PERGAMON

Phytochemistry 53 (2000) 623–637

PHYTOCHEMISTRY

www.elsevier.com/locate/phytochem

Chemotaxonomy and geographical distribution of tropane alkaloids

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Received 21 December 1998; received in revised form 14 July 1999

Abstract

This review illustrates the distribution of tropane alkaloids within the families Solanaceae, Erythroxylaceae, Proteaceae, Euphorbiaceae, Rhizophoraceae, Convolvulaceae and Cruciferae. Whereas tropane alkaloids are characteristic of the genera *Datura*, *Brugmansia* (tree datura) and *Duboisia* of the Solanaceae, the distribution is more widespread with novel tropane derivatives in families not traditionally associated with these bases. The chemical nature of more recently discovered water-soluble calystegines and the di- and trimeric forms from the Convolvulaceae (e.g. schizanthines from *Schizanthus* spp.), truxillines from Bolivian coca leaves and moonines of *Erythroxylum moonii* are highlighted. Where possible and appropriate, links between the phytochemistry and taxonomy are discussed. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Tropane alkaloids; Scopolamine; Calystegines; Schizanthines; Truxillines; Moonines; Geographical distribution; Cultivation; Solanaceae; Erythroxylaceae; Proteaceae; Euphorbiaceae; Rhizophoraceae; Convolvulaceae; Cruciferae

1. Introduction

The tropane alkaloids of *Datura* (*Datura stramonium*) were introduced to European medicine by Romany immigrants (gypsies). The generic name was derived from the Indian poison, *dhat*, used by a criminal class known as *Thugs*. Stramonium Herb was official in a 17th German herbal. *D. stramonium* has synonyms such as *Thornapple* after its hooked capsule and *Jamestown weed*. Early settlers of Jamestown (USA) used it as a pot-herb with fatal results. The Solanaceae is considered the home of tropane alkaloids. Being an important food family, the potato's lethal cousins became familiar as toxic plants and also as medicinal herbs. They were used for their hallucinogenic properties and became incorporated into folklore, i.e. witchcraft and tribal initiation ceremonies. Since tropane alkaloids have relatively simple chemical structures and were easy to extract, the majority confined to Solanaceous plants were soon isolated and identified. Then tropane alkaloids were located in other families, for example the Erythroxylaceae and Convolvulaceae, and some phylogenetic trends observed. Recently, the location of tropanes has widened with the discovery of dimeric and trimeric forms. Other tropane bases which were overlooked in previous investigations have been recognised and isolated. Parochially known as *sugar-mimic alkaloids*, they are very polar molecules that have avoided detection using traditional techniques. They have rekindled a pharmacological interest, as they seem to inhibit sugar metabolism. An excellent review given by Fodor is mainly devoted to the chemical synthesis of tropane alkaloids (Fodor, G., 1997).

2. The Solanaceae

The classification of the Solanceae into tribes by

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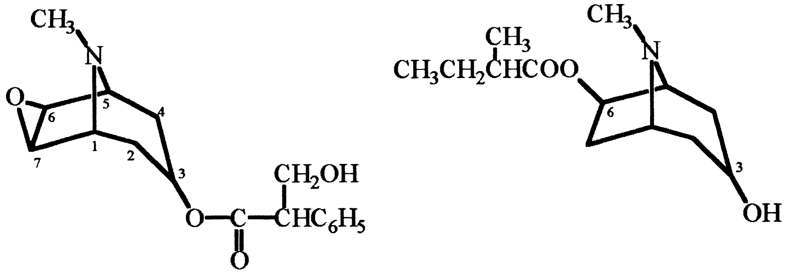
PII: S0031-9422(99)00475-6



scopolamine (hyoscine)   **6β-(2-methylbutanoyloxy)tropan-3α-ol**

Fig. 1. Basic tropane alkaloids.

Hunziker is used for the consideration of the distribution of tropane alkaloids within the family (Hunziker, 1979). Tribes and genera are treated in an order which better lends itself to the discussion of the occurrence of alkaloids.

2.1. The Solanoidae

2.1.1. The tribe Datureae

The tribe Datureae contains the greatest range of tropane alkaloids. Two genera are recognised, *Datura* and *Brugmansia*, the latter now separated from *Datura* and considered to be of generic rank (Lockwood, 1973a, 1979). *Datura stramonium* (*D. tatula*), is a herbaceous species widely distributed in the warm regions of the world, and is a noxious weed of cultivated cereal crops (Everist, 1957). The type specimen is from America. Other *Datura* species include *D. ferox* (China), *D. quercifolia* (Mexico), *D. pruinosa* (Mexico), *D. leichhardtii* (central Australia), *D. innoxia* (Mexico), *D. discolor* (W. Indies), *D. metal* (Asia), and *D. wrightii* (TX, USA). The sources of the type species are as shown, however, like all herbaceous *Datura* species, they have become widely distributed. *Datura ceratocaula* is geographically distributed throughout Mexico and central America. Rather than viewing *D. ceratocaula* as a primitive, connecting link between the herbaceous daturas and brugmansias, it seems more appropriate to view it as a highly specialised datura (Lockwood, 1973b). *Datura ceratocaula* is an aquatic, hollow-stemmed, prostrate, creeping plant known by the Mexicans as the narcotic *torna-loca* or maddening plant. The aerial parts contain little scopolamine, the major alkaloid is hyoscyamine (Schultes & Hofmann, 1973) but it also contains the novel base 6β-(2-methylbutanoyloxy)tropan-3α-ol (Fig. 1) (Beresford & Woolley, 1974). The genus *Brugmansia* is native to South America, all eight species are arborescent and appear to be cultigens unknown in the truly wild state. *Brugmansia aurea* is the most widespread species occurring throughout the Andes from Colombia to northern Chile, at elevations of 2500 to 3000 m. *Brugmansia sanguinea* with its striking red inflorescence is native from Colombia to Peru. Most of the species were of the greatest social and religious importance in ancient Andean cultures. The species currently recognised are *B. arborea*, *B. aurea*, *B.* × *candida*, *B.* × *dolichocarpa*, *B.* × *insignis*, *B. sanguinea*, *B. versicolor* and *B. vulcanicola* (Schultes & Farnsworth, 1980). The most intensive ethnic use of *Brugmansia* appears to be in Sibundoy in southern Columbia. Some species of *Datura* and *Brugmansia* have now been studied in considerable chemical detail, and all exhibit much the same type of alkaloid spectrum (Evans, 1979).

The aerial parts contain scopolamine[1] and/or hyoscyamine as principal alkaloids, with smaller amounts of derivatives of these bases. The roots contain in addition a large number of esters formed from dihydroxytropane and teloidine. Polyhydroxylated tropane alkaloids have been recently reported in *Datura* species, and were previously overlooked due to their insolubility in chloroform, and remaining undetected by Dragendorff's and iodoplatinate reagents. Calystegine B_2 (1β,2α,3β,4α-tetrahydroxynortropane) has been isolated from tubers of *Solanum* spp. and the leaves of *Datura wrightii* in low yield (Nash, Rothschild, Porter, Watson, Waigh & Waterman, 1993).

2.1.2. The tribe Solandreae

The genus *Solandra* is a relatively small genus of about 12 'vine-like' species endemic to South America, Cuba and Jamaica. *Solandra longifolia* (Cuba, Jamaica) was first investigated by Petrie (1916), however, five species (*S. grandifolia*, *S. guttata*, *S. hartwegii*, *S. hirsuta* and *S. macrantha*) have been systemically examined using modern techniques (Evans, Ghani & Woolley, 1972a). A uniform chemotaxonomic group was revealed with atropine and/or hyoscyamine and their nor-derivatives as principal alkaloids. In addition littorine and other tropane alkaloids demonstrate the range of alkaloids which are

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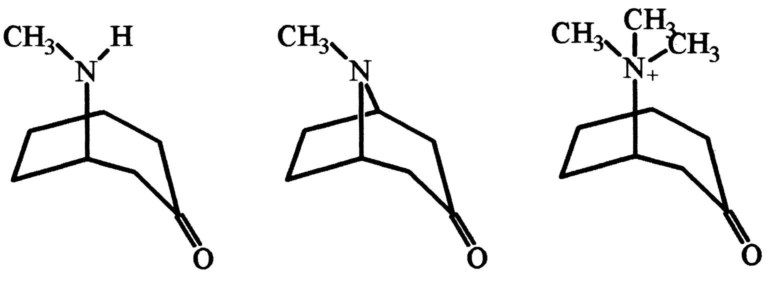
[1] Sometimes reported in the literature cited as hyoscine.



physoperuvine **tropinone** ***N,N*-dimethylphysoperuvine**

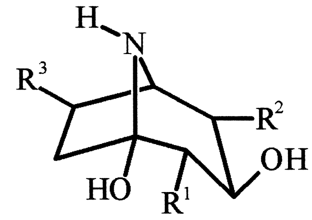
Fig. 2. Secotropane alkaloids of *Physalis peruviana*.

found in *Datura* species, however, the roots did not contain the mono- and ditigloyl esters as in *Datura*, but yielded valtropine, an alkaloid not detected in *Datura* but common in *Duboisia* species.

2.1.3. The tribe Solaneae

Atropa belladonna extensively investigated by early workers, has hyoscyamine as the principal alkaloid, other alkaloids include scopolamine and apoatropine (Evans, 1979). Hyoscyamine and scopolamine *N*-oxides are also normal plant constitutents (Phillipson & Handa, 1975). Hyoscyamine and tigloidine are found in the minor genera *Latua* and *Acristus* spp. (Evans, 1979). The Cape Gooseberry, *Physalis peruviana*, finds a variety of uses in traditional medicine. Tigloidine (3β-tigloyloxytropane) and 3α-tigloyloxytropane were isolated as root alkaloids, the tiglic acid moiety being derived from isoleucine (Beresford & Woolley, 1974). New secotropane alkaloids, also major alkaloids, were isolated from the roots and were subsequently identified as (+)-physoperuvine (the structure had previously been reported (Ray, Sahai & Sethi, 1976)), racemic physoperuvine and (+)-*N*,*N*-dimethyl-physoperuvinium salt (Fig. 2). The secoalkaloids are clearly metabolites of tropane alkaloids being shunt products rather than biosynthetic intermediates (Sahai & Ray, 1980). Extracts from both leaves and roots were examined by GC–MS. They contained 3β-acetoxytropane and *N*-methylpyrrolidinylhygrine (two isomers), first reported in this genus, and 3β-tigloyloxytropane, hygrine, physoperuvine, tropine and cuscohygrine (Kubwabo, Rollman & Tillequin, 1993). Roots of *Physalis alkekengi* yielded tigloidine, 3α-tigloyloxytropane, cuscohygrine, the hygrine dimer phygrine and some unidentified bases (total alkaloid, ca 0.02–0.025%) (Basey & Woolley, 1973). There was no scopolamine, hyoscyamine, littorine or ditigloyl esters.

Water-soluble calystegine alkaloids were later extracted from the roots of *P. alkekengi*. Two were identified as calystegines A_3 (1β,2α,3β-trihydroxynortropane) and B_2 (1β,2α,3β,4α-tetrahydroxynortropane) which had previously been isolated from *Calystegia sepium* (Convolvulaceae; Fig. 3) (Goldmann et al., 1990a). Structures of a further two alkaloids were deduced as 1β,3β,4α-trihydroxynortropane and 1β,2β,3β,4α-tetrahydroxynortropane which were assigned the names A_5 and B_3, respectively (A have 3 × OH, B have 4 × OH and C have 5 × OH). The final calystegine was B_1 (1β,2α,3β,6β-tetrahydroxynortropane) which too had been isolated from *C. sepium*. Calystegine B_2 was a potent inhibitor of β-glucosidase (Asano, Kato, Oskeki, Kizu & Matsui, 1995). The large genus *Solanum* does not contain the usual tropane alkaloids. However, some novel polyhydroxytropane alkaloids have been isolated. Calystegine A_3 (1β,2α,3β-trihydroxynortropane) has been found along with calystegine B_2 in *Datura wrightii* and in the leaves of some *Solanum* species including *S. tuberosum*, *S. dulcamara*, *S. melongena*, and in herbarium fragments



	R^1	R^2	R^3
Calystegine A_3	OH	H	H
Calystegine A_5	H	OH	H
Calystegine B_1	OH	H	OH
Calystegine B_2	OH	OH	H
Calystegine B_3	OH	OH	H

Fig. 3. The Calystegines.

of *S. dimidatum* from Texas and *S. kwebense* from southern Africa (Evans, 1979).

Mandragora roots have for many centuries enjoyed a reputation as folk medicines. *Mandragora officinalis* now comprises two distinct species, *M. autumnale* and *M. vernalis* which contain hyoscyamine, scopolamine, cuscohygrine, apoatropine, 3α-tigloyloxytropane and 3,6-ditigloyloxytropane (Jackson & Berry, 1973). Consumption of the fruits of *Salpichora organifolia* is reported as producing symptoms of drunkenness. The

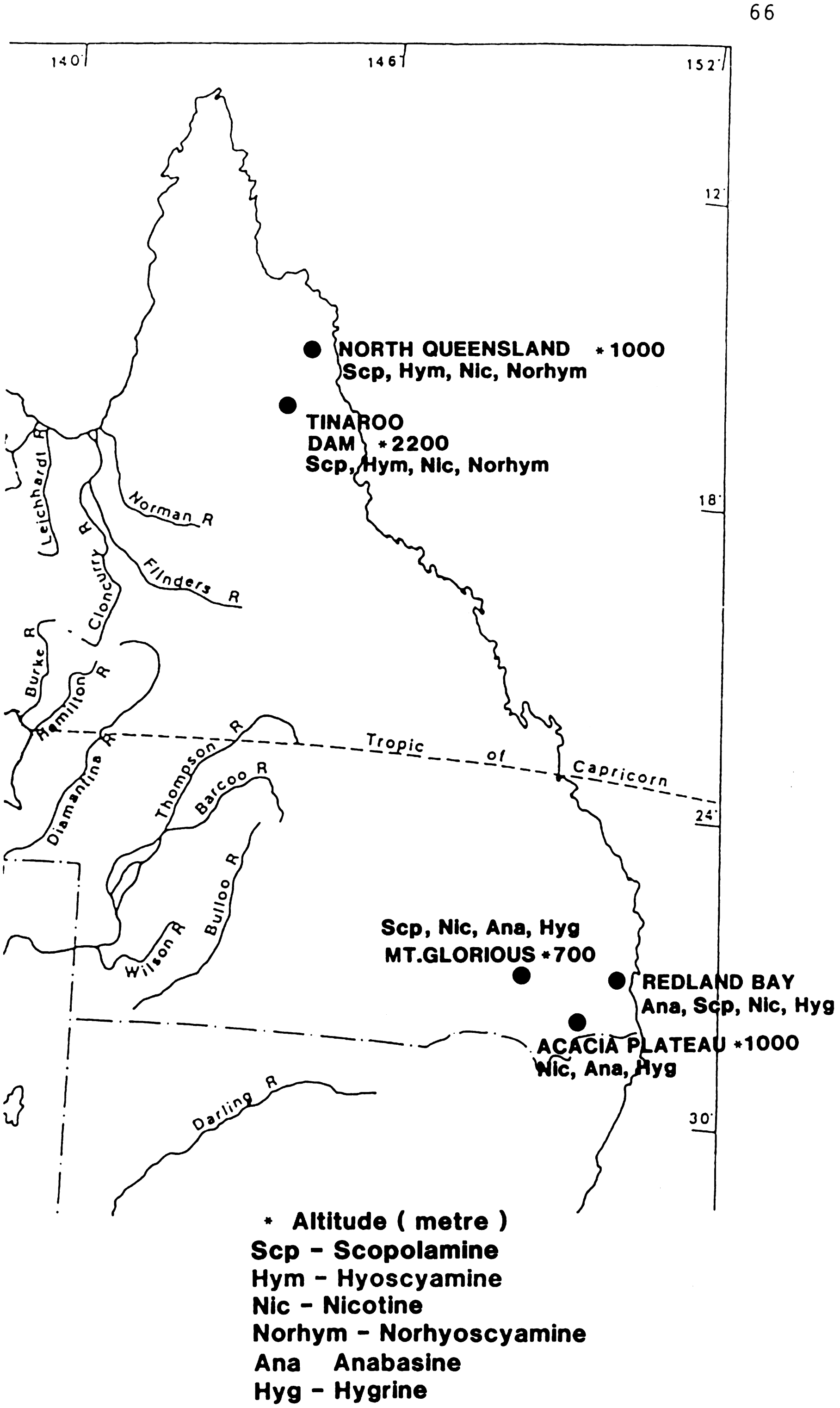


Fig. 4. Alkaloid variation in *Duboisia myoporoides* from various regions of Queensland.

roots were found to contain small quantities of cuscohygrine, pseudotropine, tropine and possibly hyoscyamine (Evans, Ghani & Woolley, 1972b). *Withania somnifera* likewise contains cuscohygrine and 3α-tigloyloxytropane (Leary, Khanna & Schwarting, 1963), and also tropine and pseudotropine (Khanna, Schwarting & Rother, 1961). The main base from the roots of *Cyphomandra betaceae* was *N*,*N*′-bis-(4-dimethylaminobutyl) hexamide. Other bases included tropinone and cuscohygrine and tentatively hyoscyamine, tigloidine, tropine and pseudotropine (Evans et al., 1972c).

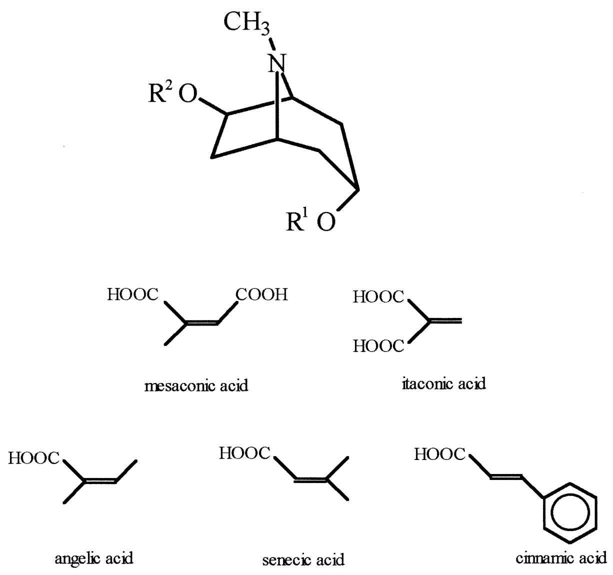
2.1.4. The tribe Hyoscyameae

N-oxides were found in *Scopolia* and *Hyoscyamus* spp. (Phillipson & Handa, 1975) which along with *Physochlaina* and *Przewalskia* spp. contain hyoscyamine as the major alkaloid with some scopolamine (Evans, 1979).

2.2. The Cestroideae

2.2.1. The tribe Anthocercideae

The tribe Anthocercideae contains seven genera, *Duboisia*, *Anthocercis*, *Cyphanthera*, *Anthotroche*, *Symonanthus*, *Grammosolen* and *Crenidium* (Haegi, 1981). *Duboisia hopwoodii*, is a small shrub seldom exceeding 2.5 m in height with narrow lanceolate leaves, smaller than those of *D. leichhardtii*. It occurs in western and central Australia (Barnard, 1952). One of the few drug-yielding plants used by the aborigine, it is known as *pituri* by central and western Australian aboriginal tribes (Watson, Luanratana & Griffin, 1983). *Duboisia myoporoides* is a tree which may grow 15 m tall, with broad-lanceolate to obovate glabrous leaves. This species occurs along the eastern coast of Australia and is also found in New Caledonia (Loftus Hills, Bottomley & Mortimer, 1953). *Duboisia myoporoides* is presumed to have chemical varieties (Loftus Hills, Bottomley & Mortimer, 1954a), scopolamine is the dominant alkaloid in a variety collected north of Gosford, NSW, while hyoscyamine appears as the major alkaloid in a variety south of Gosford. In a region known as Acacia Plateau near Killarney, Queensland, a third variety was discovered in which nicotine and anabasine are the dominant alkaloids (Mortimer & Wilkinson, 1957). More recent collections from within Queensland have confirmed the Acacia Plateau type as a distinct pyridine variety with little tropane alkaloid. Also there is some segregation towards pyridine bases in southern Queensland of the proposed scopolamine dominant northern variety (Fig. 4) (Gritsanapan & Griffin, 1991). *Duboisia leichhardtii* grows in semi-evergreen vine thickets (dry vine forests) in a location known as the south–west Burnett region of Queensland. The leaves are smaller and more narrow than those of *D. myoporoides* and the tree grows to 3 m in height. Both hyoscyamine and scopolamine dominant trees exist in natural stands, but the former were most prevalent (Loftus Hills, Bottomley & Mortimer, 1954b; Griffin, 1965). Most recently a fourth, new species of *Duboisia* was discovered (Craven, Lepschi & Haegi, 1995). *Duboisia arenitensis* occurs within the monsoon zone of northern Australia which includes the sandstone plateau of Arnhem Land (hence the species is named after the geological name for sandstone, *arenite*). No single character distinguishes the species from its congeners, it is separated on a combination of characters. The alkaloid content is less than the other species, the major alkaloid scopolamine, 0.14% and hyoscyamine at 0.04%. *Anthocercis* spp. contain either hyoscyamine or scopolamine as predominant alkaloids, frequently accompanied by their respective *apo* and *nor*-derivatives and are mainly located in south–west regions of western Australia. *Anthocercis littorea*, a shrub 3 m tall, was shown to contain mainly littorine and meteloidine (Cannon, Joshi, Meehan & Williams, 1969). Many other tropane alkaloids were later isolated that are mono- and ditigloyl esters of teloidine (Evans & Treagust, 1973). There was no suggestion of chemical variation within the species. *Anthocercis viscosa* and *A. fasciculata* contained hyoscyamine (Cannon et al., 1969). *Cyphanthera anthocercidea* (*Anthocercis frondosa*) occurring mainly in the Wimmera region of Victoria, is an erect shrub to 2 m in height containing scopolamine and hyoscyamine, but chiefly nicotine (Evans & Ramsey, 1979). *Cyphanthera albicans* (*Anthocercis albicans*) afforded butyryl esters of tropine and 6β-hydroxytropine. The genus *Anthotroche* comprises three species endemic to western Australia, *A. myoporoides*, *A. pannosa* and *A. walcottii*. They contain the tropane alkaloids hyoscyamine, norhyoscyamine, apoatropine and scopolamine (Evans & Ramsey, 1981). Evans and Ramsey (1983) investigated and reviewed the Anthocercideae including some new taxa described in Flora of Australia (Purdie, Symon & Haegi, 1982). The new genus *Symonanthus* (two spp.) is regarded as closely related to *Anthocercis* (Haegi, 1981). *Symonanthus aromaticus* (*A. aromaticus*) is chemically unique as the roots contain mono- and ditigloyl esters like *Datura* species. Both aerial parts and roots have scopolamine and its derivative aposcopolamine, as the main alkaloids. The genus *Grammosolen* (two spp.) is most closely related to *Cyphanthera* and *Anthotroche*. The alkaloid spectrum of *Grammosolen dixonii* resembles that of the nicotine-free species of *Cyphanthera*. The new genus *Crenidium* has a single species, *C. spinescens*, where hyoscyamine is the predominant alkaloid. A total of eight tropane alkaloids are present, also anabasine and ursolic acid. *Anthocercis ilicifolia* possesses a similar alkaloid spectrum to that of *A. littorea*. *Anthocercis genistoides* was shown to be



	R^1	R^2
Schizanthine A	Senecioyl-6β-oxytropan-3α-mesaconate	Senecioyl
Schizanthine B	Ethylmesaconate	Senecioyl
Schizanthine C	Tropan-3α-mesaconate	Senecioyl
Schizanthine D	3α-Hydroxytropan-6β-mesaconate	Senecioyl

Fig. 5. Tropane alkaloids of *Schizanthus* species.

most variable, meteloidine is the major alkaloid. The alkaloids of *Cyphanthera odgersii* and *C. tasmanica* were found to be consistent with other known *Cyphanthera* spp. (El-Imam & Evans, 1984).

2.2.2. The tribe Nicandreae

Esters of tropic acid are not found in the tribe Nicandrae, however, tropine was isolated from the roots of *Nicandra* species (Romeike, 1966a).

2.2.3. The tribe Salpiglossidae

The genus *Schizanthus* comprises about 27 species all indigenous to South America (Chile and Peru). Tropane-derived alkaloids have been reported in *S. pinnatus* (Ripperger, 1979). These were identified as schizanthines A and B and are 6β-senecioyloxytropan-3β-ol esters of dibasic measconic acid (A is a diester of 6-senecioyloxytropine, B is a mixed ester of 6-senecioyloxytropine and ethanol). The root alkaloids of *S. hookeri* are tropine, a pair of diastereoisomeric hygrolines and new alkaloids 3α-senecioyloxytropan-6β-ol and 6β-angeloyloxytropan-3α-ol (San Martin, Rovirosa, Gambaro & Castillo, 1980). *Schizanthus litoralis* is native to Peru and grows up to 1 m high, has doubly pinnatifid leaves and large butterfly-like, blue flowers. The genus contains a number of tropane alkaloids including hydroxytropane esters, hygrolines and the tropane diester of itaconic acid. Recently, some new alkaloids have been isolated, 6β-senecioyloxy-tropan-3α-methylmesaconate, 6β-cinnamoyloxytropan-3α-methylmesaconate, 6β-senecioyl-oxytropan-3α-ol, *cis* and *trans* *N*-(4-hydroxyphenyl) ferulamides (Munoz, Piovano, Garbarino, Hellwing & Breitmaier, 1996) and also 3α-senecioyloxytropan-6β-ol, (−)-hygroline and (+)-pseudohygroline, which had already been reported present in *S. pinnatus* (Fig. 5) (Gambaro, Labbe, Munoz & Castillo, 1983).

Schizanthines C, D, E, and a trimeric tropane alkaloid occur in *S. grahamii* (San Martin et al., 1987). The centre of this complex molecule is 2-methyl-4-phenylcyclobutane-1,2,3-tricarboxylic acid and involves an angelic acid ester. Grahamine contains a cyclobutane ring substituted by three carboxyl groups and is formed from cinnamoyltropine and mesaconic acid. Hence grahamine is related to the truxillines in coca leaf (Fig. 6).

3. The Erythroxylaceae

The genus *Erythroxylum* has some 200 species which are widely distributed in tropical regions with diversity in South America and the island of Madagascar. The comparative phytochemistry was reviewed by Evans (1981). The section *Archerythroxylum* comprises over 60 species. Of the six species examined, *Erythroxylum argentinum*, *E. cataractarum*, *E. cumanense*, *E. glaucum*, *E. mamacoca* and *E. shatona* contained total alkaloids in the range 0.06–0.20% compared with all species from the sections *Macrocalyx*, *Rhabdophyllum* and *Leptogramme* save one, which were lower in alkaloid content (0.002–0.04%) (El-Imam, Evans & Plowman, 1985). In the six *Erythroxylum* spp. of the order *Archerythroxylum*, benzoic and phenylacetic acids formed esters with alkamines, principally tropan-3-ols, tropan-3,6-diols and their derivatives. 3β-benzoyloxytropane is the most frequently occurring alkaloid and together with nortropacocaine (3β-benzoyloxynortropane) from *E. mamacoca*, comprise the very limited 3β series of alkaloids. Dihydrocuscohygrine and cuscohygrine are present in some species. Cuscohygrine as the major alkaloid of *E. cataractarum* is unique in the genus. Furthermore El-Imam and colleagues found tropacocaine, at the time a new alkaloid, in *E. ulei* (section *Leptogramme*) and in *E. mamacoca* and *E. argentinum* (section *Archerythroxylon*) but not in the sections *Marcrocalyx* and *Rhabdophyllum*. Dihydrocuscohygrine and cuscohygrine are also found in the cultivated cocaine producing species, *E. coca* and *E. novogranatense*, and its variety *truxillense*. Laurent Rivier in a review article (Rivier, 1981) reports cocaine and the *cis* and *trans* isomers of cinnamoyl cocaine in *E. coca* and *E. novogranatense* var. *truxillense* (Fig. 7). The ratios between the various alkaloids served no chemotaxonomic purpose as there was great variation within the species.

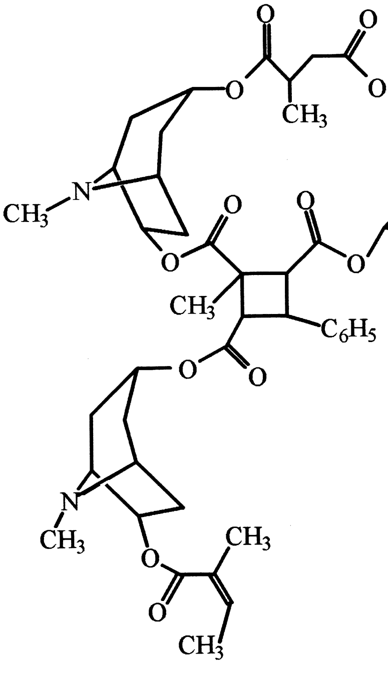


Fig. 6. Grahamine.

Cocaine is produced in quantity only in these cultivated species, even wild species which are morphologically close to *E. coca* either do not contain cocaine or do so at very low concentration (0.0005%) (Holmstedt, Jaatmaa, Leander & Plowman, 1977; Plowman & Rivier, 1983). Cocaine does not appear to be an alkaloid of Old World species. A series (α, β, γ, δ, ε) of dimeric methylecgonine (methyl ester of ecgonine, the basic moiety of cocaine) esters of truxillic acid (1,3-diphenylcyclobutane-2,4-dicarboxylic acids, dimers of cinnamic acid) was identified using GC–MS of Bolivian coca leaf, α and β-Truxillines were the most abundant (Fig. 7) (Moore et al., 1987). A new alkaloid, 1-hydroxytropacocaine, was discovered in *E. novogranatense* var. *novogranatense* and var. *truxillense*. Gas chromatographic analysis showed levels of 0.3–0.5% in glasshouse cultivated *E. novogranatense* var truxillense, the same order of magnitude as cocaine. The *novogranatense* variety contained less 1-hydroxytropacocaine (0.04–0.07%). Field grown leaf samples of *E. novogranatense* var. *novogranatense* and *E. coca* both contained less than 0.1% 1-hydroxytropacocaine (Moore, Hays, Cooper, Casale & Lydon, 1994). The base 6β-benzoyloxytropan-3α-ol occurs in both *E. cumanense* and *E. glaucum* (both section *Archerythroxylum*). Trimethoxybenzoyl esters found in the roots of *E. cumanense* were once thought to be exclusive to Old World species. *Erythroxylum macrocarpum* and *E. sideroxyloides* of the section *Packylobus*, two species indigenous to Mauritius, contain a similar range of alkaloids consisting mainly of benzoyl esters of tropan-3α-ol, tropan-3β-ol and tropan-3α,6β-diol together with their *nor*-derivatives. Three new alkaloids were discovered, 3α-benzoyloxytropan-6β-ol (from *E. sideroxyloides*), 3α-benzoyloxynortropane and 3β-benzoyloxynortropan-6β-ol (both species) (Al-Said, Evans & Grout, 1986a). *Erythroxylum hypericifolium* is found on the volcanic slopes of Mauritius and Rèunion. Considered to constitute along with four other species of Madagascan origin, the section *Venelia* of the genus (Evans, 1981), the leaves were observed to be devoid of cocaine (Schultz, 1907). The roots of a closely related species *E. previllei*, were found to contain 0.2% of alkaloids, hence the root alkaloids of *E. hypericifolium* were also examined (Al-Said, Evans & Grout, 1986b). The root bark contains the new bases 3α-(3-hyroxyphenylacetoxy)tropane, (+)3α-phenylacetoxytropan-6β-ol, 6β-acetoxy-3α-phenylacetoxytropane, 3α-phenylacetoxytropan-6β,7β-diol and 3α-phenylacetoxynortropane. 3α-Phenylacetoxytropane was also isolated. Many new alkaloids were likewise detected in the leaves (Al-Said, Evans &

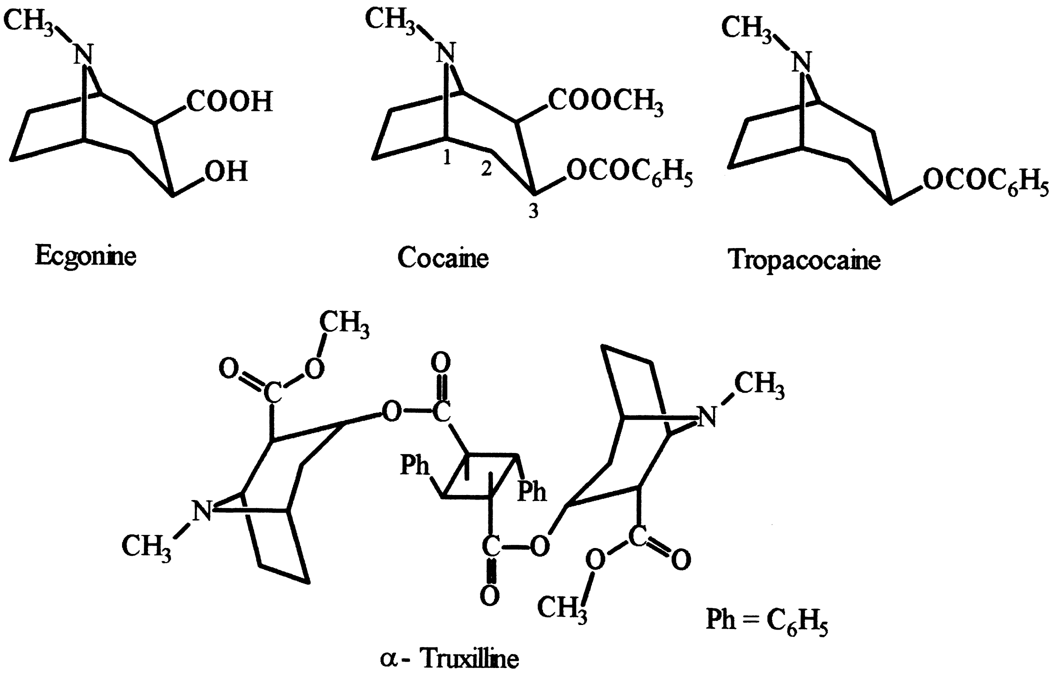


Fig. 7. *Erythroxylum* alkaloids.

Grout, 1989a). 3α-Cinnamoyloxytropan-6β-ol had previously been isolated as the (+) base from *Knightia* spp. (Lounasmaa, Pusset & Sevenet, 1980a). This is the first pseudotropane ester to be found in *Erythroxylum hypericifolium*. The benzoyl analogue is widely distributed in *Erythroxylum* spp. The new alkaloids included 3α-cinnamoyloxytropane, which has not been previously reported in *Erthroxylum* spp. but is reported in *Crossostylis* spp. (Gnecco Medina, Pusset, Pusset & Husson, 1983). Also 3α,6β-dicinnamoyloxytropane (analogous to the dibenzoyl ester found in *E. cuneatum* (El-Imam, Evans, Grout & Ramsey, 1988)), 3-cinnamoyloxytropan-6-ol (stereochemistry not established), 6β-acetoxy-3α-cinnamoyloxytropane and 6-phenylacetoxytropan-3-ol were located. Mixed cinnamate tropane dimers, esters of truxillic acid were detected (Fig. 8) (Al-Said et al., 1989a). These were identified as 3,3′-truxilloyloxy-6′-acetoxyditropane (7a), 3,3′-truxilloyl-6hydroxy-6′-acetoxyditropane (7b), and 3,3′-truxilloyloxy-6′-hydroxyditropane (7c). As in root bark, esters of phenylacetic acid predominate in the stem bark of *E. hypericifolium*. 3α-phenylacetoxynortropan-6β-ol is the mayor alkaloid. Others include 6β-acetoxy-3α-benzoyloxytropane, 3-acetoxy-6-phenylacetoxytropane and hygrine (Al-Said, Evans & Grout, 1989b).

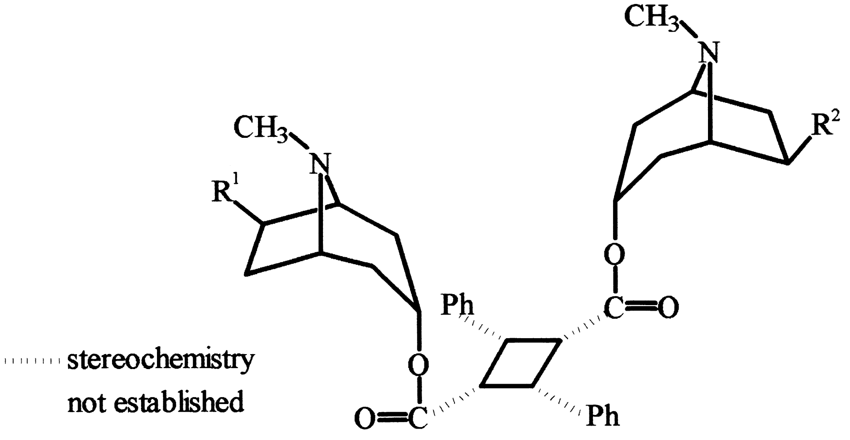


Fig. 8. Some cinnamate tropane dimers (7a–7c) from *Erythroxylum hyperfolium*.

Erythroxylum zambesiacum (section *Melanocladus*)

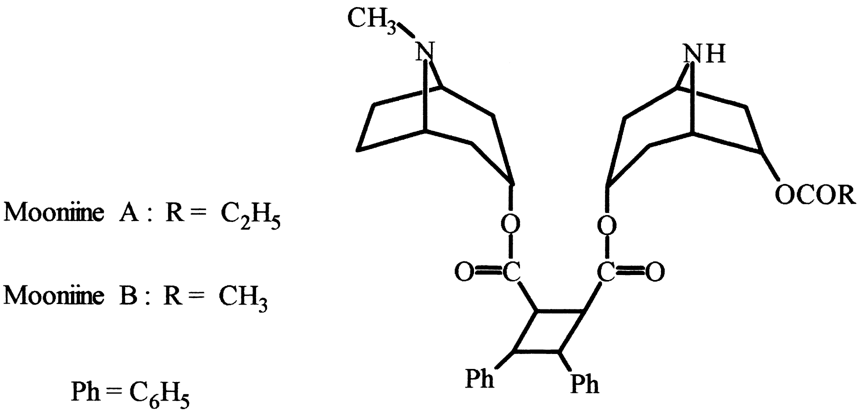


Fig. 9. Alkaloids of *Erythroxylum moonii*.

likewise has a complex mixture of root bark alkaloids (El-Imam, Evans, Grout & Ramsey, 1987). Six new alkaloids characterized from the root-bark of *E. zambesiacum* are,

3α-(3,4,5-trimethyoxybenzoyloxy)nortropane,
3α-(3,4,5-trimethoxybenzoyloxy)tropan-6β-ol,
3α-(3,4,5-trimethoxybenzoyloxy)nortropan-6β-ol,
6β-benzoyloxytropan-3α,7β-diol,
6β-benzoyloxy-3α-(3,4,5-trimethoxycinnamoyloxy)-tropan-7β-ol, and
7β-acetoxy-6β-benzoyloxy-3α-(3,4,5-trimethoxycinnamoyloxy)tropane.

Other minor bases identified include,

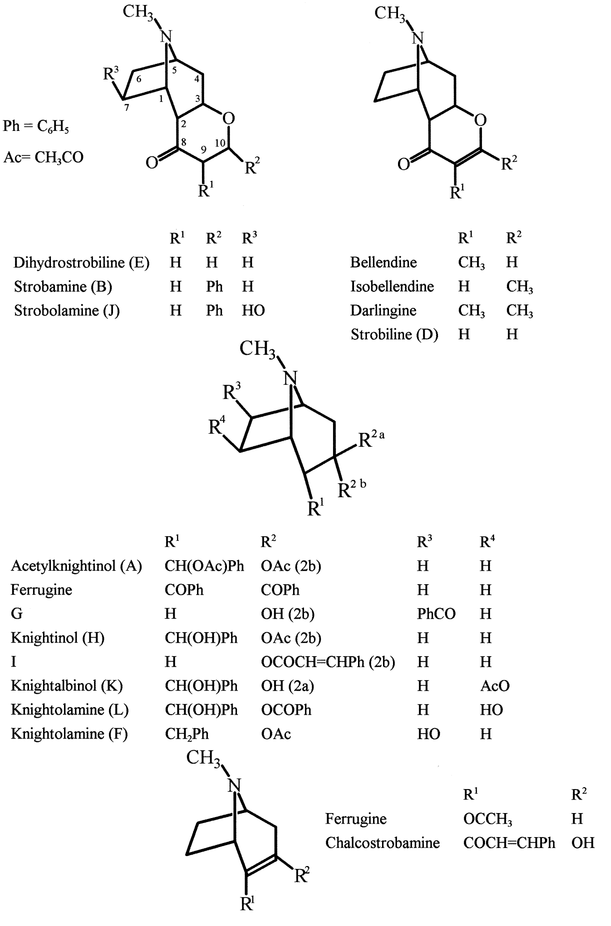
3α-(3,4,5-trimethoxybenzoyloxy)tropane,
3α-(3,4,5-trimethoxycinnamoyloxy)tropane,
3α-phenylacetoxytropan-6β-ol,
3α-(3,4,5-trimethoxybenzoyloxy)tropan-6β,7β-diol,
6β-benzoyloxytropan-3α-ol, and
6β-benzoyloxy-3α-(3,4,5-trimethoxycinnaomoyloxy)-tropane.

GC–MS of extracts from the stem bark of *E. zambesiacum* shouwed in addition a further 20 bases. Esters of phenylacetic acid predominate, others involve acetic, benzoic and trimethoxycinnamic acid. The principal alkaloid is 3α-(3′,4′,5′-trimethoxybenzoyl)oxytropane. Three new alkaloids were characterized as 6β-benzoyloxytropan-3-one and, tentatively, 6-isovaleryloxytropan-3-ol and 3-(2-methyl butyryloxy)-6,7-diol (Christen, Roberts, Phillipson & Evans, 1993). A similar investigation of the stem bark of *E. lucidum* yielded 13 bases. Most were established precursors or intermediates in the biosynthesis of tropane alkaloids, one 2,1′-dehydrohygrine is a key reputed intermediate in the formation of tropinone (Brachet, Munoz, Gupta, Veuthey & Christen, 1997). Novel dimeric tropane alkaloids although in very low yield (ca 0.003%) have been isolated from Sri Lanka species, *E. moonii* (Rahman, Khattak, Nighat, Shabbir, Hemalal & Tillekeratne, 1998). Mooniine A and mooniine B are diesters of tropine and nortropine with carboxylic dibasic acids presumably resulting from tropic acid biogenesis (Fig. 9). With the exception of tropyl esters, the tropane alkaloid spectrum of the genus *Erythroxylum* is remarkably similar to that of the Solanceae (Evans, 1979, Evans & Ramsey, 1983). *Erythroxylum australe* (section *Coelocarpus*) is a unique species as it contains tigloyl esters meteloidine, 3α-tigloyloxytropan-6β-ol, 3α-tigloyloxynortropan-6β-ol and an unknown base which was tentatively identified as 7-hydroxy-6-tigloyloxynortropan-3-yl, 2-hydroxy-3-phenylpropionate. 2-Hydroxy-3-phenyl-propionic acid, closely related to tropic acid and a component of the Solanaceous alkaloid littorine, is a further link (besides meteloidine) with the family Solanceae (Griffin, 1978). Phenylalanine, a precursor of tropoyl esters in the Solanaceae, has been established as a precursor of the benzoyl moiety of cocaine (Gross & Schutte, 1963). The tropane moieties of alkaloids within the genus *Erythroxylum*, in themselves, show little use as intra generic chemotaxonomic characters. Esterifying acids, however, are often distinctive features of certain species. The combination of acetic, phenylacetic and cinnamic acids for any one species, viz. *E. hypericifolium* (Al-Said et al., 1986b) is unique as was tiglic acid for *E. australe* (Griffin, 1978). Acid moieties, unique for certain species are the pyrrole-2-carboxylic acids of *E. vacciniifolium*, section *Archerythroxylon* (Graf & Lude, 1978) and 2-furoic acid of *E. dekindtii*, section *Lagynocarpus* (Al-Yahya, Evans & Grout, 1979).

4. The Proteaceae

Bellandena montana an endemic Tasmanian shrub, afforded the first alkaloid from the Proteaceae, bellendine, an unusual tropane alkaloid (Bick, Bremer & Gillard, 1971). Similar alkaloids were isolated from *Darlingia darlingiana*, a Queensland genus (Bick, Gillard & Huck-Meng, 1979a). The major alkaloid, darlingine is a similar pyranotropane base.

A closely related arboreal species, *D. ferruginea*, also contained darlingine, ferruginine and new tropane alkaloids ferrugine and 3α-benzoyloxy-2α-hydroxybenzyltropine (Bick, Gillard & Hung-Meng, 1979b). A further 14 alkaloids of this type were obtained from a re-investigation of *Bellendena montana* (Bick, Gillard & Huck-Meng, 1979c). These included bellendine, isobellendine and darlingine (Fig. 10). Alkaloids of a 2-benzyltropine type were obtained from the New Caledonian genus *Knightia*, *K. deplanchei* (Lounasmaa, Novkulich & Wenkert, 1975) and *K. strobilina*. Strobiline (specified D) is the major alkaloid of *K. stobiline*, also present are 3α-cinnamoyloxytropan-6β-ol (I) and the new alkaloids 3α-acetoxy-2α-acetoxybenzyltropane (acetylknightionl, A), 3α-acetoxy-2α-benzyltropan-6β-ol (knightoline, F), 6β-benzoyloxytropan-3α-ol (G), 2α-hydroxybenzyl-3α-acetoxytropane (knightinol, H) and dihydrostrobiline (E) (Lounasmaa et al., 1980a). A second paper (Lounasmaa, Pusset & Sevenet, 1980b) describes the structure of a further five new alkaloids, Strobamine B, chalcostrobamine (C), strobolamine (J), knightalbinol (K) and knightolamine (L, Fig. 10). *Agastachys odorata*, a Tasmanian species was shown to contain 6β-acetoxy-3α-tigloyloxytropane and 3α-(*p*-hydroxybenzoyloxy)trop-6-ene, the first naturally occurring tropene base (Bick, Gillard, Huck-Meng & Preston, 1979d). Speculation concerning the biogenesis of Proteaceous alkaloids was raised by Ralph Bick and his co-workers (Bick, Gillard, Huck-Meng, Lounasmaa, Pusset & Sevenet, 1981).



	R^1	R^2	R^3
Dihydrostrobiline (E)	H	H	H
Strobamine (B)	H	Ph	H
Strobolamine (J)	H	Ph	HO

	R^1	R^2
Bellendine	CH_3	H
Isobellendine	H	CH_3
Darlingine	CH_3	CH_3
Strobiline (D)	H	H

	R^1	R^2	R^3	R^4
Acetylknightinol (A)	CH(OAc)Ph	OAc (2b)	H	H
Ferrugine	COPh	COPh	H	H
G	H	OH (2b)	PhCO	H
Knightinol (H)	CH(OH)Ph	OAc (2b)	H	H
I	H	OCOCH=CHPh (2b)	H	H
Knightalbinol (K)	CH(OH)Ph	OH (2a)	H	AcO
Knightolamine (L)	CH(OH)Ph	OCOPh	H	HO
Knightolamine (F)	CH_2Ph	OAc	HO	H

	R^1	R^2
Ferrugine	$OCCH_3$	H
Chalcostrobamine	COCH=CHPh	OH

Fig. 10. Proteaceous tropane alkaloids.

5. The Euphorbiaceae, Rhizophoraceae, Convolvulaceae, and Cruciferae

Tropane alkaloids are known to exist in a further five plant families, Euphorbiaceae, Rhizophoraceae, Convolvulaceae and Cruciferae though in nature differing significantly from those alkaloids nominated so far. Tropacocaine (3β-benzoyloxytropane), 3α-acetoxy-6β-hydroxytropane and 2α-benzoyloxy-3β-hydroxytropane were isolated from *Peripentadenia mearsi*, Euphorbiaceae (Johns, Lamberton & Sioumis, 1971). Novel dithiolane esters have been found in the Rhizophoraceae (Fig. 11). Brugine (tropine 1,2-dithiolane-3-carboxylate) was obtained from *Bruguiera sexangula* (Loder & Russel, 1966), a tropical mangrove found near Lae, New Guinea which along with a related Australian species, *B. exaristata* also contained other tropine esters of acetic, propionic, *n*-butyric, isobutyric, isovaleric and benzoic acids (Loder & Russel, 1969).

Brugine is also found in *Crossostylis* spp. (*C. biflora*, *C. multiflora* and *C. sebertii*) along with tropine, 3α-benzoyl-oxytropane and two new esters of tropine, tropine cinnamate and ferulate (Gnecco Medina et al., 1983). A series of tropine esters with methoxy substituted benzoic acids is characteristic of tropane alkaloids of the family Convolvulaceae (*C. krauseanus* and *C. subhirsutus*). These include convolvine (3α-veratroyloxynortropane), convolidine (3α-vanilloyloxynortropane), (Aripova, Malikov & Yunusov, 1977; Aripova, Sharova & Yunusov, 1983), confoline (3α-veratroyl-*N*-formylnortropine) (Sharova, Aripova & Yunusov, 1980), and convolamine-*N*-oxide (Aripova, 1985). *Evolvulus sericeus* likewise contains convoline, convolamine and convolidine (Conselo & Alejandra, 1972). Baotongteng A, (2β-hydroxy-6β-acetoxynortropane) (Yao, Chen, Yi & Xu, 1981) and baotongteng B (Chen, Xu & Yao, 1986) were isolated from *Erycibe obtusifolia*. Erycibelline (2β,7β-dihydroxynortropane) occurs in two other *Erycibe* spp., *E. elliptilimba* (Lu, Yao & Chen, 1986) and *E. hainanesis* (Wang, Yao & Chen, 1990). *Cochlearia arctica* (Crucifereae) was shown to contain cochlearine and *m*-hydroxybenzoyloxytropane (Platonova & Kusovkov, 1963).

The hedge bindweed, *Calystegia sepium* (Convolvulaceae) has been shown to synthesise some novel poly-

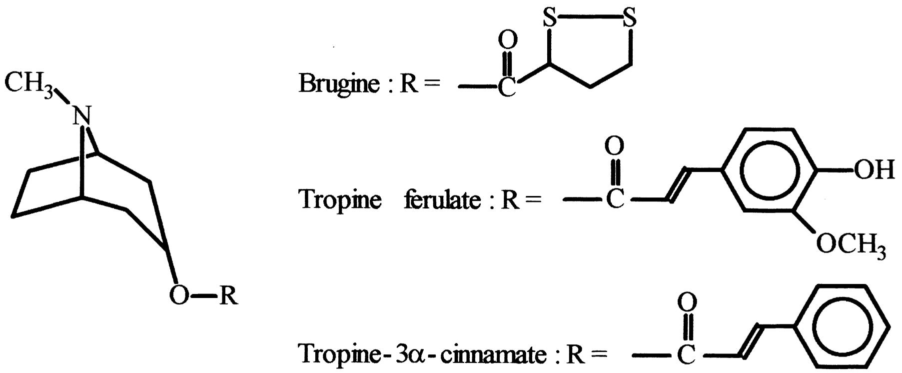


Fig. 11. Dithiolane and other esters.

hydroxynortropanes. Transformed roots of *Calystegia sepium* were extracted with water and the extract contained calystegines, which have been suggested to serve as mediators promoting the growth of *Rhizobium meliloti*.

Calystegine (calystegin) B_1 (1β,2α,3β,6α-tetrahydroxynortropane),
Calystegine B_2 (1β,2α,3β,4α-tetrahydroxynortropane) and
Calystegine A_3 (1β,2α,3β-trihydroxynortropane)

were characterised using ^{1}H- and ^{14}C- NMR (Goldmann et al., 1990b) and confirmed by synthesis (Ducrot & Lallemand, 1990).

The calystegines (Fig. 3), isolated from the roots of *Convolvulus arvensis* and transformed root cultures of *Calystegia sepium*, were proved to be potent inhibitors of β-glucosidase (Molyneux, Pan, Goldmann, Tepfer & Elbein, 1993). Calystegine B_2 was then located in *Solanum* and *Datura* spp. Calystegine A_3 and B_2 occur in the 'skin' of *Solanum tuberosum* var. *Estema* (total alkaloid, 0.01% fresh weight), also in other potato varieties and in *S. dulcamara*, *S. dimidiatum* (TX, USA), *S. kwebense* (southern Africa) and in *S. melongena* (aubergine fruits) (Nash et al., 1993). *Solanum kwebense* and *S. dimidiatum* are known to cause disorders in cattle (crazy cow syndrome). Likewise an Australian stock poison *Ipomoea* sp. off. *calobra* causes a nervous condition known as staggers. It too contains calystegine B_2 and another known glycosidase inhibitor swainsonine, a polyhydroxy indolizidine alkaloid (Molyneux, McKenzie, O'Sullivan & Elbein, 1995). *Datura wrightii* leaves also contained calystegine B_2 (Nash et al., 1993). More recently, new calystegine alkaloids were discovered in other *Solanaceous* spp. *Duboisia leichhardtii* leaves afforded calystegine C_1 (1β,2β,3β,4β,6β-pentahydroxynortropane, 0.09%) and C_2 (1β,2α,3β,4α,6β-pentahydroxynortropane) (Kato, Asano, Kizu, Matsui, Suzuki & Arisawa, 1997). A hypothesis was put forward that pseudotropine was involved in the biosynthesis of calystegines, especially in plants which were devoid of pseudotropine but possessed pseudotropine-forming tropinone reductases. Using a screening method involving GC–MS, calystegines were located in *Atropa belladonna* (all parts but mainly upper leaves), *Mandragora offinarum* (likewise, mainly spring leaves), *Scopolia carniolica* (spring leaves and flowers), *Hyoscyamus niger* (traces in all plant parts) and *Solanum tubersoum* (sprouts only) (Drager, van Almsick & Mrachatz, 1995).

6. Hybrids within the genera *Datura*, *Brugmansia* and *Duboisia*

6.1. Datura hybrids

The barriers to interspecies hybridization in herbaceous *Datura* and conditions whereby these may be overcome, have been reported by Avery, Satina & Rietsema (1959). Interspecific hybridization has been repeatedly attempted with some success, with a view to produce races with a superior alkaloid content, in particular the more esteemed scopolamine. F_1 hybrids of *D. ferox*, whose leaves contain mainly scopolamine and *D. stramonium*, having a scopolamine/hyoscyamine ratio of 1:2, are characterised by their scopolamine dominance. The F_2 generation yields an approximate 3:1 segregation into scopolamine and hyoscyamine dominant types. Chemical varieties from these hybrid plants have been developed which have the morphological form of one parent with alkaloid characteristics of the other (Romeike, 1961, 1962, 1966b. Similar hybrids back-crossed with *D. stramonium* and selecting for scopolamine, produced races which at the F_7 generation, had the morphological form and vigour of *D. stramonium*, and yet inherited the scopolamine characteristics of *D. ferox*. These hybrids were maintained through 14 generations. Interspecific crossing involving *D. leichhardtii* × *D. innoxia* and *D. stramonium* × *D. discolor* likewise concluded that although the tendency towards scopolamine production was dominant, for hybrids to maintain this, at least one parent is required which itself has little or no hyoscyamine (Evans, 1979).

6.2. *Brugmansia*[2] hybrids

All species within the genus appear to be cultigens. Bristol reported "I have seen no indication in Herbaria nor during 13 months field work, that any tree datura was not associated with human activity. The northern Andes, however, is the centre of variability and possible origin of this group. In the same region there is a conspicuous absence of seedling tree daturas" (Bristol, 1966). Thus unlike the herbaceous daturas there is considerable evidence of natural hybridization. El-Dabbas and Evans (1982) prepared reciprocal crosses of *B. aurea* and *B. candida*. The two parent species contain scopolamine 0.66% and 0.25%, respectively. The F_1 hybrids possessed a total alkaloid content and scopolamine and hyoscyamine ratios (ca., 4 : 1) very favourable for their possible utilization as sources of scopolamine. Using *B. aurea* as the male parent, gave plants similar in alkaloid characteristics to those of *B. aurea*. *Brugmansia candida* as male parent gave plants which excelled either parent in their scopolamine content. A tree datura designated *Brugmansia candida* cultivar (Flintham Hall) is of unknown origin other than it was propagated from a plant from Tangiers, is of special interest since having a salmon-coloured flower and presumed a hybrid (El-Imam & Evans, 1990), it appears to be similar to a presumed *B. candida* hybrid, which has become naturalized as a garden ornamental in subtropical Queensland, Australia (Griffin, 1966). Both contain scopolamine as the major alkaloid as well as the metabolites 6β-hydroxyhyoscyamine, hyoscyamine and norhyoscyamine. The 'Flintham Hall' hybrid contains tigloyl esters of tropine and pseudotropine. The Queensland hybrid has meteloidine as the second major alkaloid, also some new tropane alkaloids 6β,7β-dihydroxylittorine and 3α,7β-dihydroxytropan-6β-yl tiglate (6β-tigloyloxytropan-3α,7β-diol) (Griffin, 1976a). The Queensland hybrid was presumed to be sterile, however, one year a profuse seed-set was observed. Fifty seeds were germinated and cultivated over a 4 year period. There was no morphological or chemical variation although some contained traces of 6,7-epoxylittorine (Griffin, 1992). El-Imam and Evans created reciprocal crosses of *B. candida* (Flintham Hall), *B. candida*, *B. aurea* and *B. suaveolens* (El-Imam & Evans, 1990).

The parent plants respectively contained scopolamine 0.47%, 0.25%, 0.73% and 0.14%. The F_1 generation was harvested and analysed over three growing seasons. There was variation amongst the hybrids between seasons. The most superior hybrids were *B. candida* × *B. candida* (Flintham Hall), two of which had a scopolamine content of 1.45% and 1.02% decreasing to 0.73% and 0.87% after 3 years.

6.3. *Duboisia* hybrids

Forms of *Duboisia* morphologically between *D. myoporoides* and *D. leichhardtii* are found at the southern extremity of the area of distribution of *D. leichhardtii* (Loftus Hills & Kelenyi, 1946). Loftus Hills, Bottomley and Mortimer (1954c) initiated hybrids between *D. leichhardtii* and the northern variety of *D. myoporoides* (scopolamine dominant) and *D. leichhardtii* and the southern variety of *D. myoporoides* (hyoscyamine dominant). The hybrids were cultivated over 4 years. Some of the F_1 hybrids consistently produced more bases than either parent species and appeared more vigorous. The balance of alkaloids of the F_1 cross generally favoured hyoscyamine although one hybrid of *D. leichhardtii* × *D. myoporoides* (northern variety) was scopolamine dominant (2.3%). The F_2 generation on average, morphologically favoured *D. leichhardtii* and there appeared to be segregation for both hyoscyamine and scopolamine dominant types. Ikenga, Itakura and Ohashi (1979) compared scopolamine yields from reciprocal crosses of *D. myoporoides* and *D. leichhardtii*. Seven of the *D. myoporoides* parent trees contained scopolamine in the range 0.19–1.2%. Three *D. leichhardtii* parents had scopolamine 0.35–0.74%. The maximum scopolamine content of all the hybrids was 1.16%. There was no general similarity between the characters of the F_1 hybrids and the species of their parents. There is evidence that *Duboisia* species will also form intergeneric hybrids. The tribe Anthoceridae was revised by Haegi (1981) and *Anthrocercis tenuipes* was later presumed to be a hybrid of *Duboisia myoporoides* and *Cyphanthera scabella*. A related hybrid, *C. albicans* (*Anthrocercis albicans*) × *Duboisia myoporoides* was shown to contain hyoscyamine and scopolamine with smaller quantities of norhyoscyamine. The relatively high yield (total alkaloid 0.41%) contrasted with the low yields of *Cypanthera albicans* (0.05%), (Evans & Ramsey, 1983). A further naturally occurring hybrid, *Duboisia hopwoodii* × *Grammosolen dixonii* contained a total alkaloid yield of 0.29% in which the principal alkaloids were nornicotine and scopolamine (Evans, 1986). The parent species located nearby were likewise investigated. *Duboisia hopwoodii* had nornicotine and nicotine as major alkaloids (total, 1.92%), *Grammosolen dixonii*, hyoscyamine and scopolamine (total, 0.004%). Another hybrid reputed to be from *Grammosolen dixonii* × *Cyphanthera myosotidea* had as a major alkaloid, 6-hydroxyhyoscyamine. This is paral-

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[2] Sometimes reported in the literature cited as *Datura*.

leled by the F_1 *Duboisia hybrid* of commerce and the F_1 cross of *Datura ferox* × *D. stramonium* (Evans, 1986).

7. Commercial exploitation of tropane alkaloid containing species

7.1. Cultivation of Brugmansia species

Brugmansia sanguinea has been cultivated in Ecuador since 1968 some 400 metric tonnes of dried leaf are produced annually and yield about 0.8% scopolamine (Levy, 1977). The plantations have an economically useful life of about 10 years. Chemical races of *B. sanguinea* are evident, particularly ones producing relatively large amounts of 6β-acetoxy-3α-tigloyl-oxytropane (Evans, 1989). The Australian *B. candida* hybrid has been evaluated as a potential source of scopolamine. Leaves were collected at successive nodes in the main axis and demonstrated that the scopolamine yield (%) decreased as the leaf matured. The highest yield was 0.56%. Rows of plants were harvested and the young regrowth leaves, collected at monthly intervals contained scopolamine 0.34%. Unfertilised plants were calculated to yield 4360 kg of dried leaf/hectare/year corresponding to 14.8 kg of scopolamine (Griffin, 1976b). For comparison, *Duboisia* plantations with 1.25% scopolamine are calculated to yield 15.7 kg scopolamine/hectare/year. Cultivars of *Brugmansia sanguinea* have been selected and cultivated since 1978. Later cultivars were propagated through cloning by tissue culture using a system developed for the propagation of pyrethrum (Levy, 1981). Several new hybrids from reciprocal crosses of *B. aurea* and *B. candida* supplied by Dr W.C. Evans (El-Dabbas & Evans, 1982) were propagated from lateral shoot tips and cultivated at 3000 m above sea level (site 1) for 4.5 years and at 500 m (site 2) for 1 year. The alkaloid profiles of the seven hybrids were essentially similar. At site 1 the average scopolamine yield was 0.39%, at site 2 it was 0.55%. Presently the *B. sanguinea* varieties yield 16.2 kg of scopolamine/hectare/year. The *Brugmansia* hybrids were estimated to yield between 14 and 20 kg/hectare/year indicating a similarity of scopolamine productivity amongst the various species which contain this alkaloid (Levy & Regalado, 1991).

7.2. Cultivation of Duboisia species

Initially, leaves of both species, but particularly *D. myoporoides* were collected from natural stands. *Duboisia leichhardtii* shows less variability than *D. myoporoides* hence cultivation of *D. leichhardtii* in its natural location in the south–west Burnett region of Queensland was undertaken. The plantations of *D. leichhardtii* were raised from naturally set seedlings in the initial stage, later a treatment with gibberellic acid was used to promote controlled germination. *Duboisia leichhardtii* unlike *D. myoporoides* is difficult to propagate from soft wood cuttings and there is much variation with leaf of fair average quality (FAQ) yielding 0.4% scopolamine. The leaf is valued by weight and has to be above FAQ. *Duboisia myoporoides* enjoyed little cultivation and was never a preferred source due to its pyridine base content which made the isolation of scopolamine less efficient. In more recent years a hybrid of *D. leichhardtii* and *D. myoporoides* has been cultivated as it is easily propagated from cuttings and does not contain pyridine bases. Specific identification is impossible, the hybrid stock resulted from various F_1 plants that were residual from the earlier investigations of Loftus Hills and his colleagues. Effects of seasonal changes were observed when a new plantation was developed containing 45,000 hybrid trees. There was a gradual decrease in scopolamine from January to June (summer to autumn in the southern Hemisphere) and a gradual increase from June to September (Luanratana & Griffin, 1980). The decline in scopolamine could be delayed if a seaweed extract containing cytokinins was used as a spray (Luanratana & Griffin, 1982). Commercial *Duboisia* hybrid leaf was observed to contain scopolamine (1.54%), hyoscyamine (0.1%) and 6β-hydroxyhyoscyamine (0.17%) with the latter in greater yield than in any other tropane-alkaloid containing species. The hybrid contained the usual minor alkaloids of *D. leichhardtii* with only traces of pyridine alkaloids in the roots (Gritsanapan & Griffin, 1992). F_2 hybrids which were derived from self crossed and sown F_1 hybrids contained another major alkaloid, littorine (0.4%), (Griffin & Lin, 1989). The farm-gate value of the Australian Duboisia industry has fluctuated around $1 to $4 million per year in nominal terms since 1970. In 1970 the production in tonnes of leaf was 1000, by 1990, 500 tonnes. While the production tonnage appears to have fallen over the past 20 years the percentage of scopolamine has more than doubled. Most hybrid plantations yield leaf containing 1.5–2.5% scopolamine.

7.3. Cultivation of Erythroxylum species

Erythroxylum coca is the source of all commercial coca leaves from which cocaine is derived. Cultivated in the montaña zone of the eastern Andes, little is grown outside this region, which has a very favourable tropical environment with high rainfall, not too cold or hot, and with well-drained mineral-rich soil. Andean coca is cultivated from seed and matures after 2 or 3 years when the leaf is harvested. Leaf samples contained between 0.23 and 0.96% cocaine, the average being 0.63%. Columbian coca, *E. novogranatense* prefers lower elevations which are hotter and dryer than *E. coca*. The crop plant is obtained from mountain areas of Colombia, little is grown and Columbian coca is only a minor source of cocaine averaging about 0.47% yield. A related variety *E. novogranatense* var. *truxillense* constitutes 'Trujillo coca' of commerce. Cultivation occurs near the city of Trujillo in northern Peru, on the dry west-facing slopes of the Andes, up to about 1800 m, and the arid upper Marañón valley. The variety is well adapted for desert conditions and the leaf containing up to 1% cocaine (0.76–1.02%) is particularly rich in methyl salicylate which leads to its favoured use in coca-flavoured beverages. Amazonian coca, *E. coca* var. *ipadu* Plowman is widely distributed in the western Amazon and is cultivated and used by a number of native groups in Peru, Brazil and Colombia. *Ipadu* is the common Brazilian name. Having a lower cocaine content (0.4% but frequently lower) the leaf is powdered before consumption. Amazonian coca is grown from cuttings and harvested when 1–1.5 m tall, about 6 months later. Soil fertility decreases after the first harvest and the cultivated areas are abandoned after 1 or 2 years use (Plowman, 1981).

References

Al-Said, M. S., Evans, W. C., & Grout, R. J. (1986a). *Phytochemistry*, *25*, 851.

Al-Said, M. S., Evans, W. C., & Grout, R. J. (1986b). *J. Chem. Soc. Perkin Trans*, *1*, 957.

Al-Said, M. S., Evans, W. C., & Grout, R. J. (1989a). *Phytochemistry*, *28*, 3211.

Al-Said, M. S., Evans, W. C., & Grout, R. J. (1989b). *Phytochemistry*, *28*, 671.

Al-Yahya, M. A., Evans, W. C., & Grout, R. J. (1979). *J. Chem. Soc. Perkin Trans*, *1*, 2130.

Aripova, S. F., Malikov, V. M., & Yunusov, S. Yu (1977). Khim. Prir. Soedin., 2, 290 (Russ.), via C.A., 87, 98864.

Aripova, S. F., Sharova, E. G., & Yunusov, S. Yu (1983). Khim. Priv. Soedin., 6, 749 (Russ.), via C.A., 100, 171549.

Aripova, S. F. (1985). Khim. Priv. Soedin., 2, 275 (Russ.), via C.A., 103, 68274.

Asano, N., Kato, A., Oskeki, K., Kizu, H., & Matsui, K. (1995). *Eur. J. Biochem*, *229*, 369.

Avery, G. A., Satina, S., & Rietsema, J. (1959). *Blakeslee — the genus Datura*. New York: Ronald.

Barnard, C. (1952). *Econ. Bot*, *6*, 3.

Basey, K., & Woolley, J. G. (1973). *Phytochemistry*, *12*, 2557.

Beresford, P. J., & Woolley, J. G. (1974). *Phytochemistry*, *13*, 2143.

Bick, I. R. C., Bremer, J. B., & Gillard, J. W. (1971). *Phytochemistry*, *10*, 475.

Bick, I. R. C., Gillard, J. W., & Huck-Meng, Leow. (1979a). *Aust. J. Chem*, *32*, 2523.

Bick, I. R. C., Gillard, J. W., & Huck-Meng, Leow. (1979b). *Aust. J. Chem*, *32*, 2537.

Bick, I. R. C., Gillard, J. W., & Huck-Meng, Leow. (1979c). *Aust. J. Chem*, *32*, 1827.

Bick, I. R. C., Gillard, J. W., Huck-Meng, Leow, & Preston, W. (1979d). *Aust. J. Chem*, *32*, 2071.

Bick, I. R. C., Gillard, J. W., Huck-Meng, Leow., Lounasmaa, M., Pusset, J., & Sevenet, T. (1981). *Planta Medica*, *41*, 379.

Brachet, A., Munoz, O., Gupta, M., Veuthey, J., & Christen, P. (1997). *Phytochemistry*, *46*, 1439.

Bristol, M. L. (1966). *Bot. Mus. Leaft. Harvard Uni*, *21*, 229.

Cannon, J. R., Joshi, K. R., Meehan, G. V., & Williams, J. (1969). *Aust. J. Chem*, *22*, 221.

Chen, Z., Xu, P., & Yao, T. (1986). Yaoxue Xuebao, 21, 513 (Ch.), via C.A., 106, 153016.

Christen, P., Roberts, M. F., Phillipson, J. D., & Evans, W. C. (1993). *Phytochemistry*, *34*, 1147.

Conselo, F. L., & Alejandra, S. G. (1972). Rev. Colomb. Cienc. Quim,-Farm., 2, 27 (Span.), via C.A., 79, 15798.

Craven, L. A., Lepschi, B. J., & Haegi, L. A. R. (1995). *J. Adelaide Bot. Gard*, *16*, 27.

Drager, B., van Almsick, A., & Mrachatz, G. (1995). *Planta Medica*, *61*, 577.

Ducrot, P. H., & Lallemand, J. Y. (1990). *Tetrahedron Letters*, *31*, 3879.

El-Dabbas, S. W., & Evans, W. C. (1982). *Planta Medica*, *44*, 184.

El-Imam, Y. M. A., & Evans, W. C. (1984). *Planta Medica*, *50*, 86.

El-Imam, Y. M. A., Evans, W. C., & Plowman, T. (1985). *Phytochemistry*, *24*, 2285.

El-Imam, Y. M. A., Evans, W. C., Grout, R. J., & Ramsey, K. P. A. (1987). *Phytochemistry*, *26*, 2385.

El-Imam, Y. M. A., Evans, W. C., Grout, R. J., & Ramsey, K. P. A. (1988). *Phytochemistry*, *27*, 2181.

El-Imam, Y. M. A., & Evans, W. C. (1990). *Fitoterapia*, *LXI*, 148.

Evans, W. C., Ghani, A., & Woolley, V. A. (1972a). *Phytochemistry*, *11*, 470.

Evans, W. C., Ghani, A., & Woolley, V. A. (1972b). *Phytochemistry*, *11*, 469.

Evans, W. C., Ghani, A., & Woolley, V. A. (1972c). *J. Chem. Soc. Perkin Trans*, *1*, 2017.

Evans, W. C., & Treagust, P. G. (1973). *Phytochemistry*, *12*, 2505.

Evans, W. C. (1979). Tropane alkaloids of the Solanaceae. In: J. G. Hawkes, R. N. Lester & A. D. Skelding, The biology and taxonomy of the Solanaceae (p. 241). Linnean Soc. Symp. Series No. 7.

Evans, W. C., & Ramsey, K. P. A. (1979). *J. Pharm. Pharmacol*, *31*, 9P.

Evans, W. C. (1981). *J. Ethnopharmacol*, *3*, 265.

Evans, W. C., & Ramsey, K. P. A. (1981). *Phytochemistry*, *20*, 497.

Evans, W. C., & Ramsey, K. P. A. (1983). *Phytochemistry*, *22*, 2219.

Evans, W. C. (1986). Hybridisation and secondary metabolism. In W. G. D'Arcy, *Solanaceae — biology and systematics* (p. 179). New York: Columbia University Press.

Evans, W. C. (1989). In *Pharmacognosy* (13 ed) (p. 559). London: Balliere-Tindall.

Everist, S. L. (1957). Noxious weed legislation. In *Common weeds of farm and pasture* (p. 13). Queensland, Australia: Government Printer, Department of Primary Industry.

Fodor, G. (1997). In: M. Sainsbury, Second supplements to the 2nd edition of Rodd's chemistry of carbon compounds, vol. IVB (pp 251–276). Amsterdam, Elsevier Science.

Gambaro, V., Labbe, C., Munoz, O., & Castillo, M. (1983). *Phytochemistry*, *22*, 1838.

Gnecco Medina, D. H., Pusset, J., Pusset, M., & Husson, H. P. (1983). *J. Nat. Prod*, *46*, 398.

Goldmann, A., Milat, M. L., Ducrot, P. H., Lallemand, J., Maille, M., Lepingle, R., & Tepfer, D. T. (1990a). *Phytochemistry*, *29*, 2125.

Goldmann, A., Milat, M. L., Ducrot, P. H., Lallemand, J., Maille, A., Charpin, I., & Tepfer, D. T. (1990b). *Phytochemistry*, *29*, 2125.

Graf, E., & Lude, W. (1978). *Archiv der Pharmazie*, *311*, 139.

Griffin, W. J. (1965). *Aust. J. Pharm. Supp*, *36*, S128.

Griffin, W. J. (1966). *Planta Medica*, *14*, 468.

Griffin, W. J. (1976a). *Aust. J. Chem*, *29*, 2329.

Griffin, W. J. (1976b). *Econ. Bot*, *30*, 361.

Griffin, W. J. (1978). *Aust. J. Chem*, *31*, 1161.

Griffin, W. J., & Lin, G. D. (1989). *Naturwissenschaffen*, *76*, 582.

Griffin, W. J. (1992). *Phytochemistry*, *31*, 367.

Gritsanapan, W., & Griffin, W. J. (1992). *Phytochemistry*, *31*, 471.

Gritsanapan, W., & Griffin, W. J. (1991). *Phytochemistry*, *30*, 2667.

Gross, D., & Schutte, H. R. (1963). *Archiv der Pharmazie*, *296*, 1.

Haegi, L. A. R. (1981). *Telopea*, *2*, 173.

Holmstedt, B., Jaatmaa, E., Leander, K., & Plowman, T. (1977). *Phytochemistry*, *16*, 173.

Hunziker, A. T. (1979). The classification of the Solanceae. In: J. G. Hawkes, R. N. Lester & A. D. Skelding, The biology and taxonomy of the Solanaceae (p. 49). Linnean Soc. Symp. Series No. 7.

Ikenga, M. A., Itakura, A., & Ohashi, H. (1979). *Planta Medica*, *35*, 51.

Jackson, B. P., & Berry, M. I. (1973). *Phytochemistry*, *12*, 1165.

Johns, S. R., Lamberton, J. A., & Sioumis, A. A. (1971). *Aust. J. Chem*, *24*, 2399.

Kato, A., Asano, N., Kizu, H., Matsui, K., Suzuki, S., & Arisawa, M. (1997). *Phytochemistry*, *45*, 425.

Khanna, K. L., Schwarting, A. E., & Rother, A. (1961). *Lloydia*, *24*, 179.

Kubwabo, C., Rollman, B., & Tillequin, B. (1993). *Planta Medica*, *59*, 161.

Leary, J. D., Khanna, K. L., & Schwarting, A. E. (1963). *Lloydia*, *26*, 44.

Levy, L. W. (1977). *Solanaceae Newsletter*, *4*, 8.

Levy, L. W. (1981). *Environ. Exptl. Bot*, *21*, 389.

Levy, P. E., & Regalado, E. (1991). Datura hybrids: clonal micropropagation and hyoscine production at low and high altitude cultivation in Ecuador. In J. G. Hawkes, R. N. Lester, M. Nee, & N. Estrada, *Solanaceae III, taxonomy, chemistry, evolution* (pp. 69–74). London: Royal Botanic Gardens Kew and Linnean Society of London.

Lockwood, T. E. (1973a). A taxonomic review of *Brugmansia* (Solanaceae). PhD. thesis, Harvard University, Cambridge, MA.

Lockwood, T. E. (1973b). *Bot. Mus. Leaft. Harvard Uni*, *23*, 273.

Lockwood, T. E. (1979). *Journal of Ethnopharmacol*, *1*, 147.

Loder, J. W., & Russel, G. B. (1966). *Tetrahedron Letters*, *51*, 6327.

Loder, J. W., & Russel, G. B. (1969). *Aust. J. Chem*, *22*, 1271.

Loftus Hills, K., & Kelenyi, G. P. (1946). *J. Coun. Sci. Industr. Res. Aust*, *19*, 359.

Loftus Hills, K., Bottomley, W., & Mortimer, P. I. (1953). *Nature*, *171*, 435.

Loftus Hills, K., Bottomley, W., & Mortimer, P. I. (1954a). *Aust. J. Appl. Sci*, *5*, 258.

Loftus Hills, K., Bottomley, W., & Mortimer, P. I. (1954b). *Aust. J. Appl. Sci*, *5*, 276.

Loftus Hills, K., Bottomley, W., & Mortimer, P. I. (1954c). *Aust. J. Appl. Sci*, *5*, 283.

Lounasmaa, M., Novkulich, P. M., & Wenkert, E. (1975). *J. Org. Chem*, *40*, 3694.

Lounasmaa, M., Pusset, J., & Sevenet, T. (1980a). *Phytochemistry*, *19*, 953.

Lounasmaa, M., Pusset, J., & Sevenet, T. (1980b). *Phytochemistry*, *19*, 949.

Lu, Y., Yao, T., & Chen, Z. (1986). Yaoxue Xuebao 21, 829 (Ch.), via C.A., 110, 153028.

Luanratana, O., & Griffin, W. J. (1980). *J. Nat. Prod*, *43*, 552.

Luanratana, O., & Griffin, W. J. (1982). *J. Nat. Prod*, *45*, 270.

Molyneux, R. J., Pan, Y. T., Goldmann, A., Tepfer, D. T., & Elbein, A. D. (1993). *Arch. Biochem. Biophys*, *304*, 81.

Molyneux, R. J., McKenzie, R. A., O'Sullivan, B. M., & Elbein, A. (1995). *J. Nat. Prod*, *58*, 878.

Moore, J. M., Cooper, D. A., Lurie, I. S., Theodore, C. M., Carr, S., Harper, C., & Yeh, J. (1987). *J. Chromatography*, *410*, 297.

Moore, J. M., Hays, P. A., Cooper, D. A., Casale, J. F., & Lydon, J. (1994). *Phytochemistry*, *36*, 357.

Mortimer, P. I., & Wilkinson, S. (1957). J. Chem. Soc., 3967.

Munoz, O., Piovano, M., Garbarino, J., Hellwing, V., & Breitmaier, E. (1996). *Phytochemistry*, *43*, 709.

Nash, R. J., Rothschild, M., Porter, E. A., Watson, A., Waigh, R., & Waterman, P. G. (1993). *Phytochemistry*, *34*, 1281.

Petrie, J. M. (1916). *Proceedings of the Linnean Soc. of New South Wales*, *41*, 815.

Phillipson, J. D., & Handa, S. S. (1975). *Phytochemistry*, *14*, 999.

Platonova, T. F., & Kusovkov, A. D. (1963). Med. Ind. UdSSR 17, 19 via Romeike, A (1978) Bot. Notiser, 131, 85.

Plowman, T. (1981). *J. Ethnopharmacol*, *3*, 195.

Plowman, T., & Rivier, L. (1983). *Ann. Botany (London)*, *51*, 641.

Purdie, R. W., Symon, D. E., & Haegi, L. (1982). *Flora of Australia.* In *Solanaceae*, *vol. 29*. Canberra: Australian Government Printing Service.

Rahman, A. U., Khattak, K. F., Nighat, F., Shabbir, M., Hemalal, K. D., & Tillekeratne, L. M. (1998). *Phytochemistry*, *48*, 377.

Ray, A. B., Sahai, M., & Sethi, P. D. (1976). Chem. Ind. London, 454.

Ripperger, H. (1979). *Phytochemistry*, *18*, 171.

Rivier, L. (1981). *J. Ethnopharmacol*, *3*, 313.

Romeike, A. (1961). *Kulturpflanzen*, *9*, 171.

Romeike, A. (1962). *Kulturpflanzen*, *10*, 140.

Romeike, A. (1966a). *Naturwissenschaften*, *53*, 82.

Romeike, A. (1966b). *Kulturpflanzen*, *14*, 129.

Sahai, M., & Ray, A. B. (1980). *J. Org. Chem*, *45*, 3265.

San Martin, A. S., Rovirosa, J., Gambaro, V., & Castillo, M. (1980). *Phytochemistry*, *19*, 2007.

San Martin, A. S., Labbe, C., Munoz, O., Castillo, M., Reina, M., de la Fuente, B., & Gonzalez, A. (1987). *Phytochemistry*, *26*, 819.

Schultz, O. E. (1907). In A. Engler, *Das pflanzenreich*, *vol. IV* (pp. 1–174). Leipzig: Englemann.

Schultes, R. E., & Hofmann, A. (1973). *The botany and chemistry of hallucinogens*. Springfield, Illinois: Thomas (Ed. 2., 1980).

Schultes, R. E., & Farnsworth, N. R. (1980). Bot. Mus. Leaft. Harvard Uni., 28 (2).

Sharova, E. G., Aripova, S. F., & Yunusov, S. Yu (1980). Khim. Priv. Soedin., 5, 672 (Russ.), via C.A., 94, 117787.

Wang, P., Yao, T., & Chen, Z. (1990). Zhiwu Zhongyao Zazhi, 14, 739 (Ch.), via C.A., 113, 37699.

Watson, P. L., Luanratana, O., & Griffin, W. J. (1983). *J. Ethnopharmacol*, *8*, 303.

Yao, T., Chen, Z., Yi, D., & Xu, G. (1981). Yaoxue Xuebao, 16, 582 (Ch.), via C.A., 96, 48972.