AN UPDATE ON MORPHOLOGY, MECHANISM, LETHALITY, AND MANAGEMENT OF DHATURA POISONING

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Abstract

Dhatura is a part of the Solanaceae family and belongs to the genus Datura, which is thought to have both poisonous and therapeutic characteristics due to the diverse variety of bioactive ingredients. The Dhatura plant's common names are thorns apple and Jimson Weed, mad apple, and moonflower. Plants are used to cure a variety of human diseases. Alkaloids, sugars, cardiac glycosides, tannins, flavonoids, amino acids, and phenolic substances were identified in the preliminary phytochemical analysis of the Datura plant extract. Additionally, it contains dangerous tropane alkaloids like hyoscyamine, atropine, and scopolamine. Even while some research on D. stramonium has suggested possible pharmacological effects, the toxicity of the organism is still mostly unknown. Additionally, toxic symptoms have been brought on by the regular misuse of D. stramonium for recreational purposes. Therefore, its use's harmful effects and potential hazards must be understood. This paper aims to provide an overview of the plant Datura's, phytochemical makeup, pharmacological properties, toxicological properties, and treatment of Dhatura poisoning.

Keywords: Dhatura, toxic, Alkaloids, toxicological properties.

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INTRODUCTION

Dhatura is a biennial plant that occur wild throughout the nation, particularly in wastelands. It is a tiny, rough Solanaceae family shrub with a foul odor. According to its etymology, the word "Dhatura" comes from the Sanskrit word "Dhatur". The names thorn apple, jimson weed, hell's bell, and devil's trumpet are also used to refer to Dhatura. It is categorized as a brain toxin of the deliriant kind in contemporary medicine. Atropine, hyoscyamine, scopolamine, and other deadly tropane alkaloids found in the plant are what give it its therapeutic and hallucinogenic effects. They are also toxic when consumed in large doses. The plant has been categorized under class E1 of the Drug and Cosmetics Act of 1940[1]. According to Ayurveda, Dhatura is a helpful treatment for several human illnesses, such as dysmenorrhea, neuralgia, edema, wounds, inflammations, fever, and dyspnea. In India, datura poisoning is typical since the seeds are frequently used as a narcotic before robberies, kidnappings, and rapes. It is occasionally referred to as roadside poison. Inappropriate Dhatura dosages hurt the central nervous system, causing symptoms like hallucinations, seizures, memory loss, trouble swallowing, and disorientation. Although Dhatura poisoning seldom results in death, Because this plant can have both therapeutic and toxic effects on people, it must only be used under proper supervision. All plant parts are poisonous, however mature seeds have the largest concentration of alkaloids[11].

DISTRIBUTION

The Datura species are found all over the world. The plant can be found on plains and sandy flats. It's unclear where Datura Stramonium came from. The general name of Jimson weed is derived from the Sanskrit datura and the Hindustani dhatur; it may have Asian origins. Due to Datura's presence across the majority of temperate and subtropical regions of the planet, some authors claim that it is likely to have a Central American origin. It is native to India and is a prolific grower from Kashmir to Sikkim in the Himalayas. It is spread throughout the hills and valleys of Manipur as a wild plant. It is typically grown in Manipur from April to October[34].

Toxic Parts[4]: The root, fruit, seed, flower, leaves, and even the nectar of the plant is poisonous.

Fatal Dose: Approximately 60–100 Datura seeds.

Fatal Dose: 24 hours

Action[5]

- Atropine and hyoscine, which have sympathomimetic or parasympatholytic actions, block the acetylcholine receptor.
- It first accelerates the central nervous system, but later causes CNS depression, especially in the respiratory center.
- It also has a vagolytic effect that stimulates the heart.

Botanical Description[2]

Dhatura is an annual plant and the length of Dhatura plant is up to 150 cm (6 feet) tall and has a pungent odor.

Root: cylindrical, brown, rough-splintered, with lateral branches.

Stem: Cylindrical, dichotomously branched, blackish-purple to dark purple in color, with a very short internode.

Leaf: alternately arranged, with a pointed border, and a dark green color.

Flowers: have bell or trumpet shapes.

Fruit: A globular, soft-spined capsule that contains light-brown seeds.

Seed: flattened, foveate, surface finely pitted, color similar to chili pepper seeds.

Biochemical Composition of Dhatura

Datura generally contains sizeable levels of ash content, moisture, lipids, protein, carbs, and crude fifiber Alkaloids, phenolic compounds, tannins, flavonoids, and cardiac glycosides are additional important phytochemicals discovered in Datura[12]. Additionally, various amino acids have been extracted from the seeds, including alanine, phenylalanine, glutamate, and tyrosine [13]. Along with hyoscyamine and atropine, hyoscine [Scopolamine] is the main tropane alkaloid, with varying concentrations in various plant parts[14]. Hyoscyamine levels in seeds and flowers were found to be 0.426% and 0.43%, respectively, whereas atropine levels in Datura leaves were found to be 0.426%. As the D. metal plant goes through various growth stages, its alkaloid content of scopolamine and atropine gradually increases, reaching a climax when the plant completes its reproductive cycle[15]. In D. stramonium, the highest concentrations of alkaloids were discovered ten weeks after seed germination and progressively decreased as the generative phase of plants began[16]. The alkaloid percentage often changes according to the plant part and growth stage. For instance, alkaloid concentration in leaves reaches its peak during the vegetative phase before rapidly declining during the generative phase[17]. Young plants have substantial amounts of hyoscyamine in their stems and leaves. However, various plant sections in young and adult plants have varying quantities of atropine and scopolamine[18].

Pharmacological Activity of *Datura*

Datura is recognized for having narcotic, anti-inflammatory, anticancer, and antibacterial effects. Particularly because of its powerful analgesic properties, D. metal works well as a pain reliever[19]. Muscarinic antagonists such as atropine and scopolamine may be used to treat parasympathetic stimulation of the ocular, respiratory, urinary, cardiac, and gastrointestinal tracts[20]. They stop parasympathetic nerve impulses by limiting the neurotransmitter acetylcholine's ability to connect to the receptor on nerve cells [21]. The primary anti-asthmatic medication, atropine, causes the pulmonary branches of the lungs to paralyze, eliminating the lung spasms that cause asthma attacks[22]. The practice of inhaling Datura leaves through a pipe to treat allergies has its roots in Indian traditional ayurveda treatment. Because of its anticholinergic effects, D. stramonium is primarily used recreationally[23]. It is made by boiling crushed seeds. But when the fetus is exposed to D. stramonium, acetylcholine is released continuously, desensitizing nicotinic receptors and causing lifelong harm to the fetus[24].

Phytochemistry of Dhatura

The entire Datura plant contains a wide variety of alkaloids, gradually growing with the aging process [31]. Numerous withanolides, several tropane alkaloids, and numerous trigloyl esters of tropine and pseudo tropine are the major components of the datura plant. These include hyoscyamine, hyoscine, littorine, acetoxytropine, valtropine, fastusine, and fastusinine. Numerous Datura species also contain calystegines and nortropane alkaloids with glycosidase inhibitory action [32]. Atropine is present in greater concentrations in the root than in the other components. When compared to the plant's root, the aerial sections typically collected higher proportions of scopolamine and smaller proportions of atropine[31].

Pharmacognosy

Datura stramonium L. is a plant that is extensively grown and is well known for having tremendous pharmacological potential as well as great utility and employment in traditional medicine. Due to its analgesic and antitiasmic properties, it contains alkaloids, tannins, carbohydrates, and proteins[6]. The treatment of asthma using leaves[61]. In tests using a hot plate and formalin, datura stramonium seed extract significantly reduced both acute and chronic pain. This effect is most likely caused by an alkaloid that interacts with the opioid system[62]. The entire plant is dangerous, but the foliage and seeds are in particular. The anticholinergic syndrome is brought on by the inhibition of both central and peripheral muscarinic neurotrans-mission. Some of the patient's symptoms include dryness of the skin and mucosa, flushing, blurred vision, and light sensitivity, urine retention, and myoclonic jerks. Other symptoms that may be present include tremors, poor short-term memory, disorganized behavior, hallucinations, mental illness, coma, respiratory failure, and circulatory collapse.

Datura stramonium leaf extract has antimicrobial properties. Excellent antifungal activity was reported in the leaf extract of Datura stramonium L. When a mother consumes this plant to treat her asthma throughout pregnancy, the fetus will be exposed to it and this will result in a continuous release of Ach, which will desensitize nicotinic receptors and may ultimately cause irreparable damage to the fetus. Jimsonweed seeds had three main effects: reduced body weight growth, serum alkaline phosphatase, and blood urea nitrogen[63] . All plant components are poisonous, however mature seeds have the largest concentration of alkaloids[64]. They function at the peripheral and central muscarinic receptor sites as a competitive antagonist of acetylcholine[65]. As a result of poisoning, many organs with parasympathetic innervation become paralyzed[66]. Cytotoxicity and oxidative stress were brought on by datura aqueous leaf extract in human cancer cell lines. Although mortality is rare, severe toxicity has been linked to unconsciousness and seizures[67] .

Compounds obtained from Datura metel

There are a lot of important secondary metabolites that could be found in plants. It may be possible to discover bioactive substitutes for synthetic chemicals by studying useful secondary metabolites that have been identified from medicinal plants.

Several alkaloids from Datura species have been reported, including hyoscine, hyoscyamine, meteloidine, scopolamine, tigloidine, tropine, withametelline, and datumetine, among others[69]. Some of these alkaloids have been used in medicine.

Traditional Uses[4]

Several disorders can be treated with Datura, including breathing problems, fever, coughing, inflammations, swelling, headaches, madness, fatigue, hyperacidity, kidney failure, calculi, and menstrual cramps. The entire plant has therapeutic use, but the roots are particularly useful for treating rabid dog attacks. The leaf is helpful for piles and

inflammations. Lice and skin conditions are treated externally using leaf juice. It is also used to treat dandruff and lice, as well as for tooth and earaches, and stomach issues, and as an aphrodisiac.

Biological Function

Insecticide Action

Many authors have researched the insecticidal and repellant qualities of the Datura species.. In contact and spray application trials, It has been demonstrated that D. metel leaf extracts have insecticidal and repellent properties for a number of insect species. Organic extracts of D. metel revealed EC50 values of 12,000 ppm for grasshoppers and 11,600 ppm for red ants[33]. Pesticide action has been evaluated in non-polar extracts from adult individuals and larvae of different insects, both by touch and by feeding, in the case of D. stramonium[35]. When evaluated on two mosquito species, D. stramonium aqueous root extract was found to have a larvicidal efficiency of between 50% and 100% 24 hours after treatment at a 100% concentration of the extracts[38]. It has been demonstrated that various concentrations of an aqueous extract of D. stramonium leaves and seeds are efficient against flea beetles, a typical maize pest[36] . The enzymes acetylcholinesterase, carboxylesterase, acid phosphatases, and alkaline phosphatases (ALP) were also discovered to be inhibited in test subjects who survived the toxicity when Datura inoxia acetone extracts were tested for toxicity against Tribolium castaneum, Trogoderma granarium, and Sitophilus granaries[36].

Herbicide Action

When evaluated on two mosquito species, D. stramonium aqueous root extract was found to have a larvicidal efficiency of between 50% and 100% 24 hours after treatment at a 100% concentration of the extracts[38]. Flea beetles, a frequent pest of maize, can be defeated using various concentrations of an aqueous extract of D. stramonium leaves and seeds[36]. Datura inoxia acetone extracts were also discovered to inhibit the enzymes acetylcholinesterase, carboxylesterase, acid phosphatases, and alkaline phosphatases (ALP) in test subjects who survived the toxicity against Tribolium castaneum, Trogoderma granarium, and Sitophilus granarius[36].

Acaricide Activity

The methanolic preparations of D. stramonium leaves and seeds killed adult Tetranychus urticae Koch (spider mites) in 98% and 25% of instances, respectively. For leaf extracts but not seed extracts, there was a direct link between concentration and death rate[39]. In adult mite immersion tests, an ethanolic preparation made from Datura stramonium leaves resulted in 20% mortality against Rhipicephalus microplus (Asian blue tick)[40]. The D. stramonium methanolic extract dramatically decreased Rhipicephalus (Boophilus) microplus oviposition by 77%, according to in vitro research[41] .

Antifungal Activity

D. discolor, D. metel, and D. stramonium, three species of the genus, were examined for antifungal potential. In order to inhibit the growth of Aspergillus flavus, Aspergillus niger, Penicillium chrysogenum, Penicillium expansum, Fusarium moniliforme, and Fusarium poae, ethanolic and methanolic extracts from D. discolor stems and leaves were mixed with culture medium[42] . Aqueous and methanolic extracts of the leaves of D. metel suppressed the growth of Rhizoctonia solani. The methanolic extract of D. metel was up to 35% more toxic than that of the other 15 species under investigation, inhibiting mycelial growth and being utilized in the synthesis of sclerotium in both agriculture and medicine as a herbicide, an acaricide, and an insecticide[43]. A. fumigatus, A. niger, and A. flavus were all susceptible to the antifungal effects of extracts of D. metel in different solvents , with the chloroform fraction having the lowest inhibitory concentration (MIC) of 625.0 g/mL[43]. To evaluate the antifungal effects of methanol extracts from the leaves, seeds, stems, and roots of D. inoxia, A. flavus, A. niger, Alternaria solani, Fusarium solani, and Helianthus sporium were utilized[44]. Aqueous extracts of D. stramonium demonstrated the highest antifungal activity against Candida albicans (74%), whereas methanol and chloroform extracts had good inhibitory activities (69% and 65%, respectively)[45].

Antibacterial Activity

Five harmful bacteria were evaluated using D. stramonium leaf and fruit extracts with varied polarity solvents, and all tested pathogens showed growth inhibition at various doses when the extracts of methanol and chloroform from both leaves and fruits were used. All separated fruit components effectively slowed the development of Klebsiella pneumonia and Pseudomonas aeruginosa. The highest level of growth inhibition (77%) against K. pneumonia was seen in the chloroform extract of leaves[45]. The antibiotic activity of methanolic extracts (80%) of Datura inoxia against Bacillus subtilis, Staphylococcus aureus, and Escherichia coli was assessed using the paper disc diffusion method with ampicillin as a positive control. The outcomes demonstrated

action against all bacteria at the highest concentration of the extracts, except E. coli (2.5 g/mL)[46]. However, methanolic, ethanolic, and aqueous extracts of D. stramonium showed antibacterial efficacy against gram-positive and gram-negative bacteria in the paper disc diffusion method. The growth of bacteria in P. aeruginosa, K. pneumonia, and E. coli was suppressed by an ethanolic extract of leaves at a minimum inhibitory concentration of 25% w/v[47]. The methanolic leaf extract demonstrated antibacterial activity against both gram-positive and gram-negative bacteria at concentrations of 2.5, 1.25, and 0.75 mg/mL, including Staphylococcus haemolyticus, S. aureus, Shigella dysenteriae, and Bacillus cereus[47, 71].

Anti-Oxidant Activity

The antioxidant activity of D. metal stem, root, and leaf aqueous extracts ranged from 23.8 to 49.3% [48]. For the radicals, DPPH, superoxide, and radical cation ABTS, the IC50 values for the methanolic extract of D. stramonium were 35.3, 10.5, and 49.36 g/mL, respectively [49]. The antioxidant capacity, phenolic component, flavonoid concentrations, and increased antioxidant capacity (221.25 1.06 mg EPA/g) were compared to D. metel and found to be considerably higher in D. innoxia [52]. In a DPPH purification test against various solvents and plant parts, D. metel leaf methanol extract displayed the highest antioxidant capability since it has the highest concentrations of flavonoids and tannins among phenolic compounds [51,72].

Hypoglycemic Activity

Adding pulverized D. metal seeds to the diet of diabetic rats caused a significant drop in blood glucose levels after 8 hours, which was used to explore the hypoglycemic action of the seeds [52]. Despite a hydroethanolic extract of D. stramonium root was examined in diabetic mice and found to have no discernible hypoglycemic effect, diabetic mice that were orally loaded with the extract at relatively high doses (100, 200, and 400 mg/kg) experienced noticeably lower blood glucose levels [53]. D. inoxia's methanolic leaf extract demonst-rated antihyperglycemic effects on the enzymes -glucosidase, -amylase, lipase, and urease [54].

Cytotoxic Activity

When D. metel flower ethanolic extract was examined on cancer cell lines, it was discovered that the A549 (tongue), BGC-823 (gastric), and K562 (leukaemia) cell lines were all cytotoxic [57]. Similar to this, Datura stramonium seed methanolic extracts were discovered to have 66.84 percent cytotoxicity against MCF7 (breast cancer) cells at a concentration of 599 g/mL [49]. These results were consistent with those of Gupta et al. [56], who examined the cytotoxic effects of methanolic extracts of D. stramonium leaves on A549 and MCF7 cells and discovered significant immunological activation [57]. With an IC50 of 93.73 g/mL, the methanolic leaf extract of D. innoxia indicated a potentially lethal effect on MCF-7 human breast cancer cell lines [57].

When tested against human colon cancer cells, HCT 15, Rhinoxia B, a phytosterol isolated from D. inoxia leaf extracts, was reported to have antiproliferative action with an IC50 of 4 M [56].

Other Activity

Due to the presence of tropane alkaloids, datura has aphrodisiac, anaesthetic, analgesic, sedative-hypnotic, and anticholinergic (mydriatic, antispasmodic) properties. The activities of tropane alkaloids are mediated by a competitive muscarinic receptor antagonist. On the other hand, a few tropane alkaloids and derivatives have shown varying affinities to the nicotinic acetylcholine receptor, albeit to a smaller degree, and are occasionally partial agonists [58]. Because tropane alkaloids have various degrees of affinity for monoaminergic transporters, their effects on the nervous system are likewise related to the function of monoaminergic neurotransmitters [59].

Clinical (Toxic) Features[7]

The nine Ds represent the main symptoms of Dhatura poisoning.

1. Mouth dryness, thirst
2. Difficulty in swallowing
3. Wide-open pupils
4. Double Vision
5. Hyperpyrexia and dry hot skin.
6. Ataxic drunken gait, hyperthermia, and convulsions.
7. Delirium accompanied by agitation, forgetfulness, incoherence, and hallucinations.
8. Distension of the bladder, urinary retention, and dysuria
9. Rapid heart beat, arrhythmias, coma, and respiratory depression before death.

Hyperthermia and sinus tachycardia are frequent symptoms. Other frequent results include mydriasis and loss of near-vision accommodation. Eye contact can significantly enlarge the pupils and affect other systemic aspects. This might be done by coming into contact with dried and ground materials handled alongside crops by combine harvesters or through plant sap after handling the plants directly (corn-pickers eye)[25]. In one instance, accidental ocular instillation of Datura

plant sap led to the development of unilateral mydriasis in seven patients. Additionally, three of the patients had ipsilateral cycloplegia. Within a week of exposure, all individuals with these signs recovered [26].

Datura poisoning is frequently accompanied by symptoms including dry mouth, impaired GI motility, and loss of bowel noises. Swallowing becomes challenging, and speech may be difficult to understand. It may be necessary to catheterize if there is frequent urinary retention and bladder distention[27]. Some cases of hypertension have been documented. Following the consumption of Datura seeds, tachypnea with or without breathing difficulties has been seen[28]. In one instance, a young boy who consumed Datura seeds experienced acute respiratory distress syndrome that led to respiratory failure, and he eventually passed away from refractory hypoxemia [29]. Ataxia, psychosis, agitation, hostility, visual and auditory hallucinations, speech abnormalities, convulsions, myoclonus, and hypertonia are a few of the central nervous system (CNS) consequences [30].

Treatment of Dhatura Poisoning[8]

Monitoring of pulse, respiration, and body temperature, Hysostigmine 1-4 mg i.v./i.m., KMnO4 or 4–5% tannic acid for stomach washing (repeated, if necessary at intervals of 1-2 hrs.) Pilocarpine 5 mg subcutaneous, and Neostigmine 2.5 mg i.v. every three hours.

Ayurvedic Antidotes[9]: Cow milk with sugar, one pal's worth of juice from the Vrintaka fruit, Karpasasthi Pushpa Kwath, Nimbu Swarasa, and Jirka.

Postmortem Finding[10]: The enlarged pupil is a symptom of asphyxia general poisoning symptoms, The stomach, and small intestines may contain seeds or fragments. It doesn't rot and can even be found in a decomposing body.

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