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PHYTOCHEMICAL AND PHARMACOLOGICAL STATUS OF *DATURA FASTUOSA* LINN

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ABSTRACT
Medicinal plants constitute an effective source of traditional and modern medicines. Traditional system of medicine enlightened the importance of *Datura fastuosa* Linn (Solanaceae) to have a great medicinal value. The roots, dried leaves and flowering tops have been used in India for their narcotic and antispasmodic properties in the treatment of numerous ailments and conditions. The juice of fresh leaves, or a poultice of them, is used to relieve painful swellings earache. The seeds and root possess antidiarrhoeal, antipyretic properties and are used to treat insanity and fever. The present paper enlightens the chemical profile and pharmacological potential of D. *fastuosa* and encourages the traditional use to find new therapeutic effects, but under the guidance of a qualified practitioner.
KEYWORDS*: D. fastuosa,* chemical constituents, traditional uses, pharmacological potential.

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INTRODUCTION

Datura fastuosa is also known as devil's trumpet, angel's trumpet, thorn apple, Indian apple,*Datura metel*, purple datura, garden datura, horn-of-plenty, David bush, concombre zombi, cornicopio, trompette du jugement, and pomme epineuse. It is a shrub or woody herb upto 2 m in height that is often grown as an annual in temperate zones.[1] The roots, dried leaves and flowering tops have been used in India for their narcotic and antispasmotic properties in the treatment of numerous ailments and conditions. They are used in a formulations of a number of important compounds such as *Kanakasavam, tailum, Dhurdhurapatradi* coconut oil and *Mrtasanjivini.* In Ayurveda, the plant is considered bitter, acrid, astringent, germicidal, anodyne, antiseptic, antiphlogistic, narcotic and sedative. The warmed leaves are used externally to expel guinea worms in Rajasthan. The young, fresh leaves are used interally in the treatment of amenorrhoea among tribal women in central Orissa. The juice of fresh leaves, or a poultice of them, is used to relieve painfull swellings earache. Among the tribal inhabitants of Prakasam District in southern Andhra Pradesh, a paste of the leaves mixed with lime is used as external application to treat scabies. Pills made from the leaves, pounded with black pepper and garlic, are given orally to treat fever. In Ayurveda, the seeds are considered heating, tonic, febrifuge, anthelmintic, alexiteric and emetic. They are used to treat leucoderma, skin diseases, ulcers, bronchitis, jaundice and piles. In Rajasthan the seeds are reported used to treat leprosy. The seeds and root possess antidiarrhoeal, antipyretic properties and are used to treat insanity and fever. The root powder is reportedly given for 15 days after menstruation to induce sterility among Gond women in Utter Pradesh.[2]

Synonym: *D. metel* L.

Others names : English : White Thorn Apple, Hindi : Dhatura, Sanskrit : Kanaka, Gujrati : Dhanturo, Kannada : Ummatti, Madagunaki, Dathura, Malayalam : Umman, Ummatt, Ummattu, Marathi : Dhotra,Oriya : Dudura, Punjabi : Dhatura, Punjabi : Dhatura, Tamil : Umattai,Telugu : Tella-ummettha, Assamese : Dhatura, Bengali : Dhatura.[3]

Scientific classification

Kingdom:	Plantae
Division:	Magnoliophyta
Sub-division:	Angiosperms
Class:	Magnoliopsida
Sub-class:	Asterids
Order:	Solanales
Family:	Solanaceae
Genus:	*Datura*
Species:	*fastuosa*

Geographical distribution

D.fastuosa grows in waste lands, along the roadside and railway lines, and in scrub-jungles throughout the tropical parts of India, naturally in disturbed areas such as eroded sites, old fields, vacant lots, overgrazed pastures and rangeland. Apparently, disturbance and reduced competition are required for the plant to become established and grow. A wide variety of well-drained soils on both igneous and sedimentary parent materials are suitable. In Puerto Rico, the species grow naturally in areas that receive from 750 to about 1000 mm of mean annual precipitation from near sea level to about 400 m. *D.fastuosa* flowers and fruits throughout the year in some environments, but in India principally from July to September,[4] and from September through November in Nicaragua.[5]

Morphological Features

It is a spreading herb sometimes found as shrub. Leaves are ovate-lanceolate or broadly ovate, acute or acuminate, unequal at the base and often cordate, entire or dentate, sub-glabrous or with greyish tomentum, generally glandular in a long petiole of up to 10 cm in length. Flowers occur in duplicate or triplicate. Calyx in *D.fastuosa* is inflated towards the middle, persistent and reflexes in fruit. Corolla is about twice as long as the calyx, white or tinged with green, pubescent outside and with the 10 toothed limb. Capsule is globose, tuberculate or muricate, borne on a short thick peduncle. It dehisces irregularly exposing a mass of closely packed, light brown, flat seeds which nearly fill the interior. [6] The alternate leaves have petioles approximately 3 to 7 cm long and ovate to elliptic blades which are 6 to 15 cm long with sinuate to irregularly toothed edges and 1.25 to 3 mm wide, narrowly linear or lanceolate, finely acute more or less glaucous, soft, smooth, usually conspicuously distichous in the barren shoots and at the base of the stems; sheath light, glabrous or sometimes bearded, ligule a very fine ciliate rim. The yellowish-brown seeds are flat, kidney-shaped, about 5 mm long, and have a small fleshy aril. *D. fastuosa* is a shrub-like herb with large flowers. The plant can reach measuring 1.5 m in large, alternate, dark green leaves and sometimes with purple stem. The fruit is in the form of a spiny capsule. The foliage has trumpet-shaped, flowers are hermaphrodite (have both male and female organs) and are pollinated by insects.[1,5]

Microscopic Description

Root Shows 4 to 7 layers of thin-walled, rectangular cork cells, secondary cortex composed of 3 to 4 layers, thin-walled, parenchymatous cells, secondary phloem composed of usual elements, traversed by phloem rays, secondary xylem composed of usual elements. Sandy microsphenoidal crystal of calcium oxalate scattered in the secondary cortex and phloem parenchyma also present.

Stem Shows a single layered, epidermis covered by striated, thick cuticle having a few unicellular trichomes, followed by 2 or 3 layered, ruptured, rectangular cork cells. Secondary cortex consisting of 4 to 7 layered, collenchymatous and 2 to 5 layered parenchymatous cells. Endodermis contains starch grains, secondary phloem composed of sieve elements and parenchyma but fibres not present. Secondary xylem composed of vessels, tracheids, fibres and parenchyma. Starch grains oval to rounded, simple, measuring 3 to 7 µ in diameter, present in secondary cortex and phloem parenchyma.

In leaves, Petiole shows plano-convex outline, cuticularised single layered epidermis, followed by cortex composed of 7 or 8 rows of round to polygonal, thick-walled, collenchymas cells and 2 or 3 rows of thin-walled, round to polygonal, parenchyma cells. Vascular bundles prismatic crystals of calcium oxalate present in cortex and pith region. Midrib shows similar structure to that of petiole, collenchyma well developed in basal region and poorly in middle and upper region. Lamina shows cuticularised single layered epidermal cells bearing both glandular and non-glandular trichomes on both surfaces. mesophyll differentiated into palisade 30 parenchyma of single layer and spongy parenchyma of 6 to 8 layers,stomata anisocytic,present on both surfaces; stomatal index 16 to 17 on upper surface, 17 to 23 on lower surface; palisade ratio 5 to 6; vein islet number 19 to 22 per sq. mm.

Seed Shows an outline with bulges at 3 places, single layered epidermis with elongated cells; seed coat consists of thick-walled, lignified, sclerenchymatous cells forming club-shaped structure, followed by 3-5 layered more or less tangentially elongated, thin-walled, parenchymatous cells; endosperm encloses more or less curved embryo composed of polygonal, thin-walled, parenchymatous cells, filled with aleurone grains and abundant oil globules. Powder Brown and oily; shows fragments of testa of groups of thick-walled, light brown sclerenchymatous cells; polygonal, thin-walled parenchymatous cells containing oil globules and aleurone grains.[3]

Traditional Uses

D. fastuosa is used as sedative, antispasmodic and mydriatic agents. The whole plant, but especially the leaves and seed, have anaesthetic, hallucinogenic, antiasthmatic, antispasmodic, antitussive, bronchodilator, anodyne, hypnotic and mydriatic effects. In India, the plant is used in the treatment of epilepsy, hysteria, insanity, heart diseases, and for fever, diarrhea and skin

diseases. A poultice of the crushed leaves is used to relieve pain. In China, the plant is used in the treatment of asthma. In Vietnam, the dried flowers and leaves are cut into small chips and used in antiasthmatic cigarettes. About 3 to 5 g of the flower extract can be used as an anaesthetic through oral consumption which produces general anaesthesia within 5 minutes which lasted for about 5 to 6 hours. The flower of the *D. fastuosa* is used in the treatment of pain, chronic bronchitis and asthma It is also used in the treatment of burns.[7,8,9]

Chemical Constituents

The plant mainly contains alkaloids hyoscyamine, hyoscine and atropine. The total alkaloid content of the leaves is 0.426%, mainly atropine. The seeds contain 0.426% alkaloids, mainly hyoscyamine. The roots contain 0.35% hyoscyamine.The whole plant of *D.fastuosa* contains scopolamine (hyoscine) and atropine that increases gradually with the progress of developmental growth, and are most pronounced when the plant is at the end of its reproductive stage. The scopolamine accumulation is highest in the root after 16 weeks. The root contains higher amount of atropine compared to the other parts. The aerial parts usually accumulates relatively higher amounts of scopolamine and relatively lower amounts of atropine as compared with the root of the plant.[10]

A colourless crystalline constituent, daturilin has been obtained from the acid-insoluble fraction of the alcoholic extract of *D. fastuosa* leaves. This compound has been identified as l-oxo-21,24*S*-epoxy-(20*S*,22*S*-witha-2,5,25-trienolide.[11] Three withanolide compounds recognized as withametelin C, D, and E. were discovered from the leaves of *D. fastuosa*.[12] The cultured callus of *D. fastuosa* was found to contain cholesterol and 5α-pregnane3β,20β-diol. It also demonstrated the presence of C28 sterol 3β,24ξ-dihydroxy-ergosta-5,25-dienolide and the withanolide 12-deoxywithastramonolide in *in vitro* propagated shoots of *D. metel.*[13] The three new withanolide (22-hydroxyergostan-26-oic acid -lactone) compounds named baimantuoluoline A, B, and C and the two known withanolides withafastuosin E and withametelin C were isolated from the water soluble fraction exhibiting activity for psoriasis from the flower of *D. fastuosa*. The three new structures were determined as (5 ,6 ,7 ,12 ,15 ,22*R*)-6,7-epoxy-5,12,15-trihydroxy-1-oxowitha-2,24-dienolide (baimantuoluoline A), (5 ,6 ,15 ,22*R*)- 5,6,15,21-tetrahydroxy-1-oxowith-24-enolide (baimantuoluoline B), and (5 ,6 ,12 ,22*R*)-5,6,12,21-tetrahydroxy-27-methoxy-1-oxowitha-2,24-dienolide(baimantuoluolineC).[14,15] A new withanolide, secowithametelin, has been isolated from the leaves of *D. fastuosa* and its structure was determined as (20*R*,22*R*)-1-oxo-21-hydroxy-27-methoxy-witha-2,5,24-trienolide on the basis of chemical and detailed spectral analysis.[16]

A pyrrole derivative was isolated from the chloroform extract of *D.fastuosa* leaves and characterized as 2'-(3,4-dimethyl-2,5-dihydro-1*H*pyrrol-2-yl)-1' methylethyl pentanoate.[17] Also three new withanolide glycosides named daturametelins H, I, J, were isolated from the methanolic extract of the aerial parts of *D.fastuosa.* The methanolic extract also contained two new compound named as daturataturin A and 7,27-dihydroxy-1-oxowitha-2,5,24-trienolide.[18] About ten new withanolides namely withametelins I, J, K, L, M, N, O, P, 12*β*-hydroxy-1,10-*seco*-withametelin B and 1,10-*seco*-withametelin B, together with seven known withanolides were isolated from methanolic extract of the flowers of *D. fastuosa.* The structures of these 10 new withanolides compounds were elucidated by means of spectroscopic methods, and the absolute stereochemistry of withametelins I was confirmed by single-crystal X-ray analysis.[19] An antibacterial agent 5^1, 7^1 dimethyl 6^1–hydroxy 3^1, phenyl 3 a - amine b - yne sitosterol 1 has been found from *D.*fastuosa leaves. The structure of 1 was established using ^{13}C, ^{1}H NMR, IR and MS spectra. Compound 1 showed antibacterial activity against *Staphylococcus aureus, Pseudomonas aeruginosa, Proteus mirabis, Solmonella typhi, Bacillus subtilis* and *Klebsiella pneumonia* but could not inhibit *Escherichia coli*.[20]

PHARMACOLOGICAL POTENTIAL

Hypoglycemic activity

The seeds of *D. fastuosa* were evaluated for hypoglycemic and antihyperglycemic activities in normal wistar strain albino rats against diabetic rats and results were compared with gliclazide (0.56 mg/kg). A dose-dependent hypoglycemia was observed in animals treated with *D. fastuosa* seed powder. A significant reduction in blood glucose of 22.35, 31.89 and 34.26 % was observed with doses of 25, 50 and 5 mg/kg body weight, respectively. The dose dependent antihyperglycemic activity was also observed with *D. fastuosa* in alloxan-induced diabetic rats.. The finding results showed that *D. fastuosa* seed powder possessed blood glucose lowering effect in normol glycemic and in alloxan-induced hyperglycemic rats. Thus, the folk usage of the seeds of *D. fastuosa* for controlling diabetes may be validated by this study and the seeds offer promise for the development of potent phytomedicine for diabetes.[21]

Xanthine oxidase inhibitory activity

D. fastuosa is being traditionally used for the treatment of gout and related symptoms by the indigenous people of India. The xanthine oxidase inhibitory activity was

evaluated for *D. fastuosa.* More than 50% xanthine oxidase inhibitory activity (*in vitro*) was seen in the methanolic extracts of *D. fastuosa* when compared with the standard antigout drug, allopurinol, and showed 93.21% inhibition at 100 µg/ml concentration with an IC50 value of 6.75µg/mL.The aqueous and hydro alcoholic extracts of *D. fastuosa* did not produce significant activity up to 100 µg/ml concentrations. In general, the methanolic extract was found to be more active compared to the aqueous and hydro alcoholic extracts. *D. fastuosa* was found to be safe up to dosage of 2000 mg/kg body weight with no symptoms of toxicity or mortality. The methanolic extract was also screened for *in vivo* hypouricaemic activity against potassium oxonate-induced hyperuricaemia in mice, but not showed significant activity compared to the methanolic extract of *Coccinia grandis* and *Vitex negundo.*[22]

Antifungal activity

The antifungal activity of *D. fastuosa* using pathogenic species of *Aspergillus* was investigated in the hexane, chloroform, acetone and methanolic fractions of *D. fastuosa*. The chloroform fraction was found to have antifungal activity compared to the other fractions. The minimum inhibitory concentration (MIC) of the chloroform fraction of *D. fastuosa*. was 625.0 mg/mL against all the three species of *Aspergillus*, i.e. *A. fumigatus, A. flavus* and *A. niger* , using the microbroth dilution and percent spore germination inhibition assays. The MIC by disc diffusion assay was found to be 12.5 mg/disc. Results showed that the chloroform fraction of *D. fastuosa* was 9.2 times less active than amphotericin B (a standard drug for aspergillosis treatment). In brief, constituents in the chloroform extracts of *D. fastuosa* showed potential for development into better drugs against pathogenic fungi.[23]

The phytochemical investigation of the chloroform extract of the leaves of *D. fastuosa* led to the isolation of a new pyrrole derivative, which was characterized as 2'-(3,4-dimethyl-2,5-dihydro-1*H*pyrrol-2-yl)-1'-methylethyl pentanoate. This compound was found to be active against all the species tested; *Candida albicans, Candida tropicalis, Aspergillus fumigatus, Aspergillus flavus* and *Aspergillus niger*. The MIC of the compound against the various fungal species by microbroth dilution assay ranged from 21.87 to 43.75 µg/mL. Since the compound showed 90% of growth inhibitions (MIC_{90}) *D. fastuosa* leaves can be explored further to develop new antimycotic drugs.[17]

In vitro efficacy of aqueous and methanolic extracts of *D.fastuosa* was evaluated against *Ascochyta rabiei,* (the causal agent of chickpea blight) and the sensitivity of colony growth was studied in terms of inhibition zone. The inhibitory potential of all the extracts was found to be greatest at lower concentration. The aqueous and methanol extracts of *D. fastuosa* shoot caused 21-34% and 20-40% reduction in growth of *Ascochyta rabiei* whereas the root extracts proved less effective as they caused 15-25% and 11-29% reduction in growth of *A. rabiei*, respectively. [24]

Bioactive lipids as free radical scavengering in *D. fastuosa*

The fatty acids and fat-soluble bioactive of the *D. fastuosa* seeds were analyse using gas-liquid chromatography (GLC) and normal-phase high performance liquid chromatography (HPLC). The major fatty acid was linoleic acid followed by oleic, palmitic and stearic acids. The crude n-hexane extract of *D. fastuosa* and *D. innoxia* was characterized by a relatively high amount of phytosterols. The total phytosterols content was recorded at a higher level in *D. innoxia* followed by *D. fastuosa* . The next major components were stigmasterol, β-sitosterol, lanosterol,5-avenasterol and sitostanol. In this extract, γ-tocopherol was the major component present accounting for more than 80% of total tocopherols detected. *D. fastuosa* seeds contain a considerable amount of oil and maybe a good source of essential fatty acids and lipid-soluble bioactives. The presence of these constituents were responsible for antioxidant potential of *D. fastuosa.* [25]

Antiproliferative activity

The five compounds isolated from the the methanolic extract of the aerial parts of *D. fastuosa* were tested for their antiproliferative activity towards the human colorectal carcinoma (HCT-116) cell line. The compounds were withanolide glycosides named daturametelins H, I, J, daturataturin A and 7,27-dihydroxy-1-oxowitha-2,5,24-trienolide. Only the nonglycosidic compound (7,27-dihydroxy-1-oxowitha-2,5,24-trienolide) exhibited the highest antiproliferative activity in HCT-116 cells, with an IC_{50} value of 3.2±0.2 µM. [18]

Effect on CNS

D. fastuosa leaf extract contains important chemical ingredients that can be used to make viable pharmaceutical products with different biological activities on the central nervous system (CNS). The dose most tolerable is 50 ppm so that doses exceeding 100 ppm may be deleterious and may produce side effects. As such local unprescribed use should be avoided since high dose is hallucinogenic and may cause damage to the central nervous system. [26]

Herbicidal activity

D.fastuosa has been evaluated for herbicidal activity against the noxious weed parthenium (*Parthenium*

hysterophorus L.).The effect of aqueous, methanol and *n*-hexane shoot and root extracts of 5, 10, 15 and 20% w/v (on a fresh weight basis) concentration of *D. fastuosa* were tested against the germination and seedling growth of *P.hysterophorus*. Both aqueous and methanol extracts markedly suppressed the germination and seedling growth of *P.hysterophorus*. [27]

Cholinesterase inhibitory activity

D. fastuosa leaf extract, known to possess scopolamine, a tropane alkaloid, as its main constituent, was found to inhibit rat intestinal cholinesterase *in vitro*. *D. fastuosa* root extract was found to activate cholinesterase enzyme activity at optimal or higher substrate concentrations. With root and leaf extract together, the cholinesterase activity level at higher concentrations of substrate, was elevated compared with the inhibitory effect of *D. fastuosa* leaf extract alone, suggesting a potentiating action of *D. fastuosa* root extract on cholinesterase. [28]

Antispasmodic effects

The effect of *D. fastuosa* leaf and root extracts, scopolamine and acetylcholine was studied on isolated smooth muscle preparations. *D.fastuosa* extract and scopolamine showed antispasmodic effects, whereas root extract and acetylcholine caused contracture in isolated rat uterus and rectum whole muscle. The findings suggested the presence of a spasmogenic factor in the root extract of *D.fastuosa*[29].

Antimicrobial activity

Antimicrobial activity of ethyl acetate and methanol extracts of *D. fastuosa* was investigated by agar disc and well-diffusion method against HIV associated opportunistic infections causing bacterial pathogens. The plant extracts showed better inhibitory activity against the *Pseudomonas aeruginosa, Klebsiella pneumonia, Escherichia coli, Staphylococcus aureus* and *Salmonella typhi*.[30] The compound isolated from *D.* fastuosa leaves showed antibacterial activity against *Staphylococcus aureus, Pseudomonas aeruginosa, Proteus mirabis, Salmonella typhi, Bacillus subtilis* and *Klebsiella pneumonia* but could not inhibit *Escherichia coli*.[20]

Toxicities

All parts of *D. fastuosa* are poisonous. The plant is very poisonous, even in small dose which is due to its toxic tropane alkaloid. A review on traditional Chinese herbal medicines and anaesthesia revealed that herbs such as *D. fastuosa* may lead to toxicity due to the presence of anticholinergic substances such as scopolamine, hyoscyamine and atropine. The typical features of toxicity include acute confusion, fever, tachycardia, hot flushed dry skin, dilated pupils, dry mouth, urinary retention, hallucinations, headache, delirium, rapid and weak pulse, convulsions, and coma. *D. fastuosa* may cause neural toxicity due to anticholinergic poisoning.[31,32]

CONCLUSION

D. fastuosa Linn is an Indian medicinal plant widely used in phytomedicine to cure diseases such as asthmas, cough, convulsions and other various human ailments. The plant may be explored further as per its great variety of traditional uses and on the basis of its reported chemical profile. But a great caution is advised since excess doses cause severe intoxication and death. The toxic dose is very close to the medicinal dose so this plant should only be used under the guidance of a qualified practitioner. [31,32]

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