Datura Species

Subjects: Integrative & Complementary Medicine

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Datura, a genus of medicinal herb from the Solanaceae family, is credited with toxic as well as medicinal properties. The different plant parts of *Datura* sp., mainly *D. stramonium L.*, commonly known as Datura or Jimson Weed, exhibit potent analgesic, antiviral, anti-diarrheal, and anti-inflammatory activities, owing to the wide range of bioactive constituents. With these pharmacological activities, *D. stramonium* is potentially used to treat numerous human diseases, including ulcers, inflammation, wounds, rheumatism, gout, bruises and swellings, sciatica, fever, toothache, asthma, and bronchitis. The primary phytochemicals investigation on plant extract of *Datura* showed alkaloids, carbohydrates, cardiac glycosides, tannins, flavonoids, amino acids, and phenolic compounds. It also contains toxic tropane alkaloids, including atropine, scopolamine, and hyoscamine. Although some studies on *D. stramonium* have reported potential pharmacological effects, information about the toxicity remains almost uncertain. Moreover, the frequent abuse of *D. stramonium* for recreational purposes has led to toxic syndromes. Therefore, it becomes necessary to be aware of the toxic aspects and the potential risks accompanying its use.

Datura stramonium alkaloids atropine cardiac glycosides hyoscamine Ayurveda

1. Introduction

Medicinal plants present a wide range of bioactive substances known for their pharmacological activities. In fact, the majority of conventional medicines rely on plant products. One such plant species is *Datura* spp., a flowering medicinal herb that pertains to the *Solanaceae* family [1], primarily used as an intoxicant and hallucinogen [2]. It is widely cultivated in Europe, Asia, America, South Africa, and other tropical and subtropical regions [3]. *Datura* can be well-grown in average soils, but it prefers nutrient-rich and moist soil or alkaline soil [4]. Although the plant acts as a narcotic, it has distinct effects on human health, rendering it incredibly beneficial as medicine [5][6]. This may be attributed to the fact that it possesses antimicrobial, antidiabetic, anti-asthmatic, anti-inflammatory, antioxidant, analgesic, insecticidal, cytotoxic, wound healing, and neurological activities [7][8]. The *Datura* plant is also known for its larvicidal effects against red flour beetle (*Tribolium castaneum*) and mosquito repellent activities [9][10]. In addition, *Datura* spp. has also been used against animal bites such as snake bites, which helps relieve pain. *D. stramonium*, the well-known species of this family, is utilized for mystic and religious purposes along with its use as herbal medicine [11]. Moreover, *D. stramonium* seed is generally smoked to get a hallucinogenic experience [3].

The consumption of any part of *Datura* plant may lead to the severe anticholinergic effect that may cause toxicity. In fact, the entire plant is toxic to some extent, but the seeds are found to be the most toxic; neither drying out nor boiling destroys the toxic properties [12][13]. Ayurvedic system of medicine has described *D. stramonium* as a valuable therapy for numerous human illnesses such as wounds, ulcers, rheumatism, fever, inflammation, asthma,

and toothache [3][14]. A leaf extract taken orally can treat asthma along with sinus infection, and stripped bark can heal burns, swellings, and ulcers when applied externally to the affected area [9][15]. However, in the modern system of medicine, the therapeutic potentials of *D. stramonium* are dominated by its toxic effects. The intake of large doses of *D. stramonium* disturbs the central nervous system and produces symptoms like confusion, hallucinations and amnesia, and bizarre behavior [16]. In addition, the signs and symptoms of acute *D. stramonium* poisoning include dryness of the lips and the epidermis, pupil dilation, urinary retention, impaired vision, and fast heartbeat [15][17].

Several incidences of accidental or intentional *D. stramonium* poisoning have been reported from different parts of the world, when eaten directly or through decoction made from herbal prescriptions, owing to its mind-affecting properties [18]. Therefore, the therapeutic applications require extensive research and analysis of the plant from every aspect, especially its toxicity. It should be consumed only with prior knowledge of its adverse effects since the consequences can be extremely harmful. With these facts, it is necessary to be aware of the toxic aspects and the potential risks accompanying its use.

2. Biochemical Composition of *Datura*

Datura, in general, constitutes significant amounts of carbohydrates, fats, protein, moisture, ash content, and crude fiber. Besides, major phytochemicals found in *Datura* include alkaloids, phenolic compounds, tannins, flavonoids, and cardiac glycosides [19][20]. In addition, many amino acids such as alanine, phenylalanine, glutamate, and tyrosine have also been isolated from the seeds [8]. *Datura* species are particularly rich in tropane alkaloids. Hyoscine [(-)-Scopolamine] constitutes the major tropane alkaloid, along with hyoscyamine and atropine, having different concentration levels in different plant parts (**Figure 1**) [11][21]. The atropine content in the leaves in *Datura metel* was found to be 0.426%, whereas hyoscyamine levels were found to be 0.426% in the seeds and 0.43% in flower [8]. The alkaloid contents of scopolamine and atropine in the entire plant in *D. metel* increase gradually with the development of various growth stages and becomes most apparent when the plant reaches the end of its reproductive stage [22][23]. However, in the case of *D. stramonium*, the maximum amounts of alkaloids were found after ten weeks of seed germination, decreasing gradually with the beginning of the generative phase in plants [8][24]. Generally, the alkaloid concentration varies with the plant part and different growth stages in the plant. For example, leaves develop maximum alkaloid concentration in the vegetative phase, decreasing rapidly in the generative phase [25][26]. The stems and leaves of young plants contain hyoscyamine as a significant component. However, the concentrations of atropine and scopolamine differ in different plant parts in young and adult plants[9].

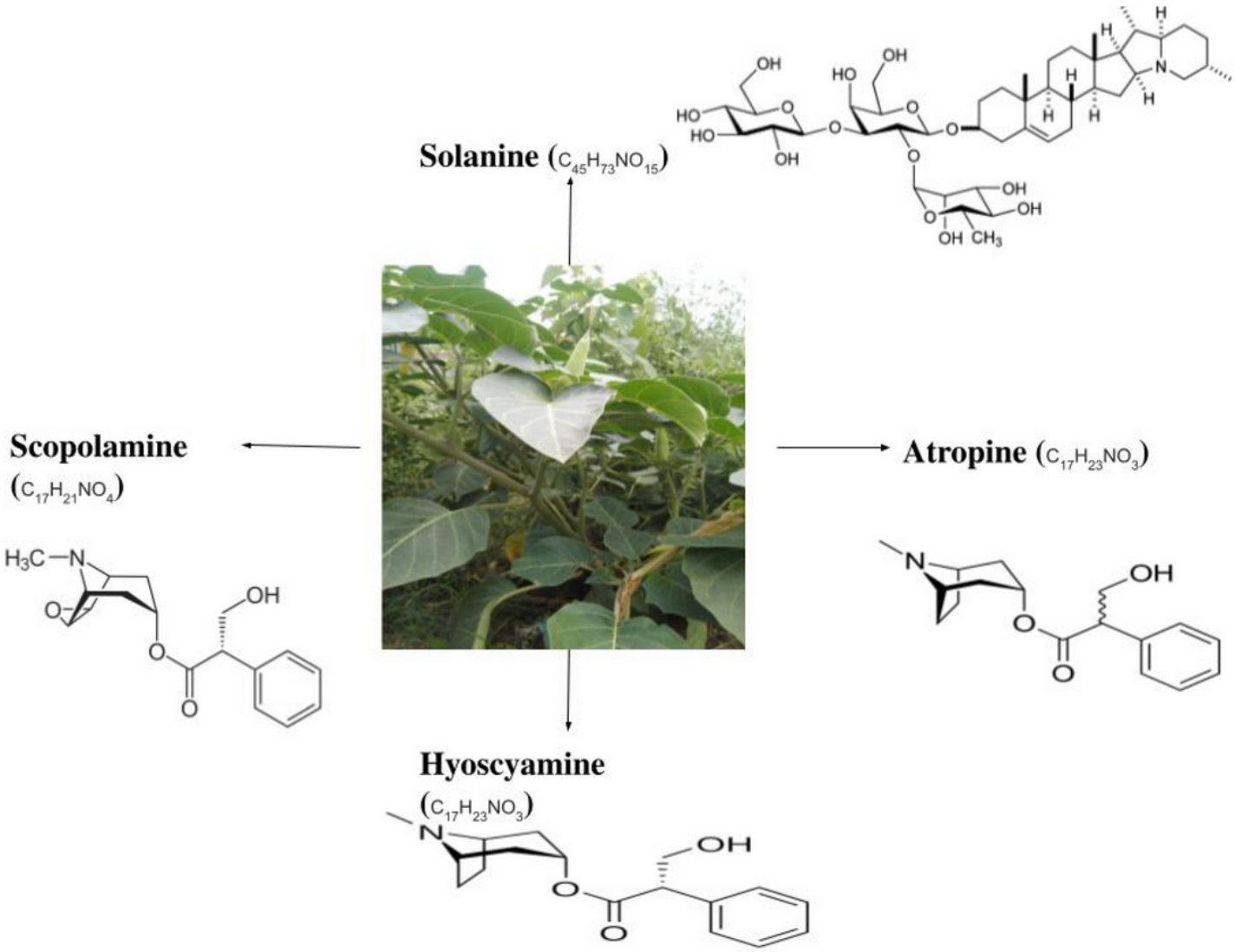

Figure 1. Identified important phytochemicals in *Datura*, as well as their chemical structures [27].

3. Pharmacological Activity of *Datura*

Datura is known to exhibit analgesic, antioxidant, anticancer, and antimicrobial properties. Especially, owing to the potent analgesic activities, *D. metel* acts as an effective painkiller. *D. stramonium* has antifungal activity against *Fusarium mangiferae* and *Fusarium oxysporum*, alkaloids found in *D. stramonium* are potential anticholinergic agents [28]. Atropine and scopolamine are muscarinic antagonists that may be utilized to cure Parkinson's disease and parasympathetic stimulation of the eye, respiratory, urinary, heart, and gastrointestinal tract [29]. They prevent parasympathetic nerve impulses by selectively blocking the binding site of the neurotransmitter acetylcholine to the receptor of nerve cells [30]. In addition, *Datura* has long been utilized as a beneficial therapy for asthma symptoms. Atropine is the active anti-asthmatic agent that triggers paralysis of pulmonary branches of the lungs, removing the spasms responsible for the asthma attacks [31].

The technique of smoking *Datura* leaves through a pipe to alleviate allergies has its origins in the standard ayurvedic medicine in India. *D. stramonium* is utilized recreationally mainly for its anticholinergic consequences

and can be produced by boiling the crushed seeds [13]. However, exposure of the fetus to *D. stramonium* causes a continuous release of acetylcholine, leading to desensitization of nicotinic receptors, resulting in permanent damage to the fetus [3].

3.1. Anti-Inflammatory and Analgesic Activities

The phytochemicals present in *Datura* species are well-known for their anti-inflammatory and analgesic properties due to their ability to suppress the production of chemical mediators responsible for the stimulation of nociceptors and induction of pain or inflammation [32][33]. The ethanolic extract of roots of *D. fastuosa* was found to exhibit anti-inflammatory activity when studied for paw edema induced by carrageenan in rats, with Indomethacin as a standard drug [34][35]. The progress of edema can be explained in different phases; release of histamine and serotonin in the initial phase, edema maintained by substances like kinin in the plateau phase, and prostaglandin release in the edema accelerating phase [34][35]. The root extracts showed considerable activity against inflammation at 200 mg/kg compared to Indomethacin (at 10 mg/kg). Moreover, the aqueous extracts of seeds and leaves possessed significant analgesic effects at 800 and 400 mg/kg dosage, respectively, when experimented on mice using a writhing test (induced by acetic acid) and hot plate reaction [8]. However, the analgesic activity induced by leaves could be potentially decreased by naloxone, while that of seed extract remained unaffected. The aqueous leaf extracts of *D. innoxia* have been evaluated for their anti-inflammatory activity to develop an active herbal pain-relieving drug [36]. The basic mechanism involved in anti-inflammatory and analgesic action is believed to be the cyclooxygenase (COX1 and COX2) inhibition, followed by suppression of prostaglandin-synthesis or probably the narcotic effects of *Datura* species [33][36].

3.2. Antioxidation Activities

The antioxidant activity of *Datura* extracts can also be attributed to the presence of phytochemical compounds, which act as potent free radical scavengers and help prevent cellular damage [37]. Analysis of *Datura* plant extracts for antioxidant characteristics revealed its ability to cure various health disorders, including cancers, since antioxidants are known to inhibit cell damage, the general pathway for cancers, aging, and several other diseases [38]. The antioxidant capacity of leaf extracts in different solvents, estimated by various in vitro methods, including hydroxyl radical scavenging activity, DPPH (2,2-diphenyl-1-picrylhydrazyl) scavenging activity, superoxide radical scavenging activity, β-carotene bleaching activity, and reducing power assay, revealed that chloroform extract of leaves possessed maximum concentration-dependent antioxidant activity [39][40]. The IC_{50} value of methanolic and hydroalcoholic seed extracts of *D. metel* recorded using the DPPH model showed that hydroalcoholic extract possesses slightly higher antioxidant activities (IC_{50} of 25.78 µg/mL) than methanolic seed extract (IC_{50} of 28.34 µg/mL) [7][39].

In the estimation of DPPH free radicals scavenging activities, a positive correlation was observed between the flavonoid and phenolic content of the *D. metel* extracts [8][39]. Maximum DPPH scavenging activity of methanolic seed extracts of *D. stramonium* was found to be 59.50% at a concentration of 60 µg/mL with IC_{50} value of 94.87 µg/mL; similarly, the maximum superoxide radical scavenging activity was 53.17% at a concentration of 60 µg/mL,

while maximum scavenging activity of hydroxyl radical was 57.88% at concentration of 30 µg/mL with IC_{50} value of 39.59 µg/mL [38]. Moreover, the hydromethanolic root extract of *D. stramonium* exhibited a significant amount of correlation with DPPH free radical scavenging activity.

3.3. Antimicrobial Potential of Datura

The antimicrobial activity against pathogenic microbes was evaluated using aqueous and ethanolic extracts of different plant parts of *D. stramonium*, and the results revealed that the ethanolic extracts showed better antimicrobial activity than the aqueous extracts [41][42]. Moreover, the leaf extracts were found to be more effective than stem and root. The branches and leaves of *Datura stramonium* extracted with different organic solvents such as benzene, chloroform, and ethanol exhibited significant antibacterial and antifungal activity when studied against *Enterobacter sp., Micrococcus luteus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus,* and *Klebsiella pneumonia* [8][43]. It was observed from the MBC (minimum bactericidal concentration) values that benzene extracts with the concentration of 3.12 mg/mL inhibited *P. aeruginosa* while the chloroform extracted with the same concentration was effective against *S. aureus*, *P. aeruginosa,* and *M. luteus*. Further, all the *D. stramonium* extracts were effective against various fungal strains such as *Aspergillus fumigatus*, *Aspergillus niger*, and *Saccharomyces cerevisiae* also, with maximum activity against *S. cerevisiae* and minimum antifungal activity against *A. niger* [8]. The methanolic and hydroalcoholic seed extracts of *D. fastuosa* also possessed considerable antimicrobial properties against bacterial (*Bacillus subtilis, Escherichia coli, Staphylococcus aureus*) and fungal (*Aspergillus niger* and *Candida albicans*) strains [8][44]. The methanolic extract acted against *E. coli* effectively with MBC of 25 µg/mL, while the hydroalcoholic extract was more effective against *B. subtilis* with both MBC and MIC (minimum inhibitory concentration) of 25 µg/mL. Methanolic plant extracts of *D. inoxia* also showed antifungal activity, and *Fusarium solani* was found more sensitive than other fungal species. The inhibition against different fungal species varied from 18.29 to 85.36%, where *F. solani* were affected more while *A. niger* showed more resistance [45]. *D. metel* seed oil had antibacterial activity against at least seven bacterial strains with the highest inhibition zone and lowest MIC against *Lactobacillus delbrueckii lactis* (19 mm) and *Pseudomonas aeruginosa* (18 mm), signifying susceptibility of bacterial strains to *D. metel* seed oil. The antibacterial activity exhibited a concentration-dependent response, and the inhibition zone increased with an increase in seed oil concentration [46].

3.4. Anti-Asthmatic and Bronchodilating Effects

Alkaloids found in *D. stramonium,* such as atropine and scopolamine, which possess significant anticholinergic and bronchodilating activities, block the muscarinic receptors (which are important for airways regulation), subsequently dilating bronchial smooth muscles [47][48]. Acetylcholine (the neurotransmitter synthesized and released by cholinergic neurons) leads to the contraction of smooth muscle after interaction with cholinergic muscarinic Acetylcholine (Ach) receptors [49]. The muscarinic receptors associated with the airway and lung tissues are M1, M2, and M3, of which M1 and M3, fully active in asthmatics, are responsible for bronchoconstriction while M2 which suppresses the release of acetylcholine, are less functional in asthmatics [50]. *Datura* administration inhibits M2 function, ultimately leading to the continued release of neurotransmitters. The anticholinergic activity of *D.*

stramonium involves blocking the functions of muscarinic receptors on airway smooth muscles and submucosal gland cells [14]. The anti-asthmatic *D. stramonium* cigarette acts as a potential bronchodilator in asthmatic patients with the mild airway. A substantial decrease in the specific airway resistance (sRaw) was observed after inhaling smoke from the cigarette [8][51]. However, when exposed to the fetus during its use by the mother for asthma, *D. stramonium* releases acetylcholine. It desensitizes nicotinic receptors, resulting in slow or no response to repetitive agonist modulatory effects on the brain's functioning, consequently damaging the fetus [3][13].

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