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Tropane Alkaloids

Sources, Chemistry, Pharmacology and Biotechnology

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Contents

Chapter 1
Tropane Alkaloids: A Biologically Important Group of Nitrogen-Containing Heterocyclic Phyto-secondary Metabolites

Lepakshi Md. Bhakshu, K. Venkata Ratnam, and T. Pullaiah

Abstract Nature provides many medicinal plants that act as biological factories of diverse groups of metabolites, including alkaloids. One of the well-known and earliest reported classes of natural secondary metabolites belongs to alkaloids, nitrogen-containing heterocyclic compounds, with diverse biological and pharmacologically active, especially neurological disorders. The major source for the tropane alkaloids belongs to Solanaceae, a botanical family with many subgroups. Tropane alkaloids have been thoroughly investigated, utilized in numerous pharmacological procedures, and employed in the creation of beneficial medicinal substances. As parasympatholytics that competitively inhibit acetylcholine, tropane alkaloids are advantageous. These alkaloids are based on the bicyclic ring of the tropane moiety, and the majority of tropane alkaloids are ester derivatives that are substituted on the atom C-3 of the tropane ring. The present revision focuses on the chemistry of tropane alkaloids and their possible biological resources that might be helpful to scientists to study further and develop nontoxic and safe medicaments.

Keywords Tropane alkaloids · Solanaceae · Scopolamine · Hyoscyamine · Recreational drugs · Anticholinergic medicaments

1.1 Introduction

Nature provides many medicinal plants that act as biological factories of diverse groups of metabolites, including alkaloids. One of the well-known and earliest reported classes of natural secondary metabolites belongs to alkaloids,

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nitrogen-containing heterocyclic compounds, with diverse biological and pharmacologically active, especially neurological disorders. Alkaloids are a well-known and historically documented class of naturally occurring secondary metabolites. These heterocyclic molecules, including nitrogen, have various biological and pharmacological activities, particularly in treating neurological illnesses (Srinivasan and Smolke 2019). The primary source of alkaloids is the Solanaceae family of plants, which has numerous subgroups. Tropane alkaloids (TAs) are one of these subgroups and have been thoroughly explored, utilized in numerous pharmacological processes, and employed in creating valuable medicinal entities. As parasympatholytics that competitively oppose acetylcholine, tropane alkaloids are helpful. These alkaloids are based on the bicyclic ring of the tropane moiety, with most tropane alkaloids being substituted on atom C-3 of the tropane ring as ester derivatives (Alsamarrai 2019). The nightshade family (Solanaceae) genera *Duboisia*, *Atropa*, *Datura*, *Hyoscyamus*, and other genera produce them mostly as anticholinergics. The World Health Organization lists several TAs, including atropine, hyoscyamine, and scopolamine, as critical medications for treating organophosphate and nerve agent poisoning, cardiac arrhythmia, gastrointestinal spasms, and Parkinson's disease symptoms (Grynkiewicz and Gadzikowska 2008; WHO 2015).

1.2 Source of Tropane Alkaloids

All compounds with a tropane ring structure are classified as tropane alkaloids (TAs), a particular class of alkaloids. TAs can be divided into three types and are either esters of 3α-tropanole (tropine) or, to a lesser extent, 3β-tropanole (pseudotropine): There are approximately 200 different TAs that have been described, including TAs from Solanaceae plants like scopolamine and hyoscyamine, coca alkaloids like cocaine from *Erythroxylum coca*, and the recently identified calystegines group, which are polyhydroxylated nortropane alkaloids (NTAs) that are primarily found in Convolvulaceae, Solanaceae, Moraceae, Erythroxylaceae, and Brassicaceae, among others (Kohnen-Johannsen and Kayser 2019).

The secondary metabolites of plants in the Solanaceae family are grouped together by the tropane skeleton and further separated into two classes: derivatives of tropine and ecgonine. Researchers continue to draw inspiration from the first category, which is represented by the well-known alkaloids atropine and scopolamine, in their efforts to create more selective muscarinic receptor antagonists. These drugs are considered model anticholinergic drugs. The second class includes cocaine, one of the most often abused narcotics. The synthesis of much-needed cocaine antagonists has not been very successful despite extensive investigation. Consequently, novel strategies for treating cocaine rely on utilizing immunology and biotechnology. More than 20 potential medicinal compounds with tropane as the central skeleton in their structure are produced by the modern pharmaceutical industry and are used as bronchodilators, mydriatics, antiemetics, and antispasmodics.

Esters of tropane have been identified in the following plant families: Proteaceae, Rhizophoraceae, Euphorbiaceae, Convolvulaceae, and Erythroxylaceae, in addition to the Solanaceae family. Some of the more than 100 genera and 3000 species in the Solanaceae family—such as *Anisodus*, *Atropa*, *Brugmansia*, *Datura*, *Hyoscyamus*, *Przewalskia*, *Scopolia*, *Physochlaina*, *Mandragora*, *Anthotroche*, *Cyphantera*, and *Duboisia*—are known to be rich in alkaloids containing the tropane moiety (Griffin and Lin 2000). The term "tropane alkaloids" (TA, Fig. 1.1) refers to a unique family of harmful alkaloids that can contaminate food and feed and naturally emerge from a wide range of plant groups, including Brassicaceae, Erythroxylaceae, and Solanaceae. (−)-Hyoscyamine and (−)-scopolamine are the two naturally occurring alkaloids that are most common in TA-producing plants. Conversely, when (−)-hyoscyamine is purified, atropine is produced, which is a racemic mixture of (+)- and (−)-hyoscyamine. Globally, temperate and tropical regions are home to a large distribution of TA-producing weeds, which can occasionally contaminate agricultural products. However, the usage of these bio-active compounds is highly restricted with specific recommendations by physicians during severe conditions of pain. Certain tropane alkaloids such as cocaine and scopolamine are neurotoxic and showed psychoactive effects, related usage, and cultural associations. Research has been initiated toward in vitro biosynthesis and bio-engineering of production of nontoxic tropane alkaloids as effective medicines.

In addition to chemical synthesis, natural compounds extracted from domesticated plants—primarily scopolamine and atropine from Australian *Duboisia*—serve as the two main sources of raw materials for this commercial activity (Grynkiewicz

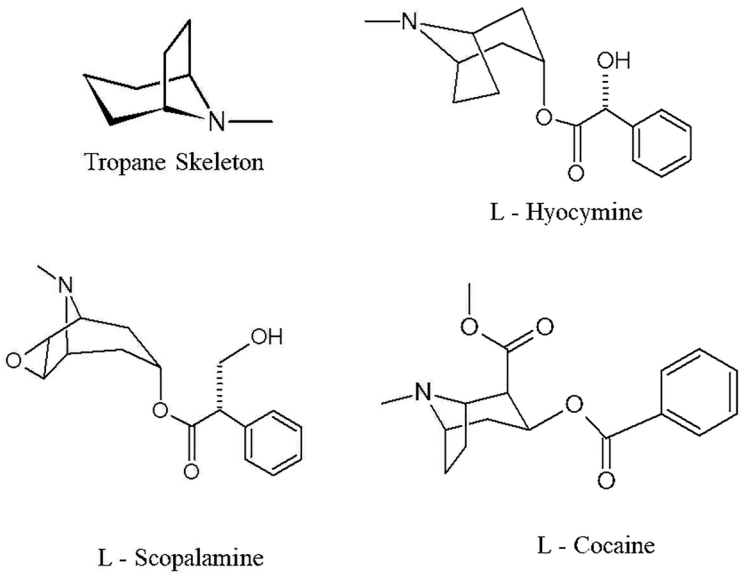

Fig. 1.1 Few popular examples of tropane alkaloids

and Gadzikowska 2008). Many plants with a moderate climate are listed in the ethnopharmacological tradition, whose extracts have been used for centuries as poisons and magic potions for various purposes (such as pain relievers, hallucinogens, etc.). It is now known that these extracts contain significant amounts of tropane alkaloids, such as up to 2% in ripe *Datura stramonium* seeds. Among these, there are species such as the poisonous nightshade (*Atropa belladonna*), mandrake (*Atropa mandragora*), henbane (*Hyoscyamus niger*, *Hyoscyamus albus*), scopola (*Scopolia carniolica*), and jimsonweed, which is also known as thorn-apple (*Datura stramonium*), stated as poisons (Griffin and Lin 2000).

1.3 Historical Aspects

Individual alkaloid compounds began to be isolated from 1830 onward, including atropine from *Atropa belladonna* L., hyoscyamine from *Hyoscyamus niger* L., and scopolamine. Meissner, who first used the term "alkaloid," was the first to recognize that the active principles of these toxic plants are alkaline and can, therefore, be isolated by extractive techniques in 1819. Tons of atropine and scopolamine derived from genetically modified cultivars are used in modern medicine, and new chemical and biotechnological manufacturing techniques are improved by constantly rising demand. Concurrently, cocaine derived from two species of *Erythroxylon*, which has limited medical applications due to its highly addictive features (Weil 1981; Rocio et al. 2004), was used illegally to manufacture and traffic "recreational drugs," which had negative socioeconomic and health effects worldwide (Grynkiewicz and Gadzikowska 2008).

Tropane alkaloids (TAs) are another type of hazardous alkaloids that have been shown to contaminate food and feed products. Plants belonging to the Brassicaceae, Solanaceae, and Erythroxylaceae families are among those that spontaneously produce these secondary metabolites. (−)-Hyoscyamine and (−)-scopolamine are the two naturally occurring alkaloids that are most common in plants that produce TA. However, when (−)-hyoscyamine is purified, atropine is produced, which is a racemic mixture of (+)- and (−)-hyoscyamine. Weeds that produce TA are found throughout the world in both temperate and tropical regions, and they can occasionally contaminate agricultural products. According to a 2013 report by the EFSA CONTAM panel, TAs are bad for human health, and weeds that contain TAs are widespread in both temperate and tropical regions, which may unintentionally contaminate agricultural products, tea, and herbal combinations (https://www.eurofins.in/food-testing/blog/tropane-alkaloids-in-tea/). The primary toxicological effects of atropine and scopolamine are due to excessive antimuscarinic activity in the central and autonomic nervous systems. The EFSA Panel has set a group acute reference dosage of 0.016 μg/kg body weight for the whole of the relevant TAs because of these impacts on human health (EFSA 2013; León et al. 2022; Martinello et al. 2022). Similar to PAs, TAs have the ability to contaminate teas, herbal blends,

animal and agricultural products, and feeds. Consequently, studies on TAs have looked at their prevalence in plants, cow's milk, seeds, bread, leafy vegetables, cereal-based baby food, honey and its derivatives, teas, and herbal infusion matrices (León et al. 2022; Martinello et al. 2022; Romera-Torres et al. 2020; Marin-Saez et al. 2019; Du et al. 2019; Klein et al. 2022; Kowalczyk and Kwiatek 2022; Versilovskis et al. 2020; Gonzalez-Gomez et al. 2022; Gumus 2023).

1.4 Industrial Applications

Tropane alkaloids (TAs), a unique class of secondary metabolites produced by medicinal plants in the Solanaceae family, have potent anticholinergic effects. Scopolamine and hyoscyamine are two tropane alkaloids and anticholinergic drugs that are used medicinally. These drugs are used in the treatment of functional gastrointestinal disorders, pain, motion sickness, Parkinson's syndrome, and asthma. Hyoscyamine is an essential component in the industrial manufacturing of ipratropium bromide and scopolamine for tiotropium bromide. Tiotropium bromide and ipratropium are required drugs for the treatment of chronic obstructive pulmonary disease. As a result, the two alkaloids are in high demand. On the other hand, scopolamine is very profitable to produce and grow due to its wide range of medical applications.

Consequently, there is an increasing global need for these chemicals, driving up commercial demand. Additionally, the World Health Organization (WHO) lists scopolamine as one of the most significant pharmaceuticals. Scopolamine and hyoscyamine come from massive plantations of *Duboisia* plants in Queensland, Australia. The synthesis of scopolamine at high levels is becoming more difficult for the food and pharmaceutical sectors because of new biotic and abiotic factors brought about by climate change (Gonzalez-Gomez et al. 2022; Kohnen-Johannsen and Kayser 2019).

1.5 Chemical Nature and its Skeleton

The bicyclic saturation structure (N-methyl-8-azabicyclo [3.2.1] octane-1) with a nitrogen bridge connecting a cycloheptane ring is called tropane. Tropane alkaloids belong to a family of about 300 alkaloids that are easily separated based on stereochemical characteristics and the amount of carbons in the tropane skeleton (Zhang et al. 2023). Despite having a similar biogenetic reaction sequence that produces the tropane skeleton and only branches at the tropinone reduction step, tropine and ecgonine derivatives are separated in scientific literature for another crucial reason. The sole well-known member of the ecgonine class is cocaine, a neurostimulant that is known to cause severe addiction (Grynkiewicz and Gadzikowska 2008). Nearly

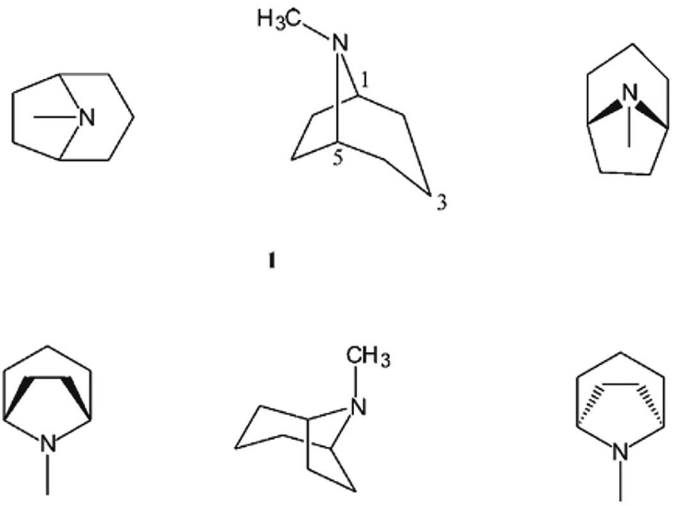

Fig. 1.2 Conventional representations of tropane structure

all TAs are structurally esters of different organic acids, such as tiglic, isovaleric, cinnamic, benzoic, and tropic acids conjugated to hydroxylated tropane derivatives (Huang et al. 2021, Fig. 1.2).

1.6 Model for the Synthesis of Hyoscyamine

The main alkaloid found in the plants is hyoscyamine, which is the ester of tropine with levorotatory {l(−)} or (S)-tropic acid. It is thought to be produced biogenetically by skeletal rearrangement of phenyllactic acid, which is created from L-phenylalanine. The 1,2-carboxy group shift, which has been widely accepted by recent treatises on alkaloid biosynthesis, is a component of the metabolic pathway from tropine phenyl lactic ester, littorine, to tropic acid ester, hyoscyamine (Scheme 3) which has recently disputed (Patterson and O'Hagan 2002; Fig. 1.3).

6-Hydroxytropine, also called anisodamine, is produced by the hyoscyamine enzyme. 6-Hydroxylase, also known as 6-(R)hydroxylase or H6H, is a precursor of scopine, another alkamine that is a basic component of hyoscine and has an extra epoxide ring. Tropine, nortropine, or hydroxylated tropines are alkamines found in minor tropane alkaloids. A range of acids, including benzoic, cinnamic, tiglic, truxillic, isovaleric, methylbutyric, and others, can esterify them at position C-3, with the noteworthy exception of anisodamine (3-tropoyl-6-hydroxytropine), which is not handled as medicines (Poupko et al. 2006).

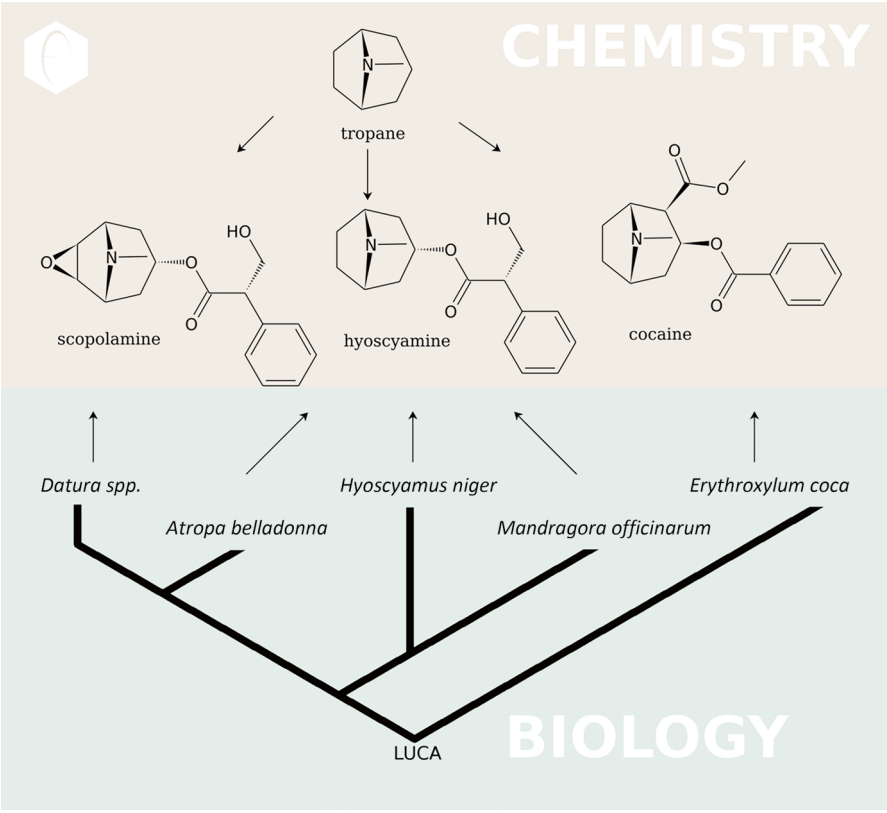

Fig. 1.3 Chemical structure and phylogeny of tropane alkaloids demonstrated the path of synthesis and their occurrence in five plant species. (Source: By Mplanine—Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=115787548)

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Chapter 2
Plant Sources of Tropane Alkaloids

T. Pullaiah

Abstract Tropane alkaloids are known to exist in plants such as those belonging to Solanaceae, Convolvulaceae, Erythroxylaceae, Brassicaceae, Euphorbiaceae, Rhizophoraceae, Moraceae, and Proteaceae. This chapter provides information on the plant sources of these alkaloids and the distribution of these plants. The valid and accepted names have been obtained from Plants of the World Online. Additionally, the text includes information on the tropane alkaloids found in different species.

Keywords Tropane alkaloids · *Atropa* · *Datura* · *Duboisia* · *Hyoscyamus* · *Erythroxylum* · *Schizanthus* · Hyoscyamine · Scopolamine

2.1 Introduction

Tropane alkaloids are a fascinating group of compounds defined by their unique structure, which includes both a pyrrolidine ring and a piperidine ring, creating the foundational skeleton of tropane. These compounds are particularly noteworthy for their anticholinergic properties, which can offer various applications in medicine and pharmacology. Understanding their structure and function can lead to further insights into their potential uses and benefits (Lockery et al. 2021). The distribution of tropane alkaloids in plants such as Solanaceae, Convolvulaceae, Erythroxylaceae, Brassicaceae, Euphorbiaceae, Rhizophoraceae, Moraceae, and Proteaceae has been reported (Griffin and Lin 2000). The chemical synthesis of tropane alkaloids remains a challenge, as there are no commercially viable methods available. However, these valuable compounds can be effectively obtained through extraction from medicinal plants, highlighting an opportunity for further research and development in this area (Hu et al. 2019; Kohnen-Johannsen and Kayser 2019). Savita et al. (2021) gave an account of the chemotaxonomic significance of tropane alkaloids.

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They listed the occurrence of tropane alkaloids in different plant families. In this chapter, plant sources of the alkaloids and the distribution of these plants have been given. Plants of the World Online has been followed for valid and accepted names. Under each family, plant species are arranged in alphabetical sequence.

2.2 Solanaceae

Solanaceae is the main source of tropane alkaloids.

2.2.1 Alkekengi

***Alkekengi officinarum* Moench** (Synonym: *Physalis alkekengi* L.)

This species' native range is SE Europe to China. It is a perennial, rhizomatous herb. Basey and Woolley (1973) reported tropane alkaloids in *Alkekengi officinarum* (synonym: *Physalis alkekengi* L.).

2.2.2 Anisodus

There are four species of *Anisodus*, all distributed in Himalayas and China.

***Anisodus acutangulus* C.Y. Wu & C. Chen**
A. acutangulus, known in Chinese as san fen san, is a perennial herb native to China. *A. acutangulus* is rich in tropane alkaloids (Geng et al. 2013). To clarify its alkaloid constituents, Geng et al. (2013) investigated *A. acutangulus* and discovered one dimeric tropane alkaloid, namely bis hyoscyamine.

***Anisodus stramoniifolius* (Wall.) G. Don** (Synonyms: *Scopolia lurida* (Link) Dunal; *Scopolia anomala* (Link & Otto) Airy Shaw; *Hyoscyamus luridus* E.H.L. Krause).

It is distributed in Himalayas and China. Air-dried leaves and stems are reported to contain 0.32% of alkaloids, comprising hyoscyamine, himaline, atropine, scopolamine, cuscohygrine, hellaradine, tropine, and scopine.

In most of the tropane alkaloid literature, this species was treated under *Scopolia lurida*.

***Anisodus tanguticus* (Maxim.) Pascher**
It grows in Nepal and Central China. *A. tanguticus* is a tropane alkaloids-producing herb (Chen et al. 2022a, b). Its roots are rich in anisodine, anisodamine, and atropine.

There are four species in *Anisodus* of which *Anisodus carniolicoides* (C.Y. Wu & C.C. Chen) D'Arcy & Zhi Y. Zhang has not been studied for tropane alkaloids.

2.2.3 Anthocercis

Evans and Ramsey (1983) reported tropane alkaloids in aerial parts of *Anthocercis anisantha*, *A. genistoides*, *A. gracilis*, *A. ilicifolia*, *A. intricata*, and *A. viscosa*.

***Anthocercis anisantha* Endl.**
This species' native range is Australia (Western to South). It is a shrub and grows primarily in the desert or dry shrubland.

***Anthocercis fasciculata* F. Muell.**
It is a shrub that grows primarily in the subtropical SW. Western Australia. *Anthocercis fasciculata* contains hyoscyamine (Cannon et al. 1969).

***Anthocercis genistoides* Miers**
It is a shrub that grows primarily in the desert or dry shrubland of Southwest Australia. Aponorhyoscine is indicated as a component of the roots of *Anthocercis genistoides* (Evans and Ramsey 1981).

***Anthocercis gracilis* Benth.**
This species is native to Southwest of Western Australia and primarily grows as a subshrub or shrub in the subtropical biome.

***Anthocercis ilicifolia* Hook.**
It is a shrub and grows in subtropical Western Australia. *Anthocercis ilicifolia* ssp. *ilicifolia* contain considerable amounts of both nicotine and nornicotine, together with lower levels of the tropane alkaloid hyoscyamine (<0.2% DW) (Ryan et al. 2015).

***Anthocercis intricata* F. Muell.**
It is a shrub native to subtropical Western Australia.

***Anthocercis littorea* Labill.**
It is a shrub and grows in the subtropical W. and S. Western Australia. *A. littorea* contains littorine and meteloidine (Cannon et al. 1969) and tropane derivatives mono- and ditigloyl esters of teloidine (Evans and Treagust 1973).

***Anthocercis viscosa* R.Br.**
It is a shrub and native to subtropical SW. Australia. *Anthocercis viscosa* contains hyoscyamine (Cannon et al. 1969).

2.2.4 *Anthotroche*

There are three accepted species of *Anthotroche*, and tropane alkaloids have been reported in all the three species. Aponoratropine has been detected in the aerial parts of *A. myoporoides*, *A. pannosa*, and *A. walcottii* (Evans and Ramsey 1981, 1983).

***Anthotroche myoporoides* C.A. Gardner**
It is a shrub and native to subtropical Western Australia.

***Anthotroche pannosa* Endl.**
It is a shrub and grows in the desert or dry shrubland of W. Western Australia. Bremner and Cannon (1968) isolated hyoscyamine from *Anthotroche pannosa*.

***Anthotroche walcottii* F. Muell.**
It is a shrub and grows in the subtropical W. Western Australia.

2.2.5 *Atropa*

Atropa is a genus with seven species distributed in temperate forests. *A. belladonna* contains hyoscyamine, scopolamine, and apoatropine as the principal alkaloids (Evans 1979). Tropane alkaloids of *A. belladonna* and *A. acuminata* were investigated by Ashtiana and Sefidkonb (2011). Banihashemi et al. (2020) investigated the production of scopolamine in hairy roots via *Agrobacterium rhizogenes* in *Atropa komarovii*. Fatemeh and Fatemeh (2011) determined the tropane alkaloid content (atropine and scopolamine) in different parts of the wild and cultivated *Atropa belladonna* and wild *Atropa acuminata* in Iran using high-performance liquid chromatography (HPLC) method.

***Atropa acuminata* Royle ex Lindl.**
This perennial herb grows in the temperate areas and has a native range from E. Iran to W. Himalaya.

***Atropa baetica* Willk.**
This perennial herb grows in CE. and S. Spain and Morocco. Zárate et al. (1997) reported tropane alkaloids in *Atropa baetica*.

***Atropa belladonna* L.**
It is a perennial herb and grows in Europe to N. Iran and NW. Africa. Baralle and Gros (1969) and Van Haga (1954) reported the presence of cuscohygrine as a constituent alkaloid of *A. belladonna*.

***Atropa komarovii* Blin. & Shalyt**
It is a perennial herb and grows in NE. Iran to S. Turkmenistan.

The following three species of *Atropa* have not been studied for the presence of tropane alkaloids: *Atropa indobelladonna* Karthik. & V.S.Kumar, *Atropa* × *martiana* Font Quer, and *Atropa pallidiflora* Schönb.-Tem.

Brugmansia

Brugmansia is a genus of seven species and two hybrids. Tropane alkaloids have been reported in most of the species. The aerial parts contain scopolamine and hyoscyamine, while the roots contain teloidine (Griffin and Lin 2000).

***Brugmansia arborea* (L.) Sweet** (Synonym: *Datura arborea* L.)

This species' native range is Ecuador to N. Chile. It is a shrub or tree that grows in the montane tropics. Cultivated in hilly regions as ornamental (Fig. 2.1).

***Brugmansia aurea* Lagerh**

It is a tree and its native range is the wet tropical Colombia to Ecuador.

***Brugmansia insignis* (Barb.Rodr.) Lockwood ex R.E.Schult.**

It is a shrub or tree that grows in the seasonally dry tropical West South America to Northwest Brazil.

***Brugmansia sanguinea* (Ruiz. & Pav.) D. Don**

This species' native range is from West South America to North Chile. It is a shrub or tree that grows in the montane tropics.

***Brugmansia suaveolens* (Humb. & Bonpl. ex Willd.) Sweet**

The native range of this species is Brazil (S. Bahia to N. Rio Grande do Sul). It is a shrub or tree and grows in the seasonally dry tropics (Fig. 2.2).

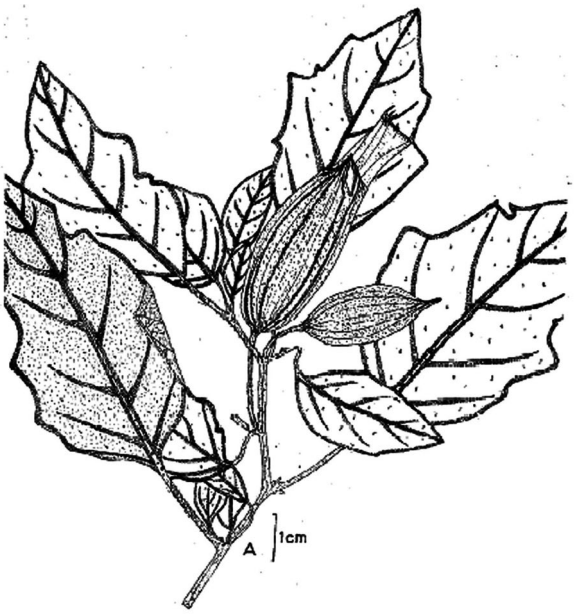

Fig. 2.1 *Brugmansia arborea* (L.) Sweet (Syn.: *Datura arborea* L.)

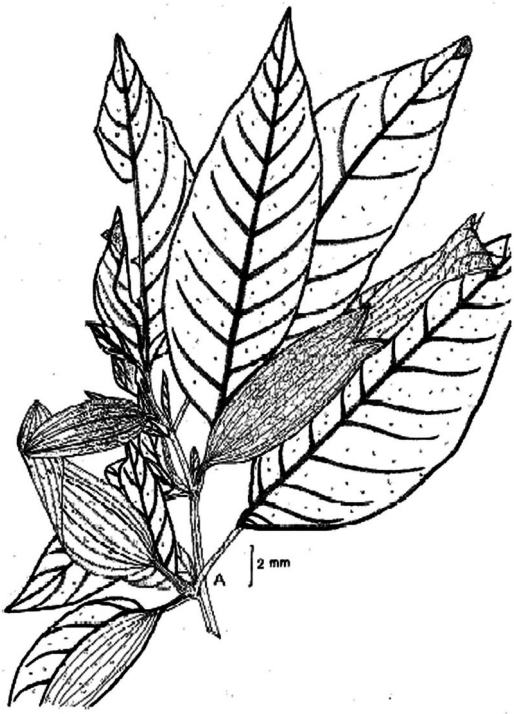

Fig. 2.2 *Brugmansia suaveolens* (Humb. & Bonpl. ex Willd.) Sweet

***Brugmansia versicolor* Lagerh.**

This species' native range is W. Ecuador. It is a tree that grows in the wet tropics.

***Brugmansia vulcanicola* (A.S.Barclay) R.E. Schult.**

This species' native range is from SW. Colombia to S. Central Ecuador. It is a shrub or tree that grows primarily in the montane tropics.

***Brugmansia* × *candida* Pers.**

It is a hybrid between *B. aurea* × *B. versicolor*. This hybrid's native range is from South Colombia to Ecuador. It is a tree that grows in the seasonally dry tropics.

***Brugmansia* × *rubella* (Saff.) Moldenke**

It is a hybrid between *B. arborea* × *B. sanguinea*. This hybrid's native range is Ecuador. It is a tree and grows in the seasonally dry tropics.

Crenidium

Crenidium spinescens primarily contains hyoscyamine as its main alkaloid but also has anabasine along with ursolic acid (El-Imam and Evans 1984). The genus *Crenidium* has only one species.

***Crenidium spinescens* Haegi**

This species' native range is S. Central Western Australia. It is a shrub that grows in the desert or dry shrubland.

Cyphanthera

The alkaloids of *Grammosolen odgersii* (synonym: *Cyphanthera odgersii*) and *Cyphanthera tasmanica* are consistent with those of other species of the genus. *Cyphanthera tasmanica* contains significant amounts of nicotine and nornicotine, along with lower levels of the tropane alkaloid hyoscyamine (<0.2% DW) (Ryan et al. 2015). Evans and Ramsey (1983) reported tropane alkaloids *in Cyphanthera albicans*, *C. anthocercidea*, *C. microphylla*, *C. racemosa*, and *C. scabrella*.

There are eight accepted species in the genus *Cyphanthera*.

***Cyphanthera albicans* (A. Cunn.) Miers** (Synonym: *Anthocercis albicans* A. Cunn.)

Cyphanthera albicans, or *Anthocercis albicans*, is a shrub found in southeastern Queensland to northeastern Victoria. It contains butyryl esters of tropine and 6β-hydroxytropine, its predominant alkaloids (El-Imam and Evans 1984). In addition to known tropane alkaloids, 3α-*iso*-butyryloxytropan-6β-ol and 3α-*n*-butyryloxytropane have been characterized as respective components of the aerial parts of *Cyphanthera albicans* (synonym: *Anthocercis albicans*) (Evans and Ramsey 1981).

***Cyphanthera anthocercidea* (F. Muell.) Haegi** (synonym: *Anthocercis anthocercidea* (F.Muell.) Druce).

Cyphanthera anthocercidea is a shrub distributed in the subtropics of Victoria (Australia). It contains hyoscyamine, scopolamine, and nicotine (which is more abundant).

Cyphanthera microphylla **Miers**

This species is a shrub and its native range is SW Australia.

***Cyphanthera myosotidea* (F. Muell.) Haegi**

This subshrub, which grows in the subtropics, is native to SE South Australia to NW Victoria.

***Cyphanthera racemosa* (F. Muell.) Haegi**

It is a shrub and its native range is W. and SW. Western Australia.

***Cyphanthera scabrella* (Benth.) Miers**

This species' native range is New South Wales (Blue Mountains). It is a scrambling shrub that grows in the subtropics.

***Cyphanthera tasmanica* Miers**

This species' native range is E. Tasmania. It is a shrub or tree that grows in the subtropics.

Cyphomandra

The primary compounds derived from the roots of *Cyphomandra betacea* include N,N′ O—bis-(4-dimethylaminobutyl) hexamide, tropinone, cuscohygrine, hyoscyamine, tigloidine, tropine, and pseudotropine. The accepted scientific name for this species is *Solanum betaceum* Cav. It is also known by the synonym *Cyphomandra betacea* (Cav.) Sendtn. This species is a tree found in the tropical regions of South America.

Datura

Datura is a genus of about 14 species of poisonous flowering plants (POWO 2024). The taxonomy of *Datura* is infamously unclear. Several other described species were later reclassified. For example, the name *D. meteloides* is ambiguous; it is usually classified as *D. wrightii*, but sporadically as *D. innoxia* (Haegi 1976; Hammer et al. 1983). *D. lanosa* was reclassified as either *D. wrightii* or *D. innoxia*, whereas *D. velutinosa* and *D. guyaquilensis* are generally accepted to be *D. innoxia* (Hammer et al. 1983).

Cinelli and Jones (2021) gave an excellent review of the alkaloids of the genus *Datura*. *Datura* species contain hyoscyamine, scopolamine, and littorine, while the roots yield valtropine. Tropane alkaloids have been reported in *Datura ceratocaula*, *Datura discolor*, *Datura ferox*, *Datura innoxia*, *Datura metel*, *Datura stramonium*, and *Datura wrightii*. Other species of *Datura* have not been studied for the presence of tropane alkaloids; these include *Datura arenicola*, *Datura kymatocarpa*, *Datura lanosa*, *Datura leichhardtii*, *D. pruinosa*, *D. quercifolia*, and *D. reburra*. Gerlach (1948) reported that *Datura innoxia* can be a potential commercial source of scopolamine.

***Datura ceratocaula* Ortega**

It is an annual herb or helophyte and grows in the seasonally dry tropical Mexico.

***Datura discolor* Bernh.**

It is an annual herb that grows in the subtropical W. Central USA to Honduras.

***Datura ferox* L.**

It is an annual herb, native to Mexico (Central, Northeast, Southwest) and Texas (USA), and introduced elsewhere.

***Datura innoxia* Mill.**

It is an annual or perennial herb—native to Arizona to Texas and Mexico—and introduced in North and South Africa (Fig. 2.3).

***Datura metel* L.** (Syn.: *Datura alba* F. Muell.; *Datura fastuosa* L.)

The native range of this species is from Texas to Colombia. It is an annual herb widespread in Old World Tropics and introduced in New World Tropics (Figs. 2.4 and 2.5).

Fig. 2.3 *Datura innoxia* Mill. (Source: A. Lalithamba with permission)

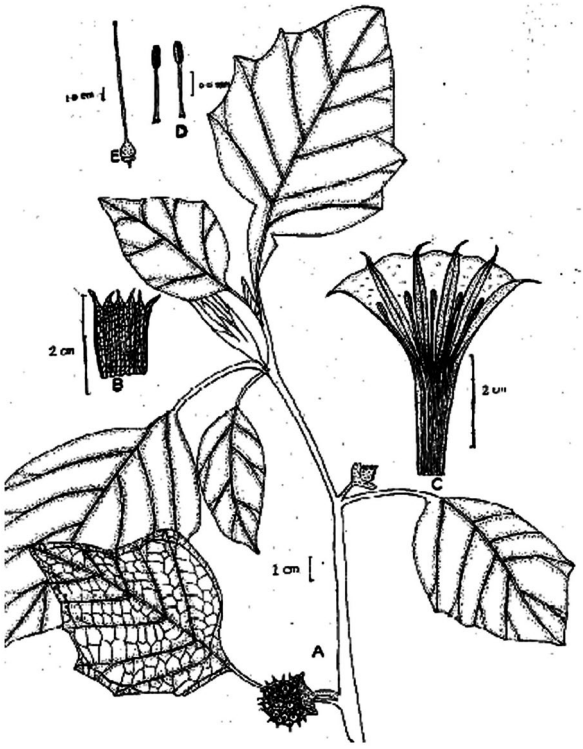

Fig. 2.4 *Datura metel* L.

Datura quercifolia H.B.K.

It is an annual, erect, small herb, up to 50 cm tall; native to Southwestern USA and Mexico; and grown as ornamental in many other countries (Fig. 2.6).

Fig. 2.5 *Datura metel* L. (Source: K. Raja Kullayiswamy with permission)

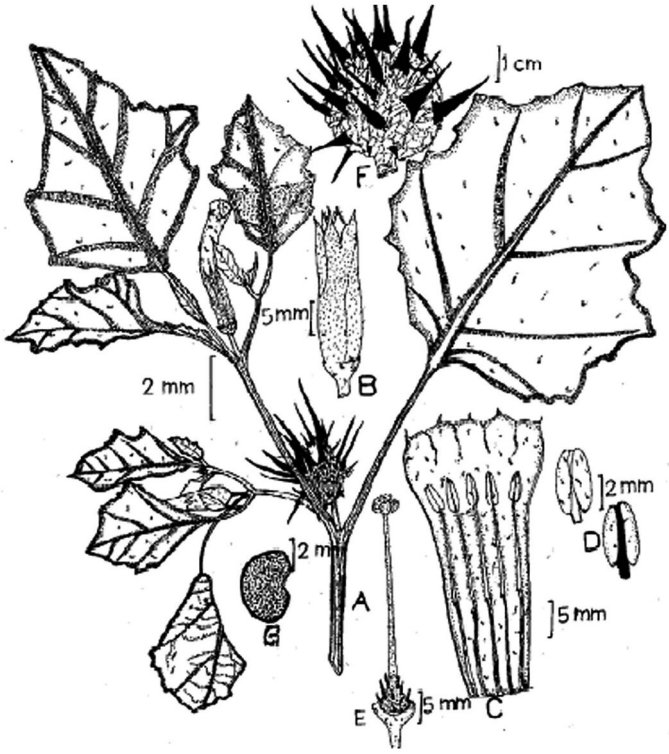

Fig. 2.6 *Datura quercifolia* H.B.K.

Datura stramonium L.

It is an annual erect herb and grows in subtropical Texas to Central America and the Caribbean and common in many warm temperate countries (Fig. 2.7).

Fig. 2.7 *Datura stramonium* L. (Source: K. Raja Kullayiswamy with permission)

Fig. 2.8. *Duboisia* (ABC Southern QLD: Jon Daly) https://www.abc.net.au/news/2021-11-13/sleepy-town-secretive-drug-centre-big-pharma-criminal-cartel/100572628

Datura wrightii Regel

This species' native range is SW. and S. Central USA to N. Mexico. It is an annual herb or subshrub that grows in subtropical regions.

Duboisia (Fig. 2.8)

There are four species of *Duboisia* and all of them contain tropane alkaloids. All the species of *Duboisia* are endemic to Australia. *D. myoporoides* contains scopolamine; *D. leichhardtii* contains hyoscyamine, scopolamine, and calystegine; *D.*

arenitensis contains hyoscyamine and scopolamine (Evans and Ramsey 1981). Luanratana and Griffin (1982) reported tropane alkaloids of *Duboisia hopwoodii*.

***Duboisia arenitensis* Craven, Lepschi, & Haegi**

It is a shrub and grows in the seasonally dry tropical N. northern territory of Australia.

***Duboisia hopwoodii* (F. Muell.) F. Muell.**

It is a shrub and grows in the desert or dry shrubland in Australia. A naturally occurring hybrid, *Duboisia hopwoodii* × *Grammosolen dixonii* contained a total alkaloid yield of 0.29% in which main alkaloids were nornicotine and scopolamine (Evans 1986).

***Duboisia leichhardtii* (F.Muell.) F.Muell.**

It is a shrub or tree and grows primarily in the desert or dry shrubland of S. Queensland in Australia.

***Duboisia myoporoides* R.Br.**

This species' native range is E. Australia and New Caledonia. It is a shrub or tree that grows in the subtropics.

Grammosolen

The alkaloids of *Grammosolen odgersii* (synonym: *Cyphanthera odgersii*) are consistent with those of other species of the genus *Cyphanthera*. Evans and Ramsey (1983) reported tropane alkaloids in aerial parts of *Grammosolen odgersii* (synonym: *Cyphanthera odgersii*) and *Grammosolen dixonii*.

***Grammosolen dixonii* (F. Muell. & Tate) Haegi**

This species' native range is CS. and SE. South Australia. It is a shrub that grows in the subtropics.

***Grammosolen odgersii* (F. Muell.) Haegi** (Synonym: *Cyphanthera odgersii*).

It is a shrub and grows in the desert or dry shrubland of SW. Australia.

Hyoscyamus

Hyoscyamus is rich in tropane alkaloids. The alkaloid composition of *H. boveanus*, *H. desertorum*, *H. muticus*, and *H. albus* was measured by El-Shazly et al. (1997). Altogether 39 alkaloids of the tropane and pyrrolidine types were identified. Many alkaloids were found in different species, e.g., 22 alkaloids in *H. boveanus*, 13 in *H. desertorum*, 24 in *H. muticus*, and 4 in *H. albus*. 3ß-Hyoscyamine, dehydrohyoscyamine, phyllalbine, 3α-phenylacetyl tropane, and phenylacetylscopine as well as phygrine and 2,3-diacetonyl-N-methyl-pyrrolidine are seemingly new for the genus *Hyoscyamus*. The aerial parts of *H. albus* contain scopolamine, atropine, and hyoscyamine (Ashraf et al. 2019).

***Hyoscyamus albus* L.**

It is an annual or biennial herb and grows in the subtropical Macaronesia and Mediterranean to N. Iraq and Arabian Peninsula.

***Hyoscyamus aureus* L.**

It is a biennial or perennial herb and grows in the subtropical E. Mediterranean to NW. Iraq.

***Hyoscyamus boveanus* (Dunal) Asch. & Schweinf.**

It is a semisucculent subshrub and grows in the desert or dry shrubland Egypt to Sinai.

***Hyoscyamus desertorum* (Asch. ex Boiss.) Täckh.**

It is an annual herb and grows in the desert or dry shrubland of Syria to Egypt and NE. Saudi Arabia.

***Hyoscyamus muticus* L.**

It is a perennial herb or subshrub and grows in the desert or dry shrubland from Sahara to India.

***Hyoscyamus niger* L.**

It is an annual or biennial herb and grows in the temperate regions from Mediterranean to Iran and cultivated in many other countries.

***Hyoscyamus pusillus* L.**

It is an annual herb and grows in the temperate S. European Russia to Mongolia and Arabian Peninsula.

***Hyoscyamus reticulatus* L.**

This species' native range is E. Mediterranean to Central Asia and Iran. It is an annual or biennial herb that grows in the subtropical biome.

***Hyoscyamus senecionis* Willd.**

It is a perennial herb and grows in the temperate N. Iraq to Afghanistan.

There are 31 species of *Hyoscyamus.* Of these the following species have not yet been studied for the presence of tropane alkaloids: *Hyoscyamus afghanicus* Pojark, *Hyoscyamus arachnoideus* Pojark, *Hyoscyamus bornmuelleri* Khat., *Hyoscyamus coelesyriacus* Bornm., *Hyoscyamus flaccidus* C. Wright, *Hyoscyamus gallagheri* A.G.Mill. & Biagi, *Hyoscyamus grandiflorus* Franch., *Hyoscyamus insanus* Stocks, *Hyoscyamus kotschyanus* Pojark, *Hyoscyamus kurdicus* Bornm., *Hyoscyamus leptocalyx* Stapf, *Hyoscyamus leucanthera* Bornm. & Gauba, *Hyoscyamus longipedunculatus* C.C.Towns., *Hyoscyamus malekianus* Parsa, *Hyoscyamus multicaulis* Rech.f. & Edelb., *Hyoscyamus nutans* Schönb.-Tem., *Hyoscyamus orthocarpus* Schönb.-Tem., *Hyoscyamus pojarkovae* Schönb.-Tem., *Hyoscyamus rosularis* Schönb.-Tem., *Hyoscyamus squarrosus* Griff., *Hyoscyamus tenuicaulis* Schönb.-Tem., and *Hyoscyamus tibesticus* Maire.

***Latua pubiflora* (Griseb.) Baill.**
There is only one species in this genus, i.e., *Latua pubiflora* (Griseb.) Baill. which is endemic to Chile. Tropane alkaloids from *Latua pubiflora* were investigated by Muñoz and Casale (2003).

Mandragora
There are four species of *Mandragora*, all of them contain tropane alkaloids. *Mandragora* spp. contain hyoscyamine, scopolamine, cuscohygrine, apoatropine, 3α-tigloyloxytropane, and 3,6-ditigloyloxytropane (Jackson and Berry 1973). Schlesinger et al. (2019) reported that *M. autumnalis* accumulates hyoscyamine, anisodamine, and scopolamine; *M. officinarum* and *M. turcomanica* lack anisodamine and scopolamine but show up to tenfold more hyoscyamine levels as compared with *M. autumnalis*. The roots of *M. caulescens* contain higher concentrations of two tropane alkaloids, viz., hyoscine and anisodamine (Zhang et al. 1994).

***Mandragora autumnalis* Bertol.**

It is a perennial herb and grows in the temperate Mediterranean to Western Iran.

***Mandragora caulescens* C.B. Clarke**

It is a perennial herb and native to Nepal to China (W. Sichuan, NW. Yunnan) and Northern Myanmar.

***Mandragora officinarum* L.** (Synonym: *Mandragora vernalis* Bertol).

It is a perennial herb with tuberous roots and indigenous to Mediterranean region.

***Mandragora turcomanica* Mitzgir.**

It is a perennial herb and native to NNE Iran to Southern Turkmenistan.

Nicandra
Nicandra species does not contain esters of tropic acid. However, tropine was isolated from the roots of *Nicandra physalodes* (Parr 1992). There are three species of *Nicandra*, among which only *Nicandra physalodes* showed tropine.

***Nicandra physalodes* (L.) Gaertn**

It is an annual, erect herb and grows in the seasonally dry tropical Peru to NW Argentina.

Physalis
There are 94 species of the genus *Physalis*. The roots of *Physalis* plants are known to contain alkaloids, especially tropane and pyrrolidine alkaloids. Tropane alkaloids have been reported in only in *Physalis peruviana* (Sahal and Ray 1980). *Physalis alkekengi*, in its roots, contains tigloidine, 3α-tigloyloxytropane, cuscohygrine, and phygrine (hygrine dimer) (Basey and Woolley 1973). Valid name of this species is *Alkekengi officinarum* Moench.