

## Medical importance of *Datura fastuosa* (syn: *Datura metel*) and *Datura stramonium* - A review

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**Abstract:-** The preliminary phytochemical investigation was performed on methanolic and hydroalcoholic extract of *Datura fastuosa* (syn: *Datura metel*) revealed the presence of alkaloids, tannins, cardiac glycosides, flavonoids, carbohydrates, amino acids and phenolic compounds, while, phytochemical analysis of *Datura stramonium* showed that it contained alkaloids, saponins, tannins, steroids, flavonoids, phenols and glycosides. The previous pharmacological studies of *Datura fastuosa* showed that it possessed antimicrobial insecticidal, antidiabetic, cytotoxic, antioxidant, antiinflammatory, analgesic, antipyretic, neurological, wound healing, reproductive and antispasmodic, while *Datura stramonium* exerted Antiepileptic, Anti-asthmatic, analgesic, antioxidant, antimicrobial, insecticidal, repellent and organophosphate protective effects. The current review highlights the chemical constituents and pharmacological effects of *Datura fastuosa* and *Datura stramonium*.

**Keywords:** *chemical constituents, pharmacology, Datura fastuosa, Datura metel, Datura stramonium.*

### I. INTRODUCTION:

The World Health Organization (WHO) estimates that 4 billion people, 80 percent of the world population, presently use herbal medicine for some aspect of primary health care [1]. Plants generally produce many secondary metabolites which were constituted an important source of many pharmaceutical drugs. Many previous reviews revealed the wide range of the pharmacological and therapeutic effects of medicinal plants [2-70]. The preliminary phytochemical investigation was performed on methanolic and hydroalcoholic extract of *Datura fastuosa* (syn: *Datura metel*) revealed the presence of alkaloids, tannins, cardiac glycosides, flavonoids, carbohydrates, amino acids and phenolic compounds, while, phytochemical analysis of *Datura stramonium* showed that it contained alkaloids, saponins, tannins, steroids, flavonoids, phenols and glycosides. The previous pharmacological studies of *Datura fastuosa* showed that it possessed antimicrobial insecticidal, antidiabetic, cytotoxic, antioxidant, antiinflammatory, analgesic, antipyretic, neurological, wound healing, reproductive and antispasmodic, while *Datura stramonium* exerted Antiepileptic, Anti-asthmatic, analgesic, antioxidant, antimicrobial, insecticidal, repellent and organophosphate protective effects. The current review will highlight the chemical constituents and pharmacological effects of *Datura fastuosa* and *Datura stramonium*.

### II. DATURA FASTUOSA (SYN: DATURA METEL)

**Synonyms:** Brugmansia waymannii Paxton, *Datura aegyptiaca* Vis., *Datura alba* Rumph. ex Nees, *Datura alba* F.Muell., *Datura alba* var. *africana* Mattei, *Datura bojeri* Delile, *Datura chlorantha* Hook., *Datura cornucopia* auct., *Datura dubia* Rich., *Datura dubia* Bianca ex Tod., *Datura fastuosa* L., *Datura fastuosa* var. *alba* Bernh., *Datura fastuosa* var. *flaviflora* O. E. Schulz ex O. C. Schmidt, *Datura fastuosa* var. *glabra* Bernh., *Datura fastuosa* var. *parviflora* Nees, *Datura fastuosa* var. *rubra* Bernh., *Datura fastuosa* var. *tuberculata* Bernh., *Datura fruticosa* Hornem., *Datura humilis* Desf., *Datura hummatu* Bernh., *Datura laevis* Schkuhr, *Datura metel* var. *dentata* Schldl. & Cham., *Datura metel* var. *fastuosa* (L.) Saff., *Datura metel* var. *flaviflora* (O.E.Schulz) Moldenke, *Datura metel* var. *muricata* (Link) Danert, *Datura metel* f. *pleniflora* O. Deg., *Datura muricata* Link, *Datura nanakii* Pandeya & A. B. Bhatt, *Datura nigra* Hassk., *Datura nilhummatu* Dunal, *Datura timoriensis* Zipp. ex Span., *Stramonium datura* Noronha, *Stramonium fastuosum* Moench, *Stramonium globosum* Bubani, *Stramonium infernale* Noronha and *Stramonium metel* Moench [71].

### TAXONOMIC CLASSIFICATION:

**Kingdom:** Plantae; **Division:** Magnoliophyta; **Subdivision:** Angiospermae; **Class:** Magnoliopsida; **Subclass:** Asterids; **Order:** Solanales; **Family:** Solanaceae; **Genus:** *Datura*; **Species:** *Datura fastuosa* (*Datura metel*) [72].

### COMMON NAMES:

**Arabic:** tatura, joz mashel, joz mathel; **Chinese:** yang jin hua; **English:** downy thorn-apple, Hindu datura, Hindu thorn-apple, hoary thorn-apple, horn-of-plenty, metel, purple thorn-apple; **Hindi:** sada dhatura; **Korean:** huindogmalpul; **Portuguese:** burbiaca; **Spanish:** burladora; **Swedish:** indisk spikklubba [73].

**Distribution:**

The possible origin is west Indies or America, now it is distributed in Asia in tropical, warm temperature regions [73].

### **DESCRIPTION:**

Herbs annual, 0.5-1.5 m tall, glabrescent. Stems often dark violet. Petiole 2-6 cm; leaf blade ovate or broadly ovate, 5-20 × 4-15 cm, membranous, glabrescent, base truncate or cuneate, asymmetrical, margin irregularly sinuate-dentate, lobed, or entire, apex acuminate; veins 4-6 pairs. Flowers erect. Pedicel ca. 1 cm. Calyx tubular, 4-9 cm. Corolla white, yellowish, or pale purple, funnelform, sometimes doubled or tripled, 14-20 cm; limb 6-10 cm in diam.; lobes elongate. Anthers 1-1.2 cm. Capsules deflexed, subglobose, ca. 3 cm in diam., tuberculate, irregularly 4-valved, subtended by remnants of persistent calyx. Seeds pale brown, reniform-discoid, ca. 3 mm in diameter [74].

### **TRADITIONAL USES:**

The dried leaves, flowers and roots were used as narcotic, antispasmodic, antitussive, bronchodilator, anti-asthmatic and as hallucinogenic. The plant was also used in diarrhea, skin diseases, epilepsy, hysteria, rheumatic pains, hemorrhoids, painful menstruation, skin ulcers, wounds and burns. In ayurveda, the plant was considered bitter, acrid, astringent, germicide, anodyne, antiseptic, antiphlogistic, narcotic and sedative [75-76].

**Parts used medicinally:** Seeds, flower, root bark and leaves[75-76].

### **PHYSICOCHEMICAL CHARACTERISTICS:**

Physicochemical evaluation of dried seeds of *Datura fastuosa* revealed that the plant contained total ash 5.6 % w/w, water soluble ash 4.5% w/w, water soluble extractive 26.35mg/gm, foaming index 18.18, swelling index 2.6 ml/g, moisture content 1.4 ml, crude fibre content 17.5% w/w and loss on drying 390 mg [77].

### **CHEMICAL CONSTITUENTS:**

The preliminary phytochemical investigation was performed on methanolic and hydroalcoholic extract of *Datura fastuosa* dried seeds revealed the presence of alkaloids, tannins, cardiac glycosides, flavonoids, carbohydrates, amino acids and phenolic compounds [77]. The proximate analysis showed that the seeds of the plant contained fat (14.72%), carbohydrate (51.22%), protein (20.73%), moisture (4.63%), ash content (5.14%), total sugar (5.63%), reducing sugar (2.65%), crude fibre (17.35%) and trace elements (mg/100gm): calcium 174.0, phosphorous 690.0, potassium 0.50, sodium 0.085, Iron 16.8, zinc 2.63, copper 6.9 and magnesium 390.0. Total saturated fatty acids was 18.03% and total unsaturated fatty acids was 81.74%, mono-unsaturated fatty acids 27.49%, poly-unsaturated fatty acids 54.25%. Fatty acid profile consisted of palmitic acid 15.31%, stearic acid 2.72 5, oleic acid 25.97, linoleic acid 54.25%, and palmitoleic acid 1.52 % [78]. The essential oil from different parts of *Datura metel*. were extracted using hydrodistillation and analysis by GC-MS. The main components of flowers were ketone (23.61%) and ethyl palmitate (15.84%). The main components of leaves were ketone (18.84%) and phytol (18.71%). Ketone (39.45%) and phytol (31.32%) were the major components of petioles. Palmitic acid (30.60%) and ethyl linoleate (21.56%) were the major components of seeds. The major ingredient of roots was palmitic acid (52.61%). The main ingredients of the stems were palmitic acid (38.38%) and ethyl linoleate (17.38%) [79]. Tropane alkaloids are a group of more than 200 compounds best known for their occurrence in the family *Solanaceae* comprising over 100 genera and 3000 plant species. Tropane alkaloids characterized by a two-ringed structure with a pyrrolidine and a piperidine ring sharing a single nitrogen atom and two carbon atoms. The amino group, typical for all alkaloids, is in most cases methylated. The most important natural tropane alkaloids are (-)-hyoscyamine and (-)-scopolamine (also known as hyoscine). High concentrations of these alkaloids have been found particularly in *Datura* species. Hyoscine [(-)-Scopolamine] represented the main tropane alkaloid in *Datura fastuosa* (*Datura metel*) [80]. However, the plant contained alkaloids, hyosyamine, hyoscine and atropine. The total alkaloid content of the leaves was 0.426% which were mainly atropine. The seeds contained 0.426% and the flower contained 0.43% hyoscyamine. Scopolamine and atropine contents in the whole plant of the plant increased gradually with the progress of developmental growth, and were most pronounced when the plant was at the end of its reproductive stage. The highest percentage of scopolamine accumulation in the root was after 16 weeks. The root was the organ which often accumulated higher amounts of atropine. The aerial parts, if compared with the root of the plant, usually accumulated relatively higher amounts of scopolamine and relatively lower amounts of atropine [81]. The leaves and flowers of *Datura fastuosa* yielded many withanolides included withafastuosins A, B, C and E; dmetelins A-D; baimantuoluoline A, B and C and withametelin [82-84]. Three new withanolide compounds named baimantuoluoline A, B, and C and the withafastuosin D, E and F and withametelin C were isolated from different parts of the plant [83, 85-86].

However, chemical investigation of a methanol extract of the flowers of *Datura metel* has led to the isolation of 10 new withanolides, withametelins I-P. Daturafolisides A-I, (22R)-27-hydroxy-7 $\alpha$ -methoxy-1-oxowitha-3,5,24-

trienolide-27-O- $\beta$ -d-gluco-pyranoside, daturataturin A, daturametelin J, daturataurin B, baimantuoluoside B and 12-deoxywithastramonalide were isolated from the leaves of the plant [87-88]. Four compounds were detected in methanolic extracts of flower, including cis-2-nitro-4-t-butylcyclohexanone (36.54%), acetic acid, trifluoro-, 2,2-dimethylpropyl ester (31.97%), 4-trifluoroacetoxyoctane (19.28%) and 1,4-cyclohexadiene, 1-methyl-(12.22%) [89]. Phytochemical investigation of the 50% ethanol fraction of macroporous resin of the flower of the plant led to the isolation of yangjinhuale A and five megastigmane sesquiterpenes [90]. Isofraxidin, scopatone, daturadiol, 1,4-benzenediol, arenarine D, vanillin, N-trans-feruloyl-tyramine, scopoletin, G-sitosterol and hyosciamilactol were isolated from the seeds of *Datura metel* from Xinjiang Province [91]. The amount of total phenolic content (TPC) and total flavonoid contents (TPC) were analysed. The highest TPC was determined in methanolic extracts of seed (268.6  $\mu$ g of gallic acid equivalence/mg of dry plant material) and the highest TPC was determined in fruit pulp (8.84  $\mu$ g of quercetin equivalence/mg dry plant material) [92].

## **PHARMACOLOGICAL EFFECTS:**

### **Antimicrobial effects:**

The antimicrobial effect of hydro-alcoholic and methanolic seed extracts of *Datura fastuosa* was evaluated against three clinical bacterial strains (*Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*) and two clinical fungal strains (*Candida albicans* and *Aspergillus niger*) by tube dilution method. Both plant extracts were active against the tested microorganisms. The methanolic extract of *Datura fastuosa* inhibited *E. coli* effectively with minimum bactericidal concentration (MBC) of 25  $\mu$ g/ml. The hydroalcoholic extract of *Datura fastuosa* seeds was found to be more potent in terms of its bactericidal concentration against *B. subtilis* with both minimum inhibitory concentration (MIC) and MBC values of 25  $\mu$ g/ml. Methanolic extract was found to be more efficient in inhibiting *S. aureus* with MIC of 12.5  $\mu$ g/ml [93]. A new antibacterial agent 5', 7'-dimethyl 6'-hydroxy 3'-phenyl 3-a-amine b-yne sitosterol was isolated from the plant leaves. It displayed antibacterial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Salmonella typhi*, *Bacillus subtilis* and *Klebsiella pneumonia* but could not inhibit *Escherichia coli* [85]. The antipathogenic effect of carbon tetrachloride, benzene and chloroform extract crude extracts of *Datura* leaf extract was studied against Enterobacter species. Carbon tetra chloride and benzene extracts (1000  $\mu$ g/ml) of the leaves of *Datura metel* showed excellent activity on comparing with that of standard drug, ciprofloxacin (100  $\mu$ g/ml) [94]. The hexane, chloroform, acetone and methanolic fractions of the plant were investigated for antifungal properties using pathogenic species of *Aspergillus* (*A. fumigatus*, *A. flavus* and *A. niger*). The chloroform fraction was found to be endowed with antifungal activity. The minimum inhibitory concentration (MIC) of chloroform fraction was 625.0 microg/ml against all the three species of *Aspergillus*, by microbroth dilution and percent spore germination inhibition assays. The MIC by disc diffusion assay was observed to be 12.5 microg/disc. The chloroform fraction of the plant, when investigated for potency, turned to be 9.2 times less active than amphotericin B [95]. 2beta-(3,4-dimethyl-2,5-dihydro-1H-pyrrol-2-yl)-1'-methylpentanoate isolated from the leaves of *Datura metel* was endowed with antifungal activity and its MIC was found to be 87.5 microg/ml [96]. The antiviral activity of atropine was evaluated by plaque reduction test against *Herpes Simplex* virus, *Influenza* virus, *New Castle Disease* virus, *Sindbis*, *Vaccinia*, *Adenovirus* and *Japanese encephalitis* virus. Viruses were cultivated on primary chick embryo (CE), HeLa S3, primary monkey kidney cells (MK). Atropine inhibited only the growth of enveloped viruses independent of the nucleic acid content of the virus. It also blocked the glycosylation of viral proteins of *Herpes* virus and hence the production of new virions. Virions formed in the presence of atropine were non infectious [97-98].

### **Insecticidal effects:**

Different percentage of methanolic extract of *Datura metel* seeds were tested against *Helicoverpa armigera* (Hubner). The 1.5 and 2% of methanolic extract showed significant adverse effects on larval survival, weight and duration, pupal period, % of pupation and adult emergence [99].

### **Antiinflammatory, analgesic and antipyretic effects:**

The anti-inflammatory activity of ethanolic and ethyl acetate extracts of root part of *Datura fastuosa* (50, 100, 150, 200 mg/kg orally) was evaluated using carrageenan induced rat paw edema. Indomethacin was used as a standard drug. All extracts showed significant activity at 200 mg/kg dose as compared to indomethacin (10 mg/kg). The percentage inhibition was calculated for all doses of different extracts. Ethanolic extract possessed significant anti-inflammatory activity [100]. Fifteen compounds isolated from the leaves of *Datura metel* were evaluated for *in vitro* anti-inflammatory potential using LPS-stimulated RAW 264.7 murine macrophages. Among them, compounds daturafolisides A and B, baimantuoluoside B and 12-deoxywithastramonalide exhibited significant inhibition of nitrite production with IC<sub>50</sub> of 20.9, 17.7, 17.8, and 18.4  $\mu$ M. Compounds daturafolisides C, D and F and daturataurin B presented moderate inhibitory activities

with  $IC_{50}$  of 59.0, 52.8, 71.2, and 53.1 $\mu$ M [88]. Dmetelins A-D, and 7 $\alpha$ ,27-dihydroxy-1-oxo-witha-2,5,24-trienolide isolated from the leaves of *Datura metel* were evaluated for their inhibitory effects on lipopolysaccharide (LPS)-induced nitric oxide (NO) production in RAW264.7 cells. Compounds, dmetelin A, D and 7 $\alpha$ ,27-dihydroxy-1-oxo-witha-2,5,24-trienolide, showed significant inhibitory activities, and compounds dmetelin B and C showed moderate inhibitory activities with  $IC_{50}$  values of 17.8, 11.6, 14.9, 33.3 and 28.6  $\mu$ M, respectively [84]. The aqueous extracts of *Datura fastuosa* leaves and seeds were evaluated for the analgesic effect on acetic acid-induced writhing and hot plate reaction in mice. The results revealed that *Datura fastuosa* leaves and seeds extracts at doses of 400 and 800 mg/kg orally induced analgesic effects. The analgesic activity of leaf extract was reduced by naloxone but not that of seed extract [101]. The leaves extract of *Datura fastuosa* exhibited analgesic effect in acetic acid test with tolerance phenomenon, but not by the seed extracts. Only the leaf extract reduced rectal temperature, apomorphine hypothermia and increased water intake [102].

#### **Antispasmodic and spasmogenic effects:**

The effect of the plant leaf and root extracts, scopolamine and acetylcholine was studied on isolated smooth muscle preparations. The leaf extract and scopolamine showed antispasmodic effects, whereas root extract and acetylcholine caused contraction of the isolated rat uterus and rectum whole muscle. The results indicated that the plant contained antispasmodic and spasmogenic constituents [103].

#### **Neurological effects:**

The neuropsychopharmacological effects of aqueous extracts of leaves and seeds of *Datura fastuosa*, were studied in rat and mice. The leaf and seed extracts at doses of 400 and 800 mg/kg increased motor activity, reduced slightly the duration of barbituric sleeping, antagonized catalepsy and ptosis induced by haloperidol and the immobility induced by forced swimming. The results also showed that, *Datura fastuosa* has some antidepressant profile at low doses [102]. The potential oral anaesthetic effect of methanolic crude extract of *Datura metel* was studied in dogs. The extract administered orally to dogs at a dose rate of 0.6, 1.2, 1.5, 2 and 2.4 g/kg respectively during establishment of a suitable pilot oral anaesthetic doses, showed a graded dose response relationship. The extract at an oral dose of 2.4 g/kg induced surgical anaesthesia in dogs with increased heart and respiratory rates (107 to 205 bpm and 36.33 to 41.33 cpm) respectively, normal rectal temperature (37.83°C), adequate tissue perfusion, good muscle relaxation but poor analgesia. The dogs recovered without any complications. The study revealed that the seed extract of *Datura metel* was relatively safe, induced sleep similar to that of thiopentone sodium anaesthesia with good anaesthetic indices [104]. 25 g/kg of methanolic crude extract induced behavioural sleep patterns (EEG) similar to that of thiopental in rats [105]. The activity of ethanolic seed extract of *Datura metel* on Nissl substances, astrocytes, axonal and neuronal integrity of the medial prefrontal cortex (mPFC) was studied in rats. Extract was given 100 and 200 mg/kg bw for 14 days. The results revealed that *Datura metel* was deleterious to the health of Wistar rats at a dose-dependent rate as observed in its actions on the medial prefrontal cortex at 100 mg/kg bw and 200 mg/kg bw. The histological study of the treated Wistar rats exhibited features of disoriented neuronal integrity such as, chromatolysis, reduced protein synthesis due to loss of Nissl substances and nuclei, neuronal loss as well as axonal injuries [106].

#### **Antioxidant effect:**

Hydroalcoholic and methanolic seed extracts of *Datura fastuosa* were evaluated for antioxidant potential, total antioxidant capacity, total amount of phenolic content, total flavonoid content, total flavonols and total proanthocyanidines contents. The  $IC_{50}$  value using DPPH model for methanolic extract of *Datura fastuosa* was 28.34  $\mu$ g/ml and for hydroalcoholic extract was 25.78  $\mu$ g/ml. The values of total antioxidant capacity, total amount of phenolic content, total flavonoid content, total flavonols and total proanthocyanidines content for methanolic extract of *Datura fastuosa* were found to be 6.83 mg/g, 9.97 mg/g, 6.34 mg/g, 5.37 mg/g and 1.42 mg/g of plant extract respectively and for hydroalcoholic extract, the values for the same parameters were 7.44 mg/g, 6.88 mg/g, 9.35 mg/g, 5.36 mg/g and 0.88 mg/g respectively [93]. The antioxidant activity of different solvent extracts from the leaves of *Datura metel* was tested by DPPH scavenging activity, hydroxyl radical scavenging activity, reducing power assay, and  $\beta$ -carotene bleaching activity. The antioxidant activity was performed at four concentrations ranging from 25-100 mg/ml. Chloroform extract exhibited highest concentration dependent antioxidant activity [107]. *In vitro* antioxidant activity of the extract was tested by 2, 2-diphenyl-1-picrylhydrazyl radical scavenging method. A positive correlation was recorded between the phenolic and flavonoid content of the *Datura metel* extracts and the free radical scavenging activities [92].

#### **Cytotoxic effect:**

Chemical investigation of a methanol extract of the flowers of *Datura metel* has led to isolation of 10 new withanolides, withametelins I-P. Four of 10 withanolides exhibited cytotoxic activities against A549 (lung),

BGC-823 (gastric), and K562 (leukemia) cancer cell lines, with IC<sub>50</sub> values ranging from 0.05 to 3.5 microM [87]. The *in vitro* cytotoxicity assay was performed in vero cell line by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay method. The IC<sub>50</sub> of a methanolic cold extract of datura fruit was found to be 3 mg/ml against vero cell line [92]. The cytotoxicity of withanolides isolated from *Datura metel* was evaluated against human lung carcinoma cells (A549) and human colorectal adenocarcinoma cells (DLD-1), respectively. 12α-hydroxydaturametelin exhibited cytotoxicity against A549 and DLD-1 cell lines, with IC<sub>50</sub> values of 7 and 2.0 μM, respectively. However, Two compounds possessed higher cytotoxic effects against DLD-1 cells with IC<sub>50</sub> values of 0.6 and 0.7 μM respectively. Both compounds blocked the cell cycle in the S-phase and induced apoptosis [108]. The roots and stems showed inhibitory effects against HepG-2 with IC<sub>50</sub> levels of 613.88 and 341.12 mg/l. The leaves and roots showed inhibitory effects against HeLa with IC<sub>50</sub> levels of 267.76 and 348.35 mg/l. All the six parts possessed inhibitory effects against SGC-7901 cell lines [79].

#### **Wound healing effects:**

The ethanolic extract of *Datura fastuosa* was evaluated for wound healing activity in Wistar albino rats using excision wound model. The extract was formulated as an ointment at two concentrations (5% and 10% w/w). Nitofurazone ointment (0.2%w/w) was used as standard. The parameters utilized for evaluation were percentage wound closure, mean epithelization time, hydroxyproline, DNA and protein level. The histopathological studies were also carried out on wound tissue. The result revealed that 10% w/w *Datura fastuosa* ointment exhibited significant wound healing activity comparable to that of the standard [109].

#### **Antidiabetic effect:**

The seed powder of the plant was tested for its hypoglycemic activity in normal and alloxan-induced diabetic rats. 25, 50 and 75 mg/kg, of the seed powder orally produced significant reduction in blood glucose at the 8 h in both normal and diabetic rats. The effect was found to be dose dependent [110].

#### **Xanthine oxidase inhibitory activity:**

The aqueous, methanol-water mixture and methanolic extract of *Datura metel* were evaluated for xanthine oxidase inhibitory activity at 100 microg/ml. The methanolic extracts of *Datura metel* showed more than 50% inhibition compared with the standard antigout drug, allopurinol, which showed 93.21% inhibition at 100 μg/ml concentrations [111].

#### **Reproductive effects:**

The antifertility activity of the acetone extracts of *Datura metel* was evaluated in female albino mouse. The crude acetone extract of *Datura metel* seeds were given orally to the female mouse in the concentration of 0.5%, 1% and 2% respectively. After 15 day of treatment the female mouse was mated with the normal male mouse. After 10 days of mating they were dissected to observe the number of implantation sites in the uterine horns. The results revealed that 2% seed extracts caused 100% anti-implantation activity followed by 1% and 0.5% seed extracts which caused 40% and 80% anti implantation activity respectively. The authors concluded that the seed extracts of *Datura metel* may be recommended as a good source of antifertility compounds with minimal side effects [112]. The effect alcoholic extract of *Datura fastuosa* ( 2,4 and 6mg/kg, for 7 weeks) on the fertility was studied in rat males. The results showed that the extract induced significant decrease in concentrations of sperm and normal sperm in all the concentrations in comparing with control group. They also significantly decreased serum levels of testosterone, LH and FSH, and weights of the testes and epididymis in the treated groups, The percentage of occurrence of pregnancy was also significantly decreased [113].

#### **Toxicity and side effects:**

*Datura fastuosa* was found to be safe up to dosage of 2000 mg/kg body weight with no symptoms of toxicity or mortality [72, 111]. The aqueous extracts of leaves and seeds of *Datura fastuosa* were well tolerated by rats. No mortality was observed up to 3200 mg /kg [102].The methanolic extract was relatively safe since when administered at the highest dose (5000 mg/kg) to mice, it produced no sign of toxicity and no death was recorded [104].However, all parts of *Datura* were poisonous because of the presence of toxic tropane anticholinergic alkaloids which caused neural toxicity. The signs of toxicity were anticholinergic toxic effects including acute confusion, fever, tachycardia, hot flushed dry skin, dilated pupils, dry mouth, urinary retention, hallucinations, headache, delirium, rapid and weak pulse, convulsions, coma and death [114-115].

Toxicological assessment shown that the extract of *Datura metel* seed induced deleterious effect on the visual cortex and frontal cortex of the brain in rats [116-117]. Histological evaluation of the organs showed decrease in organ weight, circulatory disturbance, necrotic changes in the liver architecture with increase of serum alkaline phosphatase, serum glutamic-oxaloacetic transaminase and glutamyl pyruvic transaminase in liver and heart [118].

### III. DATURA FASTUOSA (SYN: DATURA METEL)

#### SYNONYMS:

Datura bernhardii Lundstr., Datura bertolonii Parl. ex Guss., Datura cabanesii P. Fourn., Datura capensis Bernh., Datura ferocissima Cabanès & P. Fourn., Datura ferocissima Cabanès & P. Fourn., Datura ferox Nees, Datura hybrida Ten., Datura inermis Juss. ex Jacq., Datura laevis L.f., Datura loricata Sieber ex Bernh., Datura lurida Salisb., Datura microcarpa Godr., Datura muricata Godr., Datura parviflora Salisb., Datura praecox Godr., Datura pseudo stramonium Sieber ex Bernh., Datura stramonium var. canescens Roxb., Datura stramonium var. chalybaea W. D. J. Koch, Datura stramonium var. gordonii Danert, Datura stramonium f. inermis (Juss. ex Jacq.) Hupke, Datura stramonium var. inermis (Juss. ex Jacq.) Fernald, Datura stramonium var. stramonium, Datura stramonium var. tatula (L.) Decne., Datura stramonium f. tatula (L.) B. Boivin, Datura stramonium var. tatula (L.) Torr., Datura tatula L., Datura wallichii Dunal, Stramonium foetidum Scop [119-120].

#### TAXONOMIC CLASSIFICATION:

**Kingdom:** Plantae, **Division:** Magnoliophyta, **Class:** Magnoliopsida, **Order:** Solanales, **Family:** Solanaceae, **Genus:** *Datura*, **Species:** *Datura stramonium* [121].

#### COMMON NAMES

**Afrikaans:** gewone stinkblaar; **Arabic:** tatura, nafer, thagher, banj tatura, tatura shaeka, el-shajara el-muskera, **Chinese:** man tuo luo; **English:** common thorn-apple, false castor-oil, jimsonweed, moonflower, purple thorn-apple, thorn-apple; **French:** datura stramoine, herbe des taupes, pomme épineuse; **German:** Stechapel; **Italian:** indormia, stramonio commune; **Portuguese:** Estramónio, figueira-do-diabo; **Spanish:** datura manzana, estramonio, tapa, toloache; **Swedish:** violspikklubba [119].

#### DISTRIBUTION

*Datura stramonium* originates in the Americas but is now found around the world including the warmer regions of North, Central and South America, Europe, Asia, and Africa [122].

#### DESCRIPTION

The plant is an annual and grows to 1.2 m high. It has a simple or bifurcated, round, erect glabrous stem. The leaves are 20 cm long, long-petioled, ovate, dentate, glabrous and dark green. The flowers are large, white, solitary, terminal or in the branch bifurcations. The calyx has a long 5-edged and short 5-tipped tube. The corolla is funnel shaped and folded with a short 5-sectioned border. There are 5 free stamens and 1 superior ovary. The fruit is a 5 cm long 4-valved capsule, which is densely thorny and walnut-sized. The numerous seeds are 3.5 mm long, flat, reniform and black [123].

#### TRADITIONAL USES:

*Datura stramonium* has long been known for its hallucinogenic and euphoric effects. The weed was dried and smoked for hallucinations and total relaxation [122, 124].

*Datura stramonium* was used traditionally to treat asthma, gastrointestinal problems, aches, abscesses, arthritis, boils, headaches, hemorrhoids, rattlesnake bites, sprains, swellings, and tumors. It was used for relieving the pains of rheumatism and sciatica as an ointment, and easing spasms of Parkinson's disease [124]. The juice of the leaves in warm milk was used to expel intestinal worms including cestodes, seeds with palm oils used externally for insect bites and stings, in Nigeria [125-126]. In Ayurvedic medicine, the plant was used for the treatment of ulcers, wounds, inflammation, sciatica, bruises and swellings, rheumatism, gout, asthma, bronchitis and toothache [127].

#### CHEMICAL CONSTITUENTS:

Phytochemical analysis showed that the aqueous and ethanolic extract of the stem-bark of *Datura stramonium* contained alkaloids, saponins, tannins, steroids, flavonoids, phenols and glycosides [128]. Many amino acids were isolated from the seeds particularly alanine, glutamate, phenylalanine, and tyrosine [129]. The tropane alkaloids were the important anticholinergic alkaloids isolated from *Datura stramonium* [130].

Production of tropane alkaloids in *Datura stramonium* plants was found to start from the end of the second week after seed germination. The rates of atropine and scopolamine production were similar (0.05%) at this stage. The quantity of alkaloids reached maximum at the end of the tenth week after seed germination, then gradually decreased as the plants entered the generative phase. Alkaloid content depended on the plant part and the stage of

plant growth. Leaves and capsules showed the highest alkaloid content in the vegetative and generative phases, respectively. Generally the younger parts of plants contained more alkaloids than older ones. Alkaloid content decreased rapidly in leaves in the generative phase. Scopolamine was lowest (0.013%) in roots in the vegetative period, and then totally disappeared in the generative period. Atropine occurred in roots in both the vegetative (0.045%) and generative (0.056%) periods. Stems were rich in atropine (0.070%) but poor in scopolamine (0.023%) in both stages [131]. The maximum contents of atropine in different parts of *Datura stramonium* were found in the stems leaves and seeds. The maximum contents of hyoscyamine and scopolamine in different parts of *Datura stramonium* were found in the stems and leaves of young plants, hyoscyamine being always the predominant component. In the Young plants, the maximum atropine level was recorded in the stems and medium leaves  $0.915 \pm 0.015$  and  $0.831 \pm 0.014$   $\mu\text{g}/\text{mg}$  respectively, while in adult plant , the maximum level of atropine was recorded in the flowers and small leaves  $0.270 \pm 0.026$  and  $0.165 \pm 0.006$   $\mu\text{g}/\text{mg}$  respectively. On the other hand, in the Young plants, the maximum scopolamine level was recorded in the stems and flowers  $0.129 \pm 0.014$  and  $0.106 \pm 0.031$   $\mu\text{g}/\text{mg}$  respectively, while in adult plant, the maximum level of scopolamine was recorded in the seeds and flowers  $0.089 \pm 0.010$  and  $0.066 \pm 0.004$   $\mu\text{g}/\text{mg}$  respectively [132-133].

However, sixty-four tropane alkaloids have been detected in *Datura stramonium* these included: Hygrine;  $3\alpha,6\beta$ -Ditigloyloxy-7-hydroxytropane; 6-Hydroxyhyoscyamine; Pseudotropine;  $3\alpha$ -Tigloyloxytropane; Hydroxy-6-tigloyloxytropane; Phenyl acetoxytropane;  $3$ -Tigloyloxy-6-(2-methylbutyryloxy) tropane; Hyoscyamine;  $3$ -Tigloyloxy-6-isovaleroyloxy-7- Hydroxytropane; Scopolamine; Tropinone; Scopine; 6-Hydroxyacetoxytropane;  $3,6$ -Diacetoxytropane;  $3$ -Tigloyloxy-6-acetoxytropane;  $3$ -Tigloyloxy-2-methyl butyryl oxytropane;  $3\alpha,6\beta$ -Ditiglotoxytropane;  $3$ -Acetoxy-6-isobutyryloxytropoan;  $3$ -(2-Phenylpropionyloxy) tropane; Littorine; 6-Hydroxy apoatropine;  $3\alpha,6\beta$ -Ditigloyloxy-7-hydroxytropane;  $3$ -Tropoyloxy-6-acetoxytropane;  $3,6$ -Dihydroxytropane;  $3\beta$ -Tigloyloxytropane;  $3$ -Tigloyloxy-6-propionyloxy-7-hydroxytropane;  $3\alpha$ -Apotro-poxytropane; Aposcopolamine;  $3\alpha,6\beta$ -Ditigloyloxytropane;  $3$ -( $3'$ -Acetoxytropoyloxy) tropane;  $3\alpha$ -Tigloyloxy-6-hydroxytropane; Tropine;  $3$ -Acetoxytropane;  $3$ -Hydroxy-6-acetoxytropane;  $3$ -Hydroxy-6-methylbutyryloxytropane;  $3$ -Tigloxy-6-isobutyryloxytropane; Aponorscopolamine; 7-Hydroxyhyoscyamine; Meteloidine;  $3\alpha,6\beta$ -Ditigloyloxytropane; 3-phenylacetox-6, 7-epoxynortropane; 7- hydroxyapoatropine and scopoline [ 132, 134-135].

The main components of essential oil of *Datura stramonium* were sterols and their derivatives, and the major constituents were  $5\alpha$ -Ergosta-7,22-dien-3. $\beta$ -ol (16.53%), 3-Hydroxycholestan-5-yl, acetate (14.97%), and 26,26-Dimethyl-5,24(28)-ergostadien - $3\beta$ -ol (10.39%) [136].

Twelve compounds were isolated by Li *et al.*, from *Datura stramonium* seeds, they included: N-trans-feruloyl tryptamine, hyoscyamilactol, scopoletin, umckalin, daturaolone, daturadiol, N-trans-ferulicacyl- tyramine, cleomiscosin A, fraxetin, scopolamine, 1-Acetyl-7-hydrox-beta-carbol-ine, 7-hydroxy-beta-carbolinel-propionic acid [137].

## **PHARMACOLOGICAL EFFECTS:**

### **Antiepileptic effect:**

Rats were continuously administered one of three herbal treatments (*Scutellaria lateriflora*, *Gelsemium sempervirens* and *Datura stramonium*) through the water supply for 30 days, one week after the induction of status epilepticus by a single systemic injection of lithium (3 mEq/kg) and pilocarpine (30 g/kg). The numbers of spontaneous seizures per day during a 15 min observation interval were recorded for each rat during the treatment period and during an additional 30 days when only tap water was given. Rats that received a weak solution of the three herbal fluid extracts displayed no seizures during treatment. However, when this treatment was removed, the rats displayed numbers of spontaneous seizures comparable to the controls [138].

### **Anti-asthmatic effect:**

The specific airway resistance (sRaw) of twelve asthmatic patients with mild airway was measured after inhaling the smoke of one *Datura stramonium* cigarette. In 11 patients sRaw decreased substantially after the cigarette, the mean maximal decrease being 40% at the 30<sup>th</sup> minute. In seven patients the subsequent inhalation of 200 micrograms salbutamol caused no further decrease in sRaw. In the remaining four patients salbutamol induced a larger decrease in sRaw than the cigarette smoke. The inhalation, however, of a synthetic anticholinergic agent (SCH 1000, 600 micrograms) proved as effective as salbutamol in these patients. In one patient the cigarette smoke and SCH 1000 produced only a negligible amount of bronchodilatation whereas [139].

### **Antimicrobial effects:**

The antimicrobial activity of the aqueous and ethanolic extract of the stem-bark of *Datura stramonium* was investigation against *Staphylococcus aureus*, *Salmonella typhi*, *Shigella spp*, *Eschericia coli*, *Klebsiella pneumonia* and *Neisseria gonorrhoea*. Ethanolic extract showed more antibacterial activity than the aqueous

extract. It showed antibacterial activity against all the tested bacteria except *Neisseria gonorrhoea*. The aqueous extract showed activity only against *Staphylococcus aureus* [128]. The antimicrobial properties of whole plants (extracted sequentially with different organic solvents) of *Datura stramonium* were studied against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and the fungal strains *Aspergillus flavus*, *Aspergillus niger*, *Fusarium culmorum* and *Rhizopus stolonifer*. All the solvent extracts showed significant activity against all the tested microorganisms. Methanolic extract was the most active against all microorganisms, whereas all the extracts showed significant activity against *P. aeruginosa*. All the solvent extracts showed low MIC against *A. niger* [140]. The antibacterial and antifungal effects of benzene, chloroform and ethanol extracts of branches and leaves of *Datura stramonium* branches and leaves were studied against *Enterobacter* (clinical strain/PIMS), *Micrococcus luteus* (clinical strain/PIMS), *Pseudomonas aeruginosa* (clinical strain/PIMS), *E. coli* ATCC 25922, *Staphylococcus aureus* (clinical strain/PIMS) and *Klebsiella pneumonia* ATCC 700603. *Datura stramonium* chloroform extract produced maximum zone of inhibition  $16\pm0.7$ mm against *Enterobacter*, while it produced minimum zone of inhibition ( $7\pm0.7$ mm) against *K. pneumonia*. Benzene extract of the plant exhibited maximum zone of inhibition ( $15\pm0.7$ mm) against *Enterobacter* and *M. luteus*, while it produced minimum zone of inhibition ( $9\pm0.3$ mm) against *S. aureus* and *K. pneumonia*, ethanol extract of *Datura stramonium* gave maximum zone of inhibition against *K. pneumonia* and minimum against *E. coli*. The MBC values revealed that benzene extract (3.12mg/ml) was effective against *P. aeruginosa* while the same concentration of chloroform extract was very active against *S. aureus*, *P. aeruginosa* and *M. luteus*. All the extracts of *Datura stramonium* possessed significant antifungal activity against *Saccharomyces cerevisiae*, *Aspergillus fumigatus* and *Aspergillus niger* with maximum antifungal activity against *S. cerevisiae* and zone of inhibition was about  $16\pm0.2$ mm by ethanol extract,  $15\pm0.3$ mm by chloroform and  $14\pm1.6$ mm by benzene extract, while minimum antifungal activity was observed against *A. niger* [141]. *Datura stramonium* extracts were investigated for their *in vitro* activity against *Staphylococcus aurers* ATCC25923, Methicillin-resistant *S. aureus*, *Enterococcus sp.*, *Escherichia colii* ATCC25922, Enteroinvasive *Escherichia coli* and *Pseudomonas aeruginosa*. *Datura stramonium* leaf extracts exhibited a considerable antibacterial activity even at low concentrations. Methanolic leaf extracts showed the maximum inhibitory effect. The growth inhibition zone against *Escherichia coli* was 9.8mm and against *Staphylococcus aurers* was 6.8mm [142]. The antimicrobial effect of methanol extract from flower, seed and leaf of explant callus was studied against (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis* and *Bacillus subtilis*) and four fungi strains (*Fusarium semithecum*, *Fusarium colmorum*, *Ceratocystis ulmi* and *Rhizoctonia solani*). The result showed that the methanol extract from green leaf explant callus possessed inhibitory effects on the growth of *B. subtilis* (22mm) and *S. epidermidis* (23mm). The methanolic extract of the vegetative root and the flower of *Datura stramonium* show an effective antifungal activity against *Rhizoctonia solani* fungus [143]. Aqueous and organic solvent extracts of different parts of the plant were investigated for its anti-*Vibrio cholera* non-O1, and *Vibrio parahaemolyticus* using the disk diffusion method. The results revealed that *Datura stramonium* possessed a broad-spectrum vibriocidal effect [144]. The antifungal effects of acetone extracts of *Datura stramonium* seeds were studied against selected phytopathogenic fungi (*Penicillium janthinellum*, *Penicillium expansum*, *Aspergillus niger*, *Aspergillus parasiticus*, *Colletotrichum gloeosporioides*, *Fusarium oxysporum*, *Trichoderma harzianum*, *Phytophthora nicotiana*, *Pythium ultimum* and *Rhizoctonia solani*). Extracts exhibited moderate to good antifungal activity, with minimum inhibitory concentrations ranged from 0.125 mg/ml to 2.50 mg/ml [145]. Aqueous and ethanolic extracts of various parts of *Datura stramonium* were examined for their potential antimicrobial activity against pathogenic bacteria [*Bacillus subtilis*-2699, *Escherichia coli*-2803, *Staphylococcus aureus*-2602, *Proteus vulgaris*-2027, *Salmonella typhi*-2501; and pathogenic fungi such as *Aspergillus flavus*- 525, *Aspergillus niger* (local isolate), *Candida albicans*-3100 and *Rhizopus stolonifer* (local isolate)]. The results showed that the ethanolic extracts were more potent than the aqueous extracts and leaf extract possessed better antimicrobial activity than stem, and root. Aqueous extract of te leaves showed antibacterial activity against *Bacillus subtilis* and *Escherichia coli* with zone of inhibition of 16 and 10 mm respectively, while ethanolic extracts of the leaves exerted antibacterial activity against *Bacillus subtilis* (31mm), *Escherichia coli* (18mm), *Staphylococcus aureus* (24mm), *Salmonella typhi* (10mm), *Aspergillus flavus* (8mm) and *Candida albicans* (10mm) [146].

#### **Insecticidal and repellent activities:**

The ethanolic extracts of leaves of *Datura stramonium* were evaluated for larvicidal and mosquito repellent activities against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*. The LD<sub>50</sub> values for larvicidal activity were found to be 86.25, 16.07 and 6.25 ppm against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* respectively. The ethanolic leaves extract of *Datura stramonium* provided complete protection time (Mosquito repellency) of 2.73, 71.66, 117.7 mins against these insects at 1% concentration [147].

**Protective effect:**

The effectiveness of pretreatment with Datura seed extract (DSE) to increase the survival following organophosphate (dichlorvos) poisoning was evaluated in rats. *Datura stramonium* seeds were collected, crushed, and then heated in water to make a 2mg/ml atropine solution (100 seeds contain approximately 6 mg of atropine or 0.007 mg/seed). Male rats were pretreated with 7.5 mg/kg DSE given as a single intraperitoneal injection 5 minutes prior to a subcutaneous injection of 25 mg/kg of dichlorvos. The endpoint was time to death recorded by a blinded observer. The 24-hour survival rate was 90% (95% CI = 56% to 100%) for the DSE-pretreated group and 10% (95% CI = 0% to 45%) for the control group. A statistically significant longer survival was recorded for the Datura-treated animals ( $p = 0.0002$ ). Median survival time was 22 minutes and 30 seconds for the control group and greater than 24 hours for the DSE-pretreated group [148]. The protective role of *Datura stramonium* leaves ethanolic extract against acute carbaryl toxicity was studied in rats. The animal with toxic dose of carbaryl showed mainly cholinergic effect, while those with toxic dose of *Datura stramonium* extract showed mainly anticholinergic effect symptom. The result of isobolographic analysis showed that the sort of interaction was highly antagonism. There was increase in the combined LD<sub>50</sub> of carbaryl and *Datura stramoinum* extract nearly double that of each one alone, this was due to high tropane alkaloids contents of *Datura stramonium* that abolish carbaryl cholinergic toxic effect by blocking the muscarinic receptors of parasympathetic nerve ending [149].

**Analgesic effects:**

The analgesic effect of alcoholic Datura seed extract was evaluated in acute and chronic pain using hot plate and formalin tests. The extract when intraperitoneally administered to the animals, they, dose dependently, alleviated the pain, and ED<sub>50</sub> was 25 and 50 mg/kg in hot plate and formalin tests, respectively [150].

**Antioxidant effect:**

The antioxidant activity of the plant extracts was assessed on the basis of the free radical scavenging effect, using modified DPPH method. *Datura stramonium* leaf extracts exhibited potent antioxidant property [142].

**Side effects and toxicity:**

The plant contraindicated in glaucoma, suspicion of glaucoma, paralytic ileus, pyloric stenosis, enlarged prostate, tachycardic arrhythmias and acute pulmonary edema [123]. Exposure of the foetus to *Datura stramonium* when a mother used it for asthma, could resulted in permanent damage to the foetus. Therefore *Datura stramonium* containing herbal remedy should be used with caution during pregnancy [151]. The calculated median lethal dose (LD<sub>50</sub>) of the ethanolic extract of *Datura stramonium* leaves was 3185.25 mg/kg bw in rats [149]. Diets containing 0.5, 1.58 and 5.0% *Datura stramonium* seed were fed to male and female rats in a 90-day subchronic toxicity study. *Datura stramonium* fed animals showed decreased body-weight gain, serum albumin and serum calcium, increased relative liver and testes weights, serum alkaline phosphatase and blood urea nitrogen. Female rats showed more marked responses to *Datura stramonium* seed than did males. In addition to the effects seen in both sexes, the females developed decreased serum total protein and cholesterol, and increased serum glutamic-pyruvic transaminase, chloride, red blood cell count, haemoglobin concentration and packed red cell volume. No histological lesions were associated with ingestion of *Datura stramonium* seed at 5.0%. The authors concluded that *Datura stramonium* seed at concentrations of 0.5% or more in the diet produced adverse physiological changes in rats [152]. The plant is a hallucinogenic plant, all parts of the plant can cause severe anticholinergic reactions that may lead to death in human [153]. The whole plant, particularly the foliage & seeds was toxic. It produced anticholinergic symptoms as a result of inhibition of central and peripheral cholinergic neurotransmission. Intoxicated patient usually presented with dry skin and mucus membranes, mydriasis with loss of accommodation that causes blurred vision and photophobia, altered mental status, hyperpyrexia, flushing, sinus tachycardia, urinary retention, myoclonic jerking, ataxia, impaired short-term memory, disorientation, confusion, hallucinations, psychosis, agitated delirium, seizures, coma, respiratory failure and cardiovascular collapse [154-156]. Because of the central nervous system effects of the belladonna alkaloids, the patient may be agitated, combative, confused, and disoriented. Initial intervention focuses on addressing those issues that protect the patient and their caregivers. In severe cases, physostigmine, a cholinesterase inhibitor, should be used to reverse anticholinergic toxicity. Physostigmine should be given intravenously to an adult in a dose of 0.5–2.0 mg at a rate of no more than 1 mg/min; a second dose may be administered if necessary. Children should receive 0.02 mg/kg intravenously and the rate should not exceed 0.5 mg/min [156]. Lethal dosages for adults starting at 100 mg atropine (15 to 100 g of the leaf, 15 to 25 g of the seed, considerably less for children) [123].

**Dose:**

60-185 mg powder of leaf and 60-120 mg powder of seed [157].

#### IV. CONCLUSION

The current review discuss the chemical constituents and pharmacological effects of *Datura fastuosa* and *Datura stramonium* to be utilize for many therapeutic purposes as a results of wide pharmacological activities.

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