



E-ISSN: 2278-4136
P-ISSN: 2349-8234
www.phytojournal.com
JPP 2020; 9(3): 05-13
Received: 04-03-2020
Accepted: 07-04-2020

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An overview of tropane alkaloids from *Datura stramonium* L.

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Abstract

Datura stramonium L., a wild-growing plant of the Solanaceae family, is widely distributed throughout the world. It contains a variety of tropane alkaloids such as atropine, hyoscyamine, and scopolamine. In Ayurvedic medicine, *D. stramonium* has been used for curing various human ailments, including ulcers, wounds, inflammation, rheumatism and gout, sciatica, bruises and swellings, fever, asthma and toothache. A few previous studies have reported on the pharmacological effects of *D. stramonium*; however, complete information regarding the phytochemistry remains unclear. This comprehensive review includes information on botany and phytochemistry of the major tropane alkaloids produced by *D. stramonium*.

Keywords: *Datura stramonium*, tropane alkaloids, atropine, hyoscyamine, scopolamine

Introduction

Datura stramonium, also known as Jimson Weed, Locoweed, Angel's Trumpet, Thorn Apple, Devil's Trumpet is a hallucinogenic plant found in urban and rural areas. *Datura stramonium* is an annual herbaceous shrub belonging to the Solanaceae family. The plant originated in the territories of the Caspian Sea and spread to Europe in the first century. At present, the plant is found in most waste and dumpsites in Europe, Asia, America and South Africa (Weaver and Warwick, 1984) [44]. However, in other parts of the world, such as Germany and France, *D. stramonium* is cultivated (Moore, 1972) [24]. It is a wild growing flowering plant and was investigated as a local source for tropane alkaloids which contain a methylated nitrogen atom (N-CH₃) and include the anti-cholinergic drugs atropine and scopolamine.

Morphologically, the plant is described to have leaves with a toothed margin that are approximately 5-18 cm broad and 10-20 cm long. Flowers of *D. stramonium* can be described as axillary and resemble the shape of a trumpet thus giving its common name "Angel's trumpet". A spiny capsule is the fruit which is green and upon drying split opens and releases black seeds. The flowers are usually cream, yellow or purple in colour. The plant usually grows to a height of two meters (Stace, 2010) [38].

The plant is known to be a strong narcotic and poisonous. The ingestion of any part of the plant causes poisoning and may result in death. According to research based on *D. stramonium* toxicity, the seeds and fruit are known to be the most toxic. There are no treatments available that can reduce the toxic effects of the seeds or fruit. There are many cases of *Datura* poisoning, the first recorded in the early 1990's in the United States of America. It was reported that many adolescents and young adults became ill and passed on from ingesting the leaves of *D. stramonium* (Adegoke and Alo, 2013) [1]. The symptoms of Jimsonweed poisoning are associated with dryness of the mouth and skin, severe thirst, dilation of the pupil, loss of eyesight, hallucination, palpitations, restlessness and loss of consciousness.

Taxonomy and description

D. stramonium is an annual plant. The stem is herbaceous, branched and glabrous or only lightly hairy. By cultivation the plant reaches a height of about one meter (Nadkarni and Nadkarni, 1996 [25]; Jarald and Edwin, 2007 [17]). The branching stems are spreading, leafy, stout, erect, smooth and pale yellowish green in color, branching repeatedly in a forked manner. Leaves are hairy, big, simple dentate, oval glabrous, apposite veins of leaves are pale black, stalked, 4-6-inch-long, ovate and pale green. The upper surface is dark and grayish-green, generally smooth, the under surface paler, and when dried, minutely wrinkled (Figure 1a). *D. stramonium* bears funnel shaped, white or purple coloured flowers, with 5 stamens and superior ovary (Figure 1c). The average length of flower is about 3 inches. The calyx is long, tubular and swollen base surrounded by five sharp teeth. Corolla is funnel shaped. Stem stalk is pale blue or greenish white. Seeds are black, kidney shape and flat [Gary *et al.*, 2005 [11];

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Gupta, 2008) ^[12]. Fruits are as large as walnuts and full of thorns (hence the English name “thorn apple”) (Figure 1b). The plant is strong narcotic but has a peculiar action on the human which renders it very valuable as medicines. The whole plant is poisonous and the seeds are the most active; neither drying nor boiling destroys the poisonous properties. The genus name *Datura* is derived from “dhatura”, the Bengali name for the plant, while the epithet *stramonium* combines the Greek word “strychnos” for nightshade, and “makinos” meaning mad, referring to the narcotic properties of the species. Until relatively recently it had been customary to distinguish between the white-flowered *D. stramonium* and the purple-flowered *D. tatula*. However, chemotaxonomic studies have confirmed that these are both forms of *D. stramonium* (Haegi, 1976 ^[14]; Hadkins *et al.*, 1997 ^[13]). Variants of *D. stramonium* have been described with $2n = 12$,

25, 26, 36 or 48 chromosomes. Morphological variants include var. *tatula* which has purple flowers and sub-equal spines on the capsule; var. *stramonium*, with white flowers and shorter spines on the lower part of the fruit (Table 1).

Table 1: Classification of Kingdom Plantae

Domain	Eukaryota
Kingdom	Plantae
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Dicotyledonae
Order	Solanales
Family	Solanaceae
Genus	<i>Datura</i>

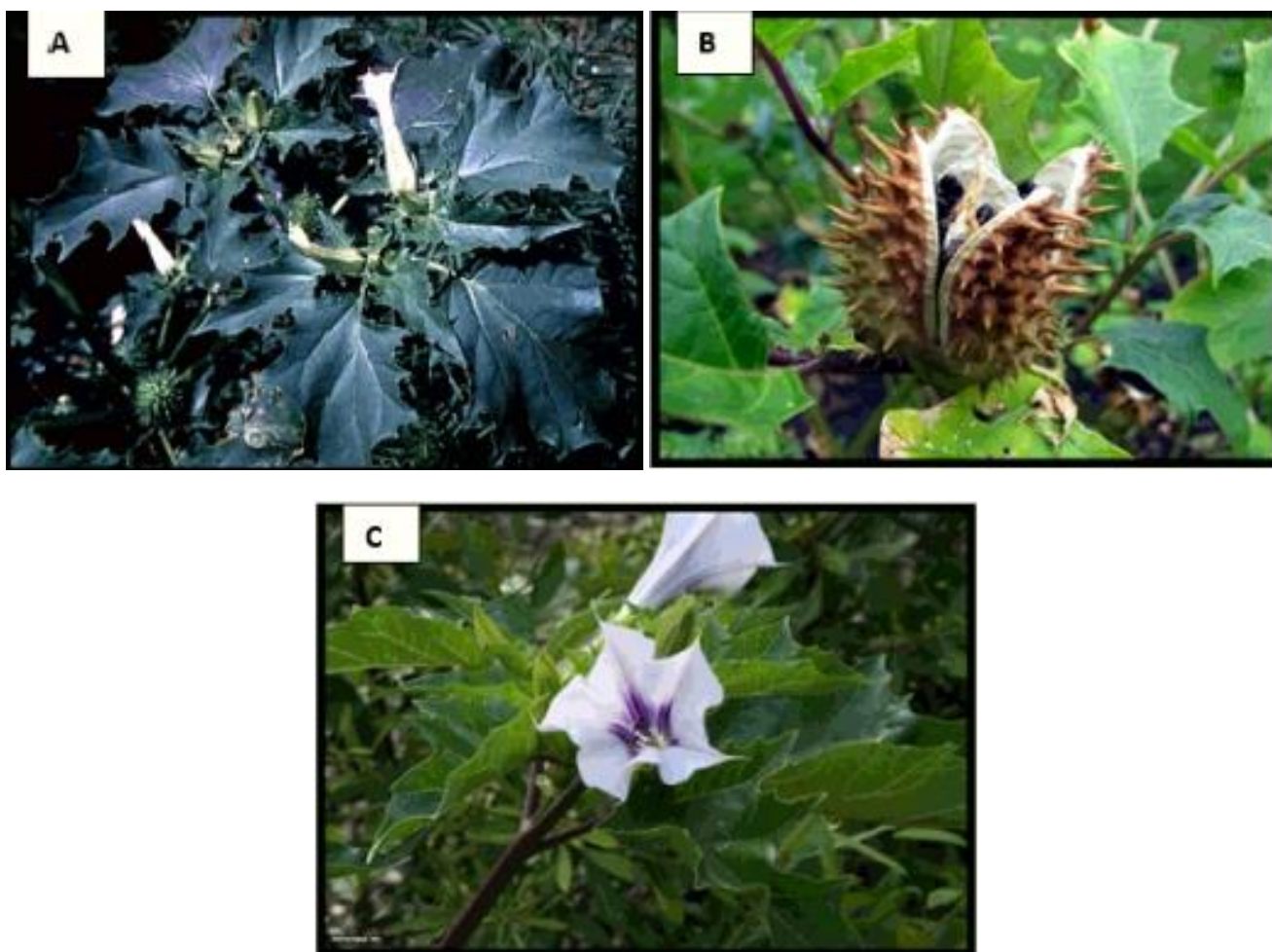


Fig 1: *Datura stramonium*. A: *Datura* plant (leaves and flowers); B: *D. stramonium* fruit; C: *D. stramonium* flower

Distribution

Datura stramonium originated in the tropical regions of Central and South America and has become a cosmopolitan weed in the warm regions of North, Central and South America, Europe, Asia, Africa and New Zealand. It is now found throughout almost all the USA except for the northwest and northern Great Plains. It was recorded in Virginia, USA, by 1676, where its seed was used as a narcotic by British soldiers. *Datura stramonium* is found on most soil types but prefers rich soils. *Datura stramonium* is a common

weed of gardens, waste places, and farmyards. In recent years, the species has started to appear as a weed of cultivated ground, particularly in soybean, bean and maize fields in southern Ontario and Quebec. It prefers open communities, and it most commonly occurs in association with annual. Biennial or short-lived perennial weeds. At present it grows in waste places in Europe, Asia, America and South Africa. *D. stramonium* is cultivated in Germany, France, Hungary, South America and throughout the world (Jarald, 2007) ^[17].

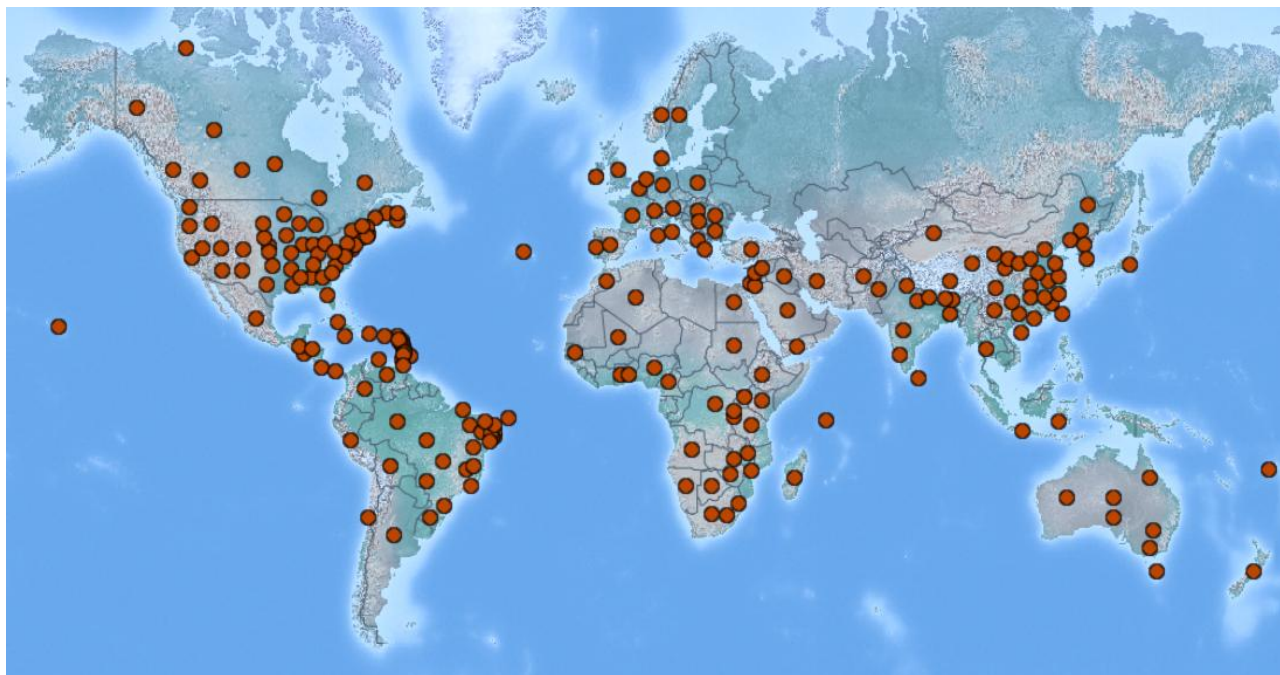


Fig 2: Present worldwide distribution (red) of *Datura stramonium*

Review procedure

Information presented in this paper was collected from different sources found online. Electronic databases such as Science Direct, ISI Web of Science, Google Scholar, Scopus and MEDLINE were used for data mining. The reviewed online sources include scientific studies published in articles, theses, books, book chapters, journals and abstracts. Potential literature sources were found by searching for the terms and/or phrases like taxonomic hierarchy, traditional medicine, folk medicine, folkloric uses, indigenous medicine, ethno medicine, ethno botany, economic uses, horticultural uses, cultural uses, phytochemistry, active compounds, biological activities and pharmacological properties of *D. stramonium*.

Ethno medicinal uses

Flower petals from *D. stramonium* are crushed and the extracted juices are used for the treatment of ear infections. The seeds are used as purgative and for the treatment of cough and fever. A small quantity of seeds are used for asthma and tonsil problems (Savithamma *et al.*, 2007) [32]. Seeds are usually smoked due to its narcotic action (Khan *et al.*, 2013) [18]. External injuries, wounds, bleedings and pain is treated with leaf paste and extract (Njoroge, 2012) [26]. Fruit oil is used for to relieve body pain (Vijendra and Kumar, 2010) [41]. Leaf or whole plant is anti-inflammatory and antispasmodic (Dwivedi *et al.*, 2008) [9]. The extract of leaves is also used for baldness and the juice of the fruit is applied to scalp for falling hairs and as an antidandruff (Khan and Khatoon, 2008) [19]. Dried leaves and seeds are used as anticholinergic and sedative (Wazir *et al.*, 2004) [43]. The leaves of *D. stramonium* L. are used for the relief of headache and vapours of leaf infusion is used to relieve the pain of rheumatism and gout (Biswas *et al.*, 2011) [6]. The smoke from the burning leaf is inhaled for the relief of asthma and bronchitis (Savithamma *et al.*, 2007) [32]. It is also applied to smooth painful wounds and sores. Seeds and leaves of *D. stramonium* were used to sedate hysterical and psychotic patients, also to treat insomnia (Khanra *et al.*, 2015) [20]. It is also used to relax the smooth muscles of the bronchial tube and asthmatic bronchial spasm. It is also used in the treatment of parkinsonism and hemorrhoids (Ivancheva *et al.*, 2006) [16].

Scopolamine is also found in the plant, which makes it a potent cholinergic-blocking hallucinogen that has been used to calm schizoid patients. Its leaves, containing hyoscyamine and atropine, can be used as an immensely powerful mind-altering drug. The seeds of *Datura* are analgesic, anthelmintic and anti-inflammatory and as such, they are used in the treatment of stomach and intestinal pain that results from worm infestation, toothache, and fever from inflammation (Ivancheva *et al.*, 2006) [16]. *Datura stramonium* plants are frequently used as antiparasitic and repellents to insect infestation (Das *et al.*, 2012) [8].

Pharmacology

D. stramonium extracts were researched for its potential pharmacological profile (Rasila Devi *et al.*, 2011 [29], Sharma *et al.*, 2014a) [36], Swathi *et al.* (2012) [39] investigated the potential of *D. stramonium* ethanolic extracts as larvicidal and mosquito repellent agents. At a concentration of 86.25 mg/L, 16.07 mg/L and 6.25mg/L, the extracts exhibited larvicidal activity against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* respectively.

D. stramonium leaf extracts, combined with extracts of other plants such as *Azadirachta indica* and *Coriandrum sativum*, were screened in vivo for their anti-inflammatory potential in albino rats. The combined ethanolic extracts were investigated using the carrageenan-induced rat paw edema method and results of these plants exhibited anti-inflammatory activity which comparable to the standard drug, diclofenac sodium. However, this anti-inflammatory activity, the synergistic effect of combined plant extracts and further studies pertaining to crude *D. stramonium* extracts is still to be conducted (Sonika *et al.*, 2010) [37].

Combined methanolic *D. stramonium* and *D. innoxia* extract, displayed antibacterial activity against Gram-positive bacteria in a dose-dependent manner. This antibacterial potential was further investigated in another study in conjunction with *W. somnifera* and *Terminalia Arjuna*. Results indicated that these extracts in combination with crude ethanolic extracts of *D. stramonium* displayed antibacterial activity against *S. aureus*, *B. subtilus*, *E.coli*, *M. luteus* and *Candida albicans* which were comparable to the standard drug ciprofloxacin (Sharma

et al., 2009)^[35]. *D. stramonium* extracts using four solvent systems (water, acetone, ethanol and methanol) was assessed for its potential antibacterial activity against clinical pathogenic isolates. The maximum antibacterial was displayed by chloroform extract against *S. aureus* with a zone of inhibition of 18 mm, whilst the least antibacterial activity was displayed by the acetone extract against *E. coli* with a zone of inhibition of 8.2 mm (Baynesagne *et al.*, 2017)^[3].

A study in 2016, investigated ethyl acetate flower extracts of *D. stramonium* for its anti-cancer activity against human liver cancer cells (HepG2) using the MTT assay. The extract exhibited anticancer activity comparable to that of the standard Gemcitabine with a CTC50 value of 131.53 µg/ml (Rajeshkanna *et al.*, 2016). Methanolic seed extracts of *D. stramonium* was also investigated for their potential antioxidant and anticancer activity. The antioxidant activity was conducted using the DPPH[•] radical, superoxide radical, ABTS^{•+} radical cation, OH[•] radical scavenging assays, Phosphomolybdenum reduction and Fe³⁺ reducing power assays, whilst the anti-cancer activity was investigated using the MTT assay against MCF (breast cancer) cell lines. The antioxidant results demonstrated IC₅₀ values for DPPH radical, superoxide radical, ABTS^{•+} radical cation, OH[•] radical scavenging assays of 35.26, 10.50, 49.36 µg/mL respectively. Cytotoxic activity for MCF7 cell line was 66.84% at 500 µg/mL (Iqbal *et al.*, 2017).

Ethanol leaf extracts of *D. stramonium* was also investigated for its potential larvicidal and mosquito repellent activities. The results for the assay demonstrated potential larvicidal against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* with LD₅₀ values of 86.25 mg/L, 16.07 mg/L and 6.25 mg/L respectively. Mosquito repellency was displayed for durations of 2.7, 71.7 and 117.7 minutes against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* respectively at higher concentrations (Swathi *et al.*, 2012)^[39].

Phytochemistry

Amongst the many phytochemicals present in *D. stramonium*, minor and major tropane alkaloids have been predominantly present in the plant. Major alkaloids include Atropine, Scopolamine, Hyoscyamine, Apo scopolamine and 7-hydroxyhyoscyamine. Studies conducted on the distribution of Atropine and Scopolamine revealed that the production of Atropine and Scopolamine occurs in different parts of the plants at different stages of its life cycle. In young stems and leaves, hyoscyamine is always the predominant alkaloid. There has been a total of 64 tropane alkaloids which has been identified in *D. stramonium*, all of which has been included in many pharmacopoeias due to its anticholinergic potential (Ryan *et al.*, 2015). Two new tropane alkaloids, 3-phenylacetoxo-6, 7-epoxynortropine and 7-hydroxyapoptropine were tentatively identified. The alkaloids scopoline, 3-(hydroxyacetoxo) tropane, 3-hydroxy-6-(2-methylbutyryloxy) tropane, 3a-tigloyloxy-6-hydroxytropane, 3,7-dihydroxy-6-tigloyloxytropane, 3-tigloyloxy-6-propionyloxytropane, 3-phenylacetoxo-6,7-epoxytropane, 3-phenylacetoxo-6-hydroxytropane, aponorscopolamine, 3a,6a-ditigloyloxytropane and 7-hydroxyhyoscyamine are reported for the first time for this species (Berkov *et al.*, 2006)^[4].

The main components of essential oil were sterols and their derivatives, and the major constituents of *Datura stramonium* essential oil are sterols and their derivatives and 5α-Ergosta-

7,22-dien-3β-ol (16.53%), 3-Hydroxycholestan-5-yl acetate (14.97%), and 26,26-Dimethyl-5, 24(28)-ergostadien-3β-ol (10.39%) (Wang and you, 2012). The seeds also contained higher concentration of phytate, tannin and oxalate than the seed coat. In seed coat calcium, iron, potassium, sodium and phosphorus were higher than the seeds (Oseni *et al.*, 2011). Polar extractives contained saponins, steroids, alkaloids, and glycosides (Shagal *et al.*, 2012)^[34]. The primary biologically active substances in *D. stramonium* are the alkaloids atropine and scopolamine (Ivancheva *et al.*, 2006)^[16].

Tropane alkaloids

Tropane alkaloids are bicyclic alkaloids that contain the tropane ring. There are secondary metabolites distributed in plants within the Proteaceae, Brassicaceae, Convolvulaceae, Rhizophoraceae, Euphorbiaceae, Solanaceae, and Erythroxylaceae family. There are approximately 2000 structures that contain the tropane rings however the most common are Atropine and scopolamine. Atropine, Scopolamine and their derivatives are commercially important as they are used as anticholinergic drugs.

The different classes of Tropane alkaloids; cocaine, scopolamine/hyoscyamine and the calystegines share a common precursor biosynthetic route beginning with the amino acids L-ornithine and L-arginine (Figure 3). In plants, ornithine and arginine are derived from glutamate, an amino acid which is directly connected to the nitrogen assimilation. Ammonia is incorporated into Glutamate via the glutamine synthetase-glutamate synthase pathway. Glutamate is the precursor in several polyamine pathways. In order to form putrescine from the amino acids ornithine or arginine, ornithine is decarboxylated by ornithine decarboxylase and arginine undergoes a three-step reaction, including decarboxylation, hydrolysis of the imine functionality of guanidine and hydrolysis of urea which is catalyzed by the enzymes arginine decarboxylase; agmatine deiminase and N-carbamoylputrescine amidase, respectively.

The activities of arginine decarboxylase and ornithine decarboxylase were suppressed in *Datura* plants by using the specific irreversible inhibitors DL-difluoromethylarginine and DL-difluoromethylornithine, respectively in order to probe the nature of these two routes to putrescine biosynthesis. These experiments indicated that the two routes do not act independently from each other and that the arginine decarboxylase exhibited a higher activity than the ornithine decarboxylase (Robins *et al.*, 1991). Putrescine (Tetramethylenediamine) is an intermediate in several metabolic pathways. It can be formed to spermidine by a spermidine synthase catalyzed reaction using decarboxylated S-adenosyl methionine and putrescine as substrates. Putrescine can also be methylated to N-methylputrescine by the enzyme putrescine N-methyltransferase (Biastoff *et al.* 2009) using S-adenosyl methionine. The next step in TA biosynthesis is the oxidative deamination of N-methylputrescine to 4-methylaminobutanal which is catalyzed by N-methylputrescine oxidase (Mizusaki *et al.*, 1972)^[23]. This diamine oxidase requires copper as a cofactor. N-methylpyrrolinium, a central intermediate, is formed by spontaneous cyclization of N-methylputrescine. Chemically, this reaction is an intramolecular Schiff base formation. N-methylpyrrolinium cation is a branchpoint in Tropane alkaloid and nicotine biosynthesis (Courdavault. 2010)^[7].

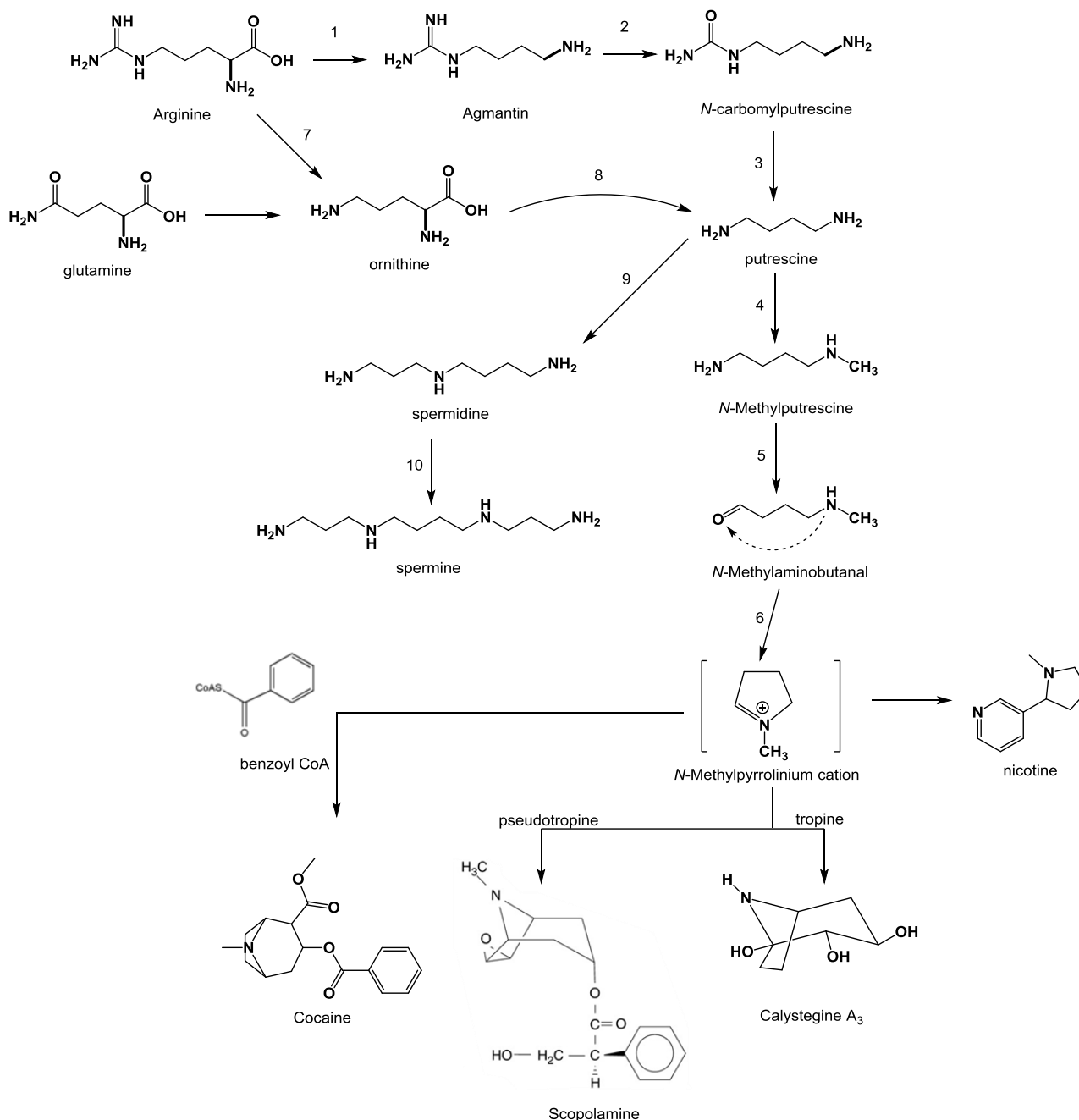


Fig 3: Early stages of Tropane Alkaloid biosynthesis; 1 = arginine decarboxylase; 2 = agmatine deiminase; 3 = N-carbamoylputrescine amidase; 4 = putrescine N-methyltransferase; 5 = N-methylputrescine oxidase; 6 = spontaneous cyclization; 7 = arginase; 8 = ornithine decarboxylase; 9 = spermidine synthase; 10 = spermine synthase

Atropine

Atropine is one of the most common tropane alkaloids used in the pharmaceutical industry (Fig. 4). It is the racemic form of Hyoscyamine and is known to bind to muscarinic receptors which block the parasympathetic cholinergic neurons. The alkaloid, acts on both peripheral and central muscarinic receptors. According to previous research, it was found that Atropine inhibits the growth of enveloped viruses independent of the nucleic acid content. The anti-viral activity of Atropine was investigated using the plaque reduction test and one step growth experiments. It was found that Atropine was effective against the Herpes simplex virus, Influenza, Sindbis, Adenovirus and Japanese encephalitis virus (Willoughby *et al.*, 2005) [45]. Atropine was discovered to block the glycosylation of viral proteins of Herpes; hence the production of virions are inhibited. Furthermore, virions which were formed in the presence of Atropine were known to be non-infectious.

The pharmaceutical application of Atropine is vast however low dosage is advised on treatment as it affects the cardiovascular system causing bradycardia. Atropine is used as an antidote to treat organophosphate poisoning as it increases acetylcholine release which inhibits cholinesterase. It is also used to dilate pupil, decrease salivation and reduce gastrointestinal activity (Sayyed and Shah, 2014) [33].

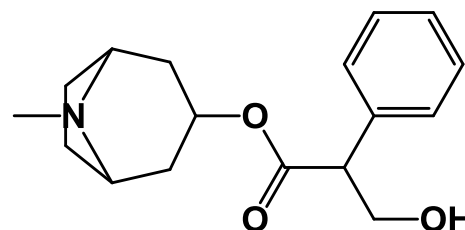


Fig 4: Chemical structure of Atropine - 1 α H, 5 α H-Tropan-3- α ol (\pm)-tropate (ester), sulfate monohydrate

Biosynthesis of Atropine

The initial stages of Atropine biosynthesis is identical to that of all tropane alkaloids. Arginine and Ornithine metabolism leads to the formation of Putrescine, Putrescine is methylated to form *N*-Methyl putrescine by the enzyme *N*-putrescine Methyltransferase. *N*-Methyl putrescine is converted to *N*-methylpyrrolinium by spontaneous cyclization. *N*-methylpyrrolinium serves as the branch point for tropane synthesis. The biosynthesis of Atropine starting

from L-Phenylalanine first undergoes a transamination forming Phenyl pyruvic acid which is then reduced to Phenyl-lactic Acid. Coenzyme A then couples Phenyl-lactic acid with Tropine forming Littorine, which then undergoes a radical rearrangement initiated with a P₄₅₀ enzyme forming hyoscyamine aldehyde. A dehydrogenase then reduces the aldehyde to a primary alcohol making Hyoscyamine, which upon racemization forms atropine.

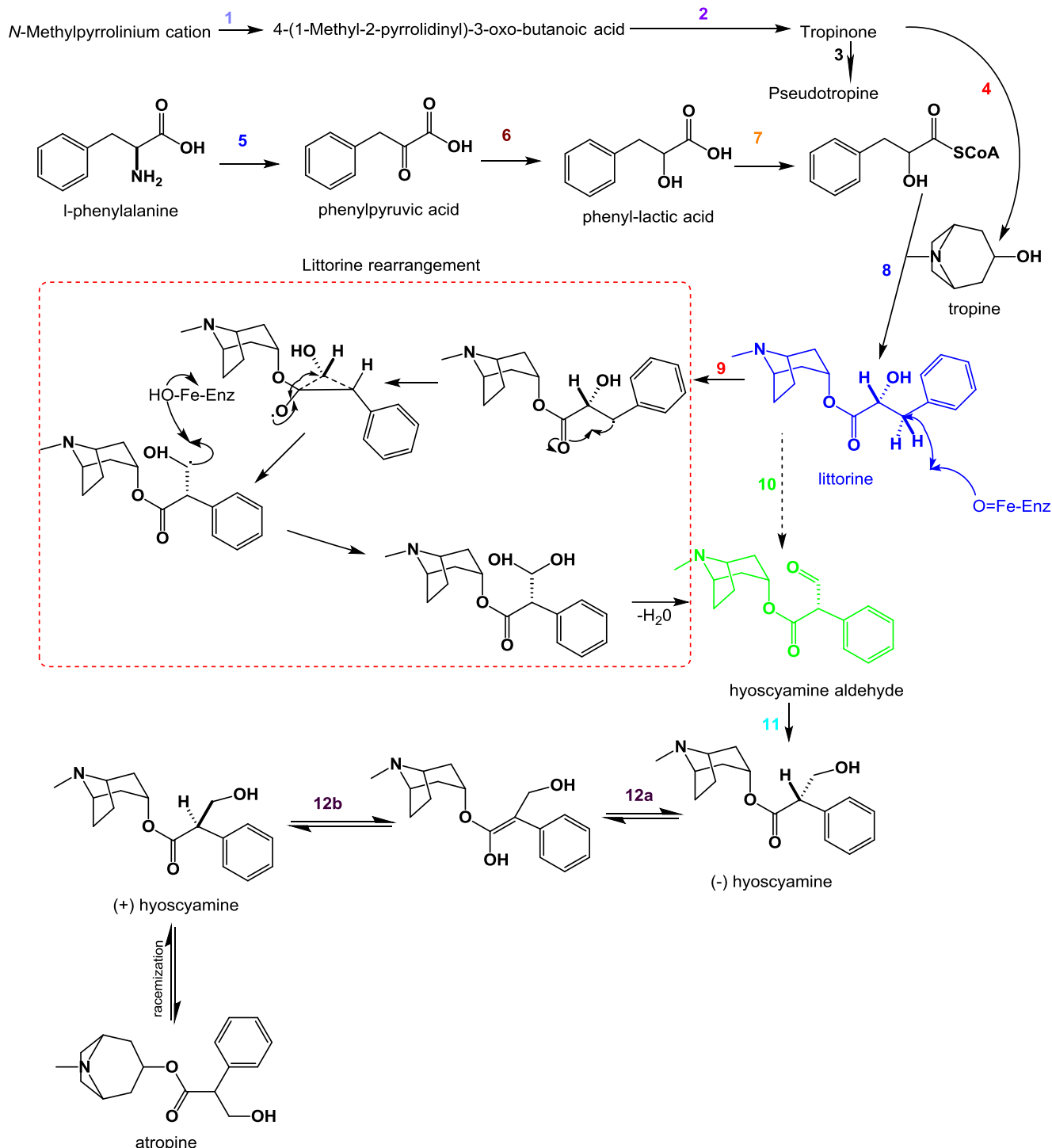


Fig 5: Atropine biosynthesis, starting with the L-phenylalanine; 1 = polyketide synthase; 2 = cytochrome P450 enzyme; 3,4 = tropinone reductase I/II; 5 = L-phenylalanine deaminase; 6 = D-phenyl lactate dehydrogenase; 7 = phenyl lactate CoA-transferase 8 = littorine synthase; 9 and 10 = cytochrome P450 littorine mutase/monooxygenase; 11 = unidentified alcohol dehydrogenase; 12a and 12b = hyoscyamine 6 β -hydroxylase

Scopolamine and Hyoscyamine

Initially, Scopolamine was used in neuropsychopharmacology as an antidepressant and as a standard drug for the induction

of age and dementia-related cognitive deficiency in healthy humans and animals (Furey *et al.*, 2010) [10]. However, the demand for Scopolamine in the pharmaceutical industry has

grown due to its multiple applications and administrations. Scopolamine is currently administered as a syrup or tablet for the treatment of nausea and vomiting. It has also been administered for the treatment of gastrointestinal spasms associated with irritable bowel syndrome and has also been used for eye inflammation. The current hype of Scopolamine is associated with its use in creating a transdermal patch for treating motion sickness. This type of Scopolamine is known as the “the transdermal scopolamine”. In 1979, the very first transdermal Scopolamine was manufactured by a company Alza Corporation. Over the years its sale has grown as transdermal Scopolamine is the preferred choice for treating motion sickness. This is due to its easy administration, cost-effectiveness and availability. It has been envisaged that in the period of 2016 -2024, the expected CAGR growth rate for Scopolamine will be 6.7%.

Hyoscyamine is an antagonist of muscarinic acetylcholine receptors. It blocks the action of acetylcholine at parasympathetic sites in sweat glands, salivary glands, stomach secretions, heart muscle, sinoatrial node, smooth muscle in the gastrointestinal tract, and the central nervous system. It increases cardiac output and heart rate, lowers blood pressure, and dries secretions. Hyoscyamine is used to

provide symptomatic relief to various gastrointestinal disorders including spasms, peptic ulcers, irritable bowel syndrome, pancreatitis, colic, and cystitis. It has also been used to control some of the symptoms of Parkinson’s disease.

Biosynthesis of Scopolamine and Hyoscyamine

The biosynthesis of scopolamine begins with the decarboxylation of l-ornithine to putrescine by ornithine decarboxylase. Putrescine is methylated to N-methylputrescine by putrescine N-Methyltransferase (Ziegler and Facchini, 2008) [46]. Putrescine oxidase that specifically recognizes methylated putrescine catalyzes the deamination of this compound to 4-methylaminobutanal which then undergoes a spontaneous ring formation to N-methylpyrrolium cation. In the next step, the pyrrolium cation condenses with acetoacetic acid yielding hygrine. No enzymatic activity could be demonstrated that catalyzes this reaction. Hygrine further rearranges to tropinone. Subsequently, tropinone reductase I converts tropinone into tropine which condenses with phenylalanine-derived phenylacetate to littorine. A cytochrome P450 classified as Cyp80F1 (Li *et al.*, 2006) [22] oxidizes and rearranges littorine to hyoscyamine aldehyde. Hyoscyamine aldehyde is further reduced to hyoscyamine. Finally, hyoscyamine is converted to scopolamine by an unidentified alcohol dehydrogenase.

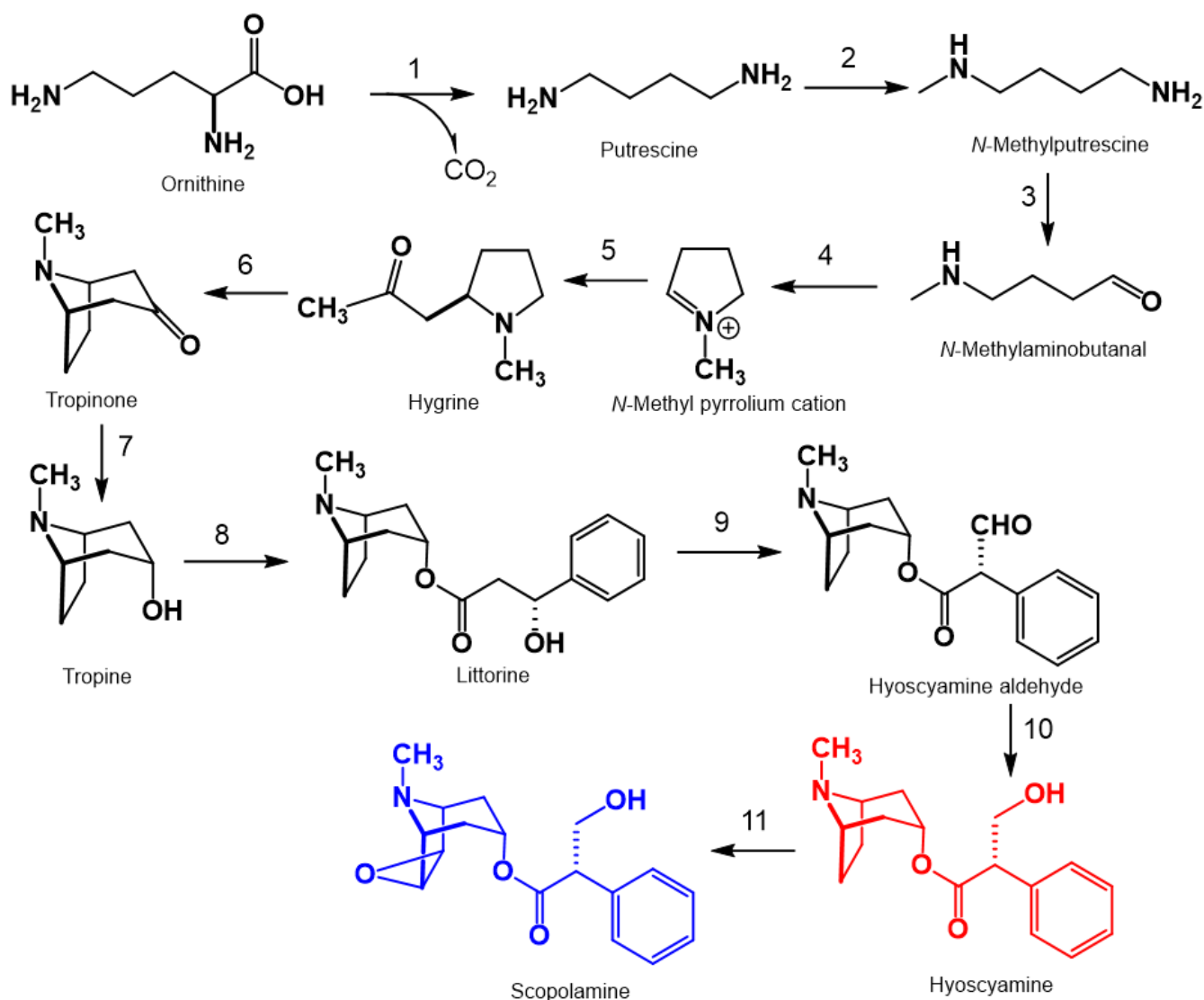


Fig 6: Scopolamine and Hyoscyamine biosynthesis, starting with Ornithine. 1 = ornithine decarboxylase; 2 = putrescine N-Methyltransferase; ; 3 = N-Methylputrescine oxidase; 4 = spontaneous cyclization; 5 = unknown enzyme; 6 = spontaneous cyclization; 7 = tropinone reductase I; 8 = littorine synthase; 9 = littorine mutase/ monooxygenase (CYP80F1) 3 = PYKS = polyketide synthase; CYP82M3 = cytochrome P450 enzyme TR-I/II = tropinone reductase I/II; littorine synthase not known; littorine mutase/ monooxygenase (CYP80F1); 10 = 11 = unidentified alcohol dehydrogenase; 11 = hyoscyamine 6 β -hydroxylase (H6H)

Scopolamine (Fig. 7A) is the 6, 7- β -epoxide of hyoscyamine (Fig. 7B) which is formed from hyoscyamine by means of 6 β -hydroxyhyoscyamine. The hydroxylation of hyoscyamine to 6 β -Hydroxy-hyoscyamine is catalyzed by a 2-oxy-glutarate

dependent dioxygenase, Hyoscyamine 6 β -hydroxylase. The epoxidation of 6 β -hydroxyhyoscyamine to Scopolamine is also catalyzed by hyoscyamine 6 β -hydroxylase.

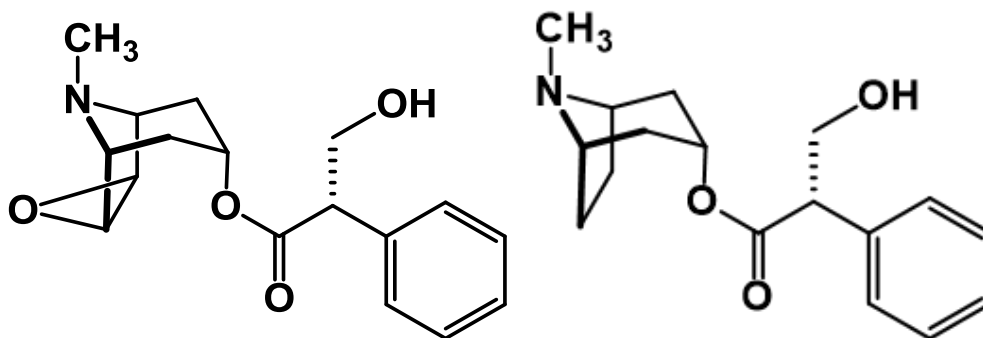


Fig 7: Chemical structure of Scopolamine [9-methyl-9-oxido-3-oxa-9-azoniatricyclononan-7-yl 3-hydroxy-2-phenylpropanoate] - (A) and Hyoscyamine [(1S, 5R)-8-methyl-8-azabicyclo [3.2.1] octan-3-yl] (2S)-3-hydroxy-2-phenylpropanoate] - (B)

Conclusion

The phytochemistry of *D. stramonium* has been documented in this in depth review. In view of its multiple pharmaceutical applications, more pharmaceutical screening and quantitative structure-activity relationship and molecular docking studies need to be conducted. The metabolic pathways and metabolomic production of the major tropane alkaloids presented in this review would be helpful in promoting research with emphasis on the manipulation of metabolic pathways for the enhanced production of the secondary metabolites. This review will also provide a new platform for the research and development of new secondary metabolites for medical application and agroindustry.

Acknowledgments

The National Research Foundation of South Africa and the Durban University of Technology are acknowledged for financial and infrastructural support.

Conflict of Interest

No conflict of interest exists amongst authors.

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