?+	—	—	—
S. gilo Rad.	A	Roots	+	—	—	—
Series *Lathyrocarpa* (Dun.) D'Arcy						
S. carolinense L.	A	Roots	+[e]	+[e]	+[e]	+[e]
Section *Leprophora* (Dun.) D'Arcy						
S. elaeagnifolium	A	Roots	—	—	—	—
Section *Lasiocarpum* (Dun.) D'Arcy						
S. quitoense Lam.	A	Roots	+[f]	?+	—	—
S. tequilense Dun.	A	Roots	—	+[g]	—	+
S. robustum Wendl.	B	Roots	—	—	—	—
S. grandiflorum Ruiz et Pav. (*S. wrightii* Benth.)	C	Roots	+[h]	—	+[h]	—
S. ferox L.	E	Roots	?+	+	+	—
Section *Torvum* Nees von Esenbeck						
S. torvum Sw.	F	Roots	?+[i]	—	—	—
S. schimperianum Hochst.	H	Roots	—	—	—	+
Section *Giganteiforma* (Bitt. pro serie sectionis *Torvi*), Child (in edit.)						
S. giganteum Jacq.	D	Roots	—	—	—	+
Section *Acanthophora* Dun.						
S. atropurpureum Schrank	D	Roots	—	—	—	—
S. ciliatum Lam.	B	Roots	+	—	—	—
S. mammosum L.	A	Roots	+[j]	—	—	—
S. khasianum C.B. Clarke	G	Roots	+	—	—	?+

Table 1. (*Continued*)

	Plant source*	Organs investigated	Cusohygrine	Amines†	Amides‡	Detection of other bases
S. prinophyllum R. Br. (Australian sp. with some correspondence to this taxon)	A	Roots	–	–	–	–
Section *Graciliflorum* (Dun.) Seithe						
S. bahamense L.	A	Aerial parts	–			? +
Section *Cryptocarpum* Dun. sen. str.						
S. sisymbriifolium Lam.	E	Roots	+[k]	+[k]	+[k]	–
		Aerial parts	–	–	+	–
Section *Campanulatum* Symon nom. nud.						
S. campanulatum R. Br.	A, B	Roots	–	–	–	–
Section *Androceras* (Nutt.) Bitt. ex Marz.						
S. citrullifolium A. Br.	D	Roots	+	+	+	–
S. rostratum Dun.	D	Roots	+	–	–	–
Genus *CYPHOMANDRA* Mart. ex Sendt.						
Section *Cyphomandropsis* (Bitt.) D'Arcy						
Cyphomandra amotapensis (Svenson) Child (in edit.)	A	Roots	–	+	?+	–
C. clavata (Rusby)	A	Roots	–	+[l]	+[l]	–
C. luteoalba (Pers.) Child	A-S42 accession det. Child	Roots	?+	+[m]	+	+
C. stuckertii (Bitt.) D'Arcy	D	Roots	–	+	–	+
Section *Cyphomandra*						
C. crassifolia (Ort.) Kuntze	E	Roots	+[n]	+[n]	+[n]	+[n]
[syn. *C. betacea* (Cav.) Sendt.]		Aerial parts	–	+[n]		–
Genus *LYCIANTHES* Hassler						
Lycianthes rantonnettii (Carr.) Bitt.	A	Roots	?+	–	–	–
Genus *MARGARANTHUS* Schlecht						
Margaranthus solanaceus Schlecht	A	Aerial parts	–	–	–	–
		Roots	+[o]	–	–	

Key: * Plant sources: A = plant material supplied by Dr. R. N. Lester, Department of Plant Biology, University of Birmingham, U.K., B = plant material supplied by Dr. Chr. Lehmann, Zentralinstitut für Genetik und Kulturpflanzenforschung, 4325-Gattersleben, DDR: C = plant material raised in Nottingham from seeds supplied by Dr. R. N. Lester (as A); D = plant material raised in Nottingham from seeds supplied by Dr. Chr. Lehmann (as B); E = University of Nottingham Collection; F = collected (W.C.E.), University Campus, Kumasi, Ghana; G = supplied by Dr. R. Hardman, School of Pharmacy, Bath University; H = supplied by the late Dr. C. Melville, Pharmacy Department, University of Manchester.

† Compounds having the chromatographic properties and colour reactions of solamine (**1a**).

‡ Compounds having the chromatographic properties and colour reactions of solacaproine (**1d**) and solapalmitine (**1b**).

[a]Roots (50 g), yielded by preparative TLC, bases having the R_f values of solamine and solacaproine respectively; they failed to yield crystalline picrates.

[b]The principal base of the roots could not be freed of a minor component; it possessed the same R_f value and IR spectrum as solamine.

[c]Total basic content of roots 0.5%. An extract of 30 g gave by partition chromatography the principal base solamine (picrate and R_f value indistinguishable from that of the authentic derivative), cuscohygrine (picrate, mp 209–210° with IR spectrum as that of authentic picrate) and small amounts of other bases including two with the same R_f values as those of tetramethylputrescine and solacaproine, respectively.

[d]Cuscohygrine (picrate, mp 211–212°, mmp 210–211°, with IR spectrum identical with that of authentic compound) was obtained from an extract of the roots (5 g) by preparative TLC.

[e]See ref. [9].

[f]Roots (50 g) afforded, by preparative TLC, cuscohygrine (picrate, mp 201–202° with IR spectrum identical with that of authentic material); a trace of solamine was indicated by TLC.

[g]Roots (23 g) gave, by partition chromatography, solamine (picrate, mp 143–145° with IR and MS identical with those of authentic compound); other minor components, one having a similar R_f value to that of tetramethylputrescine, were also detected.

[h]Roots (10 g) gave, by preparative TLC, cuscohygrine (picrate, mp 199–200° with IR spectrum identical to that of authentic compound) and a solacaproine-like base which failed to give a crystalline derivative.

[i]The cuscohygrine indicated by TLC could not be confirmed by isolation from the roots (20 g).

[j]Cuscohygrine appears to be the principal nonterpenoid base; the roots (5 g) yielded cuscohygrine (picrate, mp 199–201°, IR spectrum as authentic material).

[k]Aerial parts contained a small amount of a base with an R_f value similar to that of solacaproine (**1d**). Roots contained *ca* 0.05% total bases. Repeated column partition chromatography (pH 6.8 and 8) of a root (11 g) extract gave solacaproine picrate, mp 140–141°, IR spectrum identical with that of solacaproine dipicrate; MS gave *m/e* 313 (47.9%) (M^+ for base), cuscohygrine (picrate, mp 194–195° and IR spectrum identical with authentic dipicrate) and solamine (comparison of R_f value of base and IR spectrum with those of authentic compound).

[l]Total basic content of roots 0.24% (as solamine). Column partition chromatography of the root (24 g) extract gave solamine as the principal base (picrate, mp 113–115° having an IR spectrum identical with that of solamine tripicrate), a base possessing the same colour reactions and R_f value (TLC system C) as solacaproine but of which no crystalline picrate could be obtained, and small amounts of other alkaloids.

[m]Solamine (picrate, mp 139–141° and IR spectrum identical with that of authentic material) obtained by preparative TLC (system C) of a root (30 g) extract; another base (picrate, mp 102–104°) was not identified.

[n]See ref. [8].

[o]Roots (5 g) yielded by preparative TLC (system C) cuscohygrine (picrate, mp 204–205°, mmp 207° with IR spectrum as that of authentic material) and an unidentified base of high R_f value.

any chemotaxonomic deductions, certain pointers to the further investigation of the distribution of the relevant compounds emerge. Thus *Cyphomandra* species appear to be disposed towards the production of amides and amines in contrast to the almost complete absence of the latter in *Solanum*, sections *Solanum*, *Holophyllum* and *Melongena*. A more extensive investigation of sections *Lathyrocarpa* and *Aculeigerum* would seem desirable. Reference to Table 1 also indicates a close similarity, within sections, of the phytochemical spectrum of a number of species. The occurrence of the above ornithine-derived compounds appears unrelated to the distribution of steroidal alkaloids.

EXPERIMENTAL

The sources of the plant materials are given in Table 1. For the preliminary screening of plants for solamine and related bases, cuscohygrine, amides and other bases, the powdered material (0.2–0.4 g) was moistened with NH_4OH (15% soln) and shaken with EtOH–$CHCl_3$ (1:1) (2 ml) for 0.5 hr. The extract was strained through cotton wool and the marc treated with $CHCl_3$ (3 × 2 ml). After removal of the combined solvents, the residue was redissolved in $CHCl_3$ (2 ml), shaken (×3) with 0.05 N H_2SO_4 (2 ml) and the basic material finally recovered in $CHCl_3$ (4 × 2 ml). The evapd extracts were examined by 4 chromatographic systems, viz.. A, Al_2O_3–Et_2O; B, Al_2O_3–Et_2O–EtOH (1:1); C, Si gel–Et_2NH–$CHCl_3$ (1:9); D, Si gel–Me_2CO–18 M NH_4OH (4:1). Basic components were visualized by modified Dragendorff and iodoplatinate reagents. Appropriate reference compounds were employed and the sprayed chromatograms compared for colour reactions and R_f values.

Those plants which gave reasonable, positive tests as above, and for which sufficient material was available, were then examined in more detail employing prep. TLC (in systems B and C above) and standard partition chromatography (see ref. [8]) for the isolation of individual components.

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