

REVIEW ON *DATURA METEL*: A POTENTIAL MEDICINAL PLANT

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ABSTRACT

Plants have been an exemplary source of medicine. Ayurveda, traditional medicine, tribal medicine and other Bangladeshi literatures mention the use of plants in the treatment of various human ailments. Bangladesh has about 6,000 plant species and among them, around five thousands have been claimed to possess medicinal properties. Researches conducted in the last few decades on exploring plants mentioned in ancient literature or used traditionally for treating diseases is increasing. *Datura metel* is well known for its insecticidal, herbicidal, anti-fungal, anti-bacterial, anti-cancer, anti-inflammatory and anti-rheumatoid activity. *Datura* is also rich in Alkaloidal compounds. The present paper summarizes the phyto-chemistry, traditional uses and pharmacological actions of the plant *Datura metel*.

Keywords: *Datura metel*, Medicinal Plants, Alkaloid compounds, Phyto-chemistry, Pharmacology, Antifungal activity, Anti-cancer activity.

INTRODUCTION

Datura metel L., with local bengali name “Dhutura”, is an erect shrub with spreading branches. A perennial herbaceous plant, belonging to the Solanaceae family can reach a height of 1.5m. Leaves are simple, alternate, dark green, broadly ovate, shallowly lobed and glabrous. Flowers are large, solitary, and trumpet-shaped with a sweet fragrance usually appreciated in the mornings and evenings, with a wide range of colours, ranging from white to yellow and light to dark purple. The flowers are hermaphrodite and are pollinated by insects. The fruit is in the form of a capsule covered with short spines. *Datura* can tolerate average soil but prefers soil which is rich and moist or even very alkaline soil but hardly survives under shade. It prefers a warm temperature and is distributed in warmer regions of the world (Drake et al., 1996). *Datura* probably is of American origin and widely cultivated in all tropical and subtropical regions for its beautiful flowers (Glotter et al., 1973). *D. metel* can also be found in East Asia or India, and is used in traditional Bangladeshi herbal medicine. In Traditional Chinese Medicine, the flowers of *D. metel* are known as baimantuoluo and used for skin inflammation and Psoriasis (Wang et al., 2008). In Ayurvedic medicine, seeds of *D. metel* are used to treat Skin rashes, Ulcers, Bronchitis, Jaundice and Diabetes (Agharkar et al., 1991). In Brazil, seeds are used for tea making which would serve as a sedative and flowers are dried and smoked as cigarettes (Agra et al., 2007). There are various species of *Datura* which are now cultivated for the production of secondary metabolites.

Phytochemistry

Many different Alkaloids are found in the whole plant of *Datura*, which increased gradually with increase in age of the plant (Afsharypuor et al., 1995). Main constituents of the *Datura* plant are a huge number of tropane alkaloids (hyoscyamine, hyoscine, littorine, acetoxypine, valtropine, fastusine, fastusinine), a number of withanolides and various triglycol esters of tropine and pseudotropine (Table 1). Calystegines, the

nortropane alkaloids with glycosidase inhibitory activity, have also been found in various *Datura* species (Ghani, 2003). The root contains higher amount of atropine compared to the other parts. The aerial parts usually accumulated relatively higher amounts of scopolamine and relatively lower amounts of atropine as compared to the root of the plant (Afsharypuor et al., 1995).

Pharmacological action

D. metel contains tropane alkaloids and are used as sedative, anti-spasmodic and mydriatic agents (Nuhu, 2002). The whole plant, but especially the leaves and seed, have anaesthetic, hallucinogenic, anti-asthmatic, anti-spasmodic, anti-tussive, narcotic, bronchodilator, anodyne, hypnotic and mydriatic effects. Leaves are used as a local application for rheumatic swellings of the joints, Lumbago, Sciatica, Neuralgia, painful Tumors, Scabies, Eczema, Allergy and glandular Inflammations, such as Mumps; used externally for earache and smoked to relieve spasmodic Asthma. Seeds are also used externally for piles (Yusuf et al., 2009). Seeds, leaves and roots are used in insanity, fever with catarrh, diarrhea, skin diseases and cerebral complications.

Arthritis Treatment

Gout is a disease that results from an overload of uric acid in the body, leads to the formation of tiny crystals of monosodium urate monohydrate that deposit in tissues of the body, especially the joints (Virsaladze et al., 2007), also called gouty arthritis (Kamienski, and Keogh, 2006). The xanthine oxidase inhibitory activity was assayed for *D. metel* which is traditionally used for the treatment of gout (Umamaheswari, 2007). More than 50% xanthine oxidase inhibitory activity (*in vitro*) was seen in the methanolic extracts of *D. metel* which was comparable with the standard antigout drug, allopurinol which showed 93.21% inhibition at 100 µg/mL concentration with an IC₅₀ value of 6.75µg/mL. The methanolic extract was also screened for *in vivo* hypouricaemic activity against potassium

oxonate-induced hyperuricaemia in mice and the extract was found effective (Umamaheswari, 2007).

Hyoscyamine and scopolamine are the two commercially important anesthetic, anti-

spasmodic and anticholinergic drugs, also the two most important alkaloids produced in roots and then translocated to the aerial parts of *Datura* plants (Hashimoto and Yamada, 1994; Zhang et al., 2004).

Table 1. Alkaloidal constituents of *D. metel*.

Plant Parts	Alkaloid content (%)	Main Constituents	References
Leaves	0.426-	Atropine, hyoscyamine and scopolamine, 1-oxo-21,24S-epoxy-(20S,22S-witha-2,5,25-trienolide, pyrrole derivative (2'-(3,4-dimethyl-2,5-dihydro-1Hpyrrol-2-yl)-1'-methylethyl pentanoate)	Dabur et al., 2005; Rastogi and Mehrotra, 1993, Siddiqui et al., 1987
Seeds	0.426	Hyoscyamine, daturanolone and fastusic acid and many other tropane alkaloids	Ghani, 2003
Roots	0.35	Hyoscyamine, 3 α , 6 β -Ditigloyloxytropine, 3 α , 6 β -ditigloyloxytropan-7 β -ol, tigloidine, apohyoscyne, hyoscyne, 3 α -tigloyloxytropine, norhyoscyne, meteloidine, hyoscyamine, cuscohygrine and tropine	Ghani, 2003
Flowers	-	Withanolide (baimantuoluoline A, B, and C and withafastuosin E and withametelin C), withametelins I, J, K, L, M, N, O, P, 12 β -hydroxy-1,10-seco-withametelin B and 1,10-seco-withametelin B	Agharkar, 1991; Manickam et al., 1993; Yang et al., 2010a
Fruit (Pericarp)	-	β -sitosterol, triterpene, daturanolone and daturadiol	Ghani, 2003
Cultured callus	-	Cholesterol and 5 α -pregnane3 β ,20 β -diol	De, 2003
<i>In vitro</i> propagated shoots	-	C28 sterol 3 β ,24 ξ -dihydroxy-ergosta-5,25-dienolide and the withanolide 12-deoxywithastramonolide.	De, 2003

Insecticidal Activity

Different percentage (at 2.5, 5.0, 7.5 and 10.0%) of methanolic extract of *Datura metel* seeds, were tested against *Helicoverpa armigera* (Hubner), the cotton bollworm, is a moth, the larvae of which fed on a wide range

of plants, including many important cultivated crops. The 1.5 and 2.0% fractions of methanolic extract showed significant adverse effects on various biological parameters viz. larval survival, weight and duration, pupal period, % of pupation and adult emergence (Singh and Singh 2008).

Herbicidal Activity

Aqueous and organic solvent (methanol and n-hexane) 0, 5, 10 and 15% (w/v) extracts of shoot and root of *Datura metel* L. (Syn, *Datura alba* Nees.) were studied against *Phalaris minor* Retz., one of the most problematic weeds of wheat. 5-15% of methanol and 15% n-hexane root extract significantly reduced the germination, shoot and root length was significantly suppressed by all the employed concentrations of aqueous as well as organic solvent extracts in fact reduce the biomass a lot (Javaid et al., 2008).

Anticancer Activity and Antiproliferative Activity

Nitrogen-containing polyhydroxylated heterocyclic compounds are competitive inhibitors of various glycosidases, found most effective against various diseases including diabetes, cancer, and viral infections, along with additional activities, such as immunomodulatory properties and inhibition of glycolipid synthesis (Jacob, 1995). Withanolides was isolated from *D. metel* which are a group of steroidal lactones, many of these compounds exhibit a variety of biological activities, including anti-inflammatory, antioxidant, antitumor, and immunosuppressive properties. Withanolides can inhibit tumor cell proliferation and angiogenesis and induce the phase II enzyme quinone reductase (Pan et al., 2007). Calystegines have been isolated in several Solanaceous species and found to occur in different genera: including *Datura* (Nash et al., 1993). Three withanolide glycosides named daturametelins, together with two known ones, daturaturin and 7,27-dihydroxy-1-oxowitha-2,5,24-trienolide, were isolated from the methanolic extract of the aerial parts of *Datura metel* L. All compounds were tested for their antiproliferative activity towards the human colorectal carcinoma (HCT-116) cell line. The nonglycosidic compound exhibited the highest activity of the tested withanolides, with an IC₅₀ value of 3.2±0.2 μM (Ma et al., 2006).

Antifungal Activity

Different polar and nonpolar solvent extracts of *D. metel* showed significant antifungal activity against many different fungal species. The hexane, chloroform, acetone and methanolic fractions of *Datura metel* L. were investigated for antifungal properties using pathogenic species of *Aspergilli*. The chloroform fraction was found to be endowed with antifungal activity. The minimum inhibitory concentration (MIC) of chloroform fraction of *D. metel* L. was 625.0 mg/ml against all the three species of *Aspergilli*, (*A. fumigatus*, *A. flavus* and *A. niger*) by microbroth dilution and percent spore germination inhibition assays (Sharma, 2002). The MIC by disc diffusion assay was observed to be 12.5 mg disc. Methanolic extracts of *Datura metel* were analyzed against pathogenic *Aspergilli*, (*A. flavus* and *A. niger*) and in vitro MICs were found to be 1.25–2.50 mg/ml by both microbroth dilution and percent spore germination assays (Dabur et al., 2004; Khan and Nasreen, 2010). A novel compound 2-(3,4-dimethyl-2,5-dihydro-1H-pyrrol-2-yl)-1-methylethyl pentanoate was isolated from *Datura metel* L. and *in vitro* activity of this dihydropyrrole derivative against *Aspergillus* and *Candida* species was evaluated. The compound was found to be active against all the species tested, namely *Candida albicans*, *C. tropicalis*, *A. fumigatus*, *A. flavus* and *A. niger* (Dabur et al., 2005). The post-antifungal effect (PAFE) of the antifungal compound 2-(3,4-dimethyl-2,5-dihydro-1Hpyrrol-2-yl)-1-methylethyl pentanoate (DHP) on *A. fumigatus* was investigated and the secretory protein inhibited by DHP was identified but mechanism whereby DHP inhibit these proteins is unknown (Dabur et al., 2007). Aqueous and methanolic extracts of *Datura metel* was evaluated in vitro against *Ascochyta rabiei*, (the causal agent of chickpea blight), 21-34% and 20-40% reduction in growth of *A. rabiei* with aqueous and methanol extracts of shoot of *D. metel* respectively and 21-34% and 15-25% and 11-29% reduction was reported with root extracts (Bajwa et al., 2008).

Antibacterial Activity

Crude aqueous and ethanol extracts of leaf, stem bark and roots of *D. metel* were investigated against eight clinical bacterial isolates (*Streptococcus betahemolytic*, *S. dysenteriae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Bacillus cereus* and *Salmonella typhi*). The leaf and stem bark extracts was antagonistic against the test bacteria species with inhibitory zones and *Staph. aureus* was the most inhibited majorly with the ethanol extract (Akharaiyi, 2011).

Hypoglycemic Activity

The seeds of *D. metel* were investigated for hypoglycemic and antihyperglycemic activities in normal Wistar albino rats and diabetic rats. *D. metel* seed powder was suspended in 1% sodium CMC and given to normal (in the form of mucilage), diabetic rats, blood glucose levels above 300 mg/dL (orally) at doses of 25, 50 and 75 mg/kg body weight. Blood sampling in different time frame within 24h and dose dependent hypoglycemia was observed in animals treated. The dose dependent antihyperglycemic activity was also observed with *D. metel* in alloxan-induced diabetic rats. Seed powder of *D. metel* possessed blood glucose lowering effect in normoglycemic and in alloxan-induced hyperglycemic rats. Thus, the folk usage of the seeds of *D. metel* for controlling diabetes may be validated by this study and the seeds offer promise for the development of potent phytomedicine for diabetes (Murthy et al., 2004).

Free radical scavenging activity

D. metel seeds were analysed for the fatty acids and fat-soluble bioactive compounds. The amount of total lipid in *D. metel* seeds was 55g/kg in weight and mainly linoleic acid followed by oleic, palmitic and stearic acids. The crude n-hexane extract was characterized by a relatively high amount of phytosterols along with stigmasterol, β -sitosterol, lanosterol, Δ 5-avenasterol and sitostanol. In this extract, γ -tocopherol was the major component present

accounting for more than 80% of total tocopherols detected. n-hexane extract of *D. metel* seeds was able to quench only 40 % of DPPH radical. *D. metel* seeds contain a considerable amount of oil and may be a good source of essential fatty acids and lipid-soluble bioactives. The presence of tocopherols and sterols may have medicinal importance for human being (Ramadan et al., 2007).

Antioxidant Activity

The aqueous extracts of leaf, stem bark and roots of *D. metel* showed phytochemical and antioxidant activities. The aqueous extract of the plant displayed antioxidant activity of between 49.30-23.82% and can consider the plant as a natural source of antioxidants (Akharaiyi, 2011).

Toxicities and Cytotoxicity Activity

All of the plant parts of *Datura* are poisonous. Even a small dose is very poisonous because of the presence of toxic tropane alkaloid or the presence of anticholinergic substances such as scopolamine, hyoscyamine and atropine can cause neural toxicity (Ko, 1999). The toxicity sign and symptoms 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 and even death (Kam and Liew 2002; Ko, 1999). Using the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay cytotoxic activity of withametelins I, J, K, L, M, N, O, P, 12- β -hydroxy-1,10-seco-withametelin B and 1,10-seco-withametelin B isolated from methanolic extracts of *D. metel* were investigated. The withametelins I, K, L and N exhibited cytotoxic activities against A549 (lung), BGC-823 (gastric), and K562 (leukemia) cancer cell lines, with IC₅₀ values ranging from 0.05 to 3.5 μ M. Withamelin J showed moderate cytotoxic activity against BGC-823 and K562 but less cytotoxicity against A549 (Pan et al., 2007).

Table 2. Bioactive compound and fraction with activity.

Name of the Compound	Extraction procedure	Plant parts	Activity	References
Baimantuoluoline A	50% EtOH eluate fraction	Flower	Exhibiting activity for psoriasis	Yang et al., 2007
Withanolides	50% EtOH eluate fraction	Flower	Exhibiting activity for psoriasis	Yang et al., 2007
Withafastuosin	50% EtOH eluate fraction	Flower	Exhibiting activity for psoriasis	Yang et al., 2007
(E)-methyl 4-(3-(4-hydroxyphenyl)-N-methylacrylamido)butanoate	Extracted with 70% EtOH	Flower	Treatment of psoriasis	Yang et al., 2010a
6,7-dimethyl-1-D-ribityl-quinoxaline-2,3(1H,4H)-dione-5'-O-β-Dglucopyranoside	Extracted with 70% EtOH	Flower	Treatment of psoriasis	Yang et al., 2010a
(5α,6α,7β,22R)-5,6,7,27-tetrahydroxy-1-oxowitha-2,24-dien-27-O-β-D-glucopyranoside	Extracted with 70% EtOH	Flower	Treatment of psoriasis	Yang et al., 2010
(5α,6β,7α,22R)-5,6,7,27-tetrahydroxy-1-oxowitha-2,24-dien-27-O-β-D-glucopyranoside	Extracted with 70% EtOH	Flower	Treatment of psoriasis	Yang et al., 2010
(5α,6β,7α,12β,22R)-5,6,7,12,27-pentahydroxy-1-oxowitha-2,24-dien-27-O-β-D-glucopyranoside	Extracted with 70% EtOH	Flower	Treatment of psoriasis	Yang et al., 2010
(5α,6β,22R)-5,6,27-trihydroxy-1-oxowitha-2,24-dien-27-O-β-D-glucopyranoside	Extracted with 70% EtOH	Flower	Treatment of psoriasis	Yang et al., 2010
Withametelins	Methanol extract	Flower	Cytotoxic	Pan et al., 2007
1, 10-seco-withametelin B	Methanol extract	Flower	Cytotoxic	Pan et al., 2007
12 β -hydroxy-1,10-seco-withametelin B	Methanol extract	Flower	Cytotoxic	Pan et al., 2007
alkaloid datumetine	p-methoxybenzoic acid	Leaves	Antispasmodic drug	Siddiqui et al., 1986
2-(3,4-dimethyl-2,5-dihydro-1H-pyrrol-2-yl)-1-methylethyl pentanoate		Leaves	Antifungal activity	Dabur et al., 2005
Serotonin	Methanol	Flower	Induced during stress	Murch et al., 2009
Melatonin	Methanol	Flower	Cold stress	Murch et al., 2009

Traditional use

Datura has a wide range of traditional applications, including the treatment of epilepsy, hysteria, insanity, heart diseases, and for fever with catarrh, diarrhea and skin diseases. Crushed leaves are 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 5g of the flower extract can be used as an anesthetic through oral consumption that produces general anesthesia within 5 minutes, which lasted for about 5 to 6 h. The flower of the *D. metel* is used in the treatment of pain, chronic bronchitis and asthma (Kam and Liew 2002; Ko, 1999). In Bangladesh, leaves are used for scabies, eczema and allergy (Chowdhury et al., 1996). Dried whole plant powder is used to smoke to cure excessive or abnormal breathing, applied around the eyes to enlarge pupils. Application or drinking of leaf juice relieves pain and swelling. Leaf juice is mixed with a little opium and applied to the affected area to reduce swelling of gums or base of ears. Leaf juice is mixed with lime and turmeric and applied to the breasts to reduce breast pain (Rahmatullah et al., 2010). The flowers of *Datura metel* have been used in traditional Bangladeshi medicine for the treatment of asthma, convulsions, pain, and rheumatism for centuries.

In-vitro production of tropane alkaloids

Adventitious shoots that generated from young leaves of *D. metel* and shoot buds developed on MS medium with 2 mg/l benzylaminopurine (BAP) and elongated on hormone-free solid basal medium. The micro shoots failed to produce alkaloids (De, 2003). In unorganized plant tissue culture of *Datura* failed to produce tropane alkaloids scopolamine and hyoscyamine due to the suppression of alkaloid biosynthesis in dedifferentiated cells (Savary and Dougall, 1990). In callus tissues of *D. metel*, alkaloids were not present

(Duttagupta et al., 1980) but after redifferentiation of organ like shoots or roots in the dark alkaloids synthesized (Duttagupta et al., 1984). A hairy root line of *Datura metel* was reported following infection of aseptic stem segments with *Agrobacterium rhizogenes* strain A4 and cultured in hormone-free B5 solid medium. The growth and production of hyoscyamine and scopolamine (mg/g dry wt.) of these root cultures was optimized with reducing salt to half in B5 liquid medium and adding 8.7% to 70% permeabilizing agent Tween 20 and obtained a better biomass yield (2.3mg/l/day) and secreted scopolamine (0.84 mg/l/day) (Cusido et al., 1999).

Compounds isolated from *Datura metel* l.

Plants are a potential source of a large number of valuable secondary metabolites. Studying valuable secondary metabolites isolated from medicinal plants can open new possibilities to find bioactive alternatives to synthetic chemical. A number of alkaloids including hyoscyamine, hyoscyamine, meteloidine, scopolamine, tigloidine, tropine, withametelline and datumetine etc. have been reported from *Datura* species (Rastogi et al., 1998). Some of these alkaloids have found application in health care. Some of the bioactive compounds or fractions with their suggested activity from *D. metel* are summarized in Table 2.

CONCLUSION

D. metel L. is a medicinal plant used as phyto-medicine to treat traditionally a wide range of health complications. This plant can be explored further as per its diversity of traditional uses and on the basis of wide range of chemical compounds reported to be present in various parts of the plant. In the present investigation, Phyto-chemistry, Pharmacology and traditional uses of *D. metel* has been reviewed. Furthermore, the undocumented knowledge on this plant species has to recorded and should be explored widely so that it could serve the Humanity.

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