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POTENTIAL AND PHARMACOLOGICAL ACTIONS OF DHATURA SAFED (*DATURA METEL* L.): AS A DEADLY POISON AND AS A DRUG: AN OVERVIEW

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ABSTRACT: Plants have great potential for the treatment and management of many diseases and have been used in many countries for the treatment of different diseased conditions. The medicinal value of plants lies in their bioactive phytochemical constituents that produce definite physiological actions in living beings. Many medicinal plants contain some chemical constituents that may cause harmful effects to humans if consumed in large quantities. Alkaloids occurring in large amounts could make plants poisonous despite its medicinal effects. *Datura metel* L., a member of the family Solanaceae, is known as Jimson weed and in Arabic known as "Jaozmasel", is one of the well-known folk medicinal herbs with wide application, Chemical investigation of which revealed its components as alkaloids, carbohydrates, and proteins among which alkaloids including scopolamine, hyoscyamine and atropine are the main active ingredients that exhibits various activities, such as anti-asthmatic, sedative, analgesic and anti-rheumatoidal effects. Besides of medicinal usage, *D. metel* is one of the most abused plants all over the world because of its unrestricted availability, especially in Africa, Southeast Asia and in India, mainly for spiritual or religious purposes with negative reports are far more than other psychoactive substances. Its over-dose or abuse produced poisonous effects similar to anti-cholinergic, delirium, mydriasis, mental confusion, psychosis, and even violent behaviors. In this review, various interesting findings of the medicinal value of *Datura metel* has been mentioned, apart from its toxicity and ornamental importance to prove it as a potent chemotherapeutic agent. Thus concerted efforts in the relevant areas are still necessary to establish rational and to prevent sustainable exploitation of the world's biodiversity.

INTRODUCTION: The universal role of plants in the treatment of disease is exemplified by their employment in all the major systems of medicine irrespective of the underlying philosophical premises.

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The use of single pure compounds, including synthetic drugs, is not without its limitations, and in recent years, there has been an immense revival in interest in the herbal and homeopathic systems of medicine, both of which rely heavily on plant sources.

Undoubtedly, the plant kingdom still holds many species of plants containing substances of medicinal value, which have yet to be discovered; large numbers of plants are constantly being screened for their possible pharmacological value [1]. WHO defined traditional medicine as the health

practices, approaches, knowledge, and beliefs incorporating plant, animal and mineral-based medicines, spiritual therapies, manual techniques, and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses or maintain wellbeing [2].

Concerning patients, despite the advances made in orthodox medicine, there has been an increasing interest in the complementary systems, particularly by those who have not been benefited from previous treatment, by those who have apprehensions concerning the toxicity and safety of modern drugs, and by those who benefit from the holistic approach [3]. The World Health Organization (WHO) estimates that about 80% of the world's population relies on herbal medicines for some aspects of primary health care [2], herbal medicine is a major component in all traditional medicines and a common element in homeopathic, naturopathic, traditional orients and Indian medicines. Governments of Third World countries, unable to sustain a complete coverage with Western-type drugs, have encouraged the rational development of traditional treatments. At present, the World Health Organization is taking an official interest in such developments in order to facilitate its aim of making health care available for all [3].

It has been reported that inappropriate use of traditional medicines or practice can have negative or dangerous effects and that further research is needed to ascertain the efficiency and safety of several of the practice and medicinal plants used by traditional medicinal systems. The growing interest in herbal medicine demands toxicity risk assessment of the various indigenous preparations used in the treatment of disease [4]. One such plant used for medicinal purposes, which may be toxic to biological organs such as liver and kidney, is *Datura metel*. There are many different species in the Datura genus. It is commonly known as Thorn apple belonging to the family Solanaceae, found growing as a weed in abandoned farmlands and/or dumpsites, but it is sometimes cultivated. Different parts (leaves, flowers, and seeds) of the plant can be used for many purposes and in several ways mostly for its psychoactive activities due to which Primarily has been used as an intoxicant and hallucinogen [5]. This could make the different parts of *Datura metel* to be abused by some youths who are more users and are prone to dangers of smoking and drug abuse. Globally it is considered as a poisonous plant when taken in large doses. The extract of Datura, however, is a potent poison, and the indiscriminate use of the plant parts may lead to delirium and acute poisoning that may lead to death. The chemical constituents include flavonoids, alkaloids, essential oils, saponins, terpenoids, tannins, phenolic compounds, *etc*. Many medicinal plants contain some chemical constituents that could cause harmful effects to humans if taken in large quantities. Alkaloids occurring in a large amount could make plants poisonous despite its medicinal effects [6].

It is one of the most important medicinal herbs used worldwide due to its anti-inflammatory property, and several studies also reported the use of the plant for its antibacterial and antioxidant activities [7]. With the latest advances in medicinal chemistry and knowledge of the biosynthetic route for the development of lead, compounds have opened new perspectives in the field of drug chemistry.

Dhatura Safed, Joz Mashel, (*Datura Metel* L.)
Taxonomic Classification:

Kingdom	:	Plantae
Division	:	Magnoliophyta
Subdivision	:	Angiospermae
Class	:	Magnoliopsida
Subclass	:	Asterids
Order	:	Solanales
Family	:	Solanaceae
Genus	:	Datura
Species	:	*Datura metel* (Datura fastuosa) [8]

Vernacular Names: Arabic: Joz mashel, joz mathel; Bengali: Dhutura, Dhatura; 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; Gujrati:Dhanturo, Dhaturo; Kannada: Umbem Madhunika; Korean: Huindogmalpul; Punjabi: Dattura, Tattur; Portuguese: Burbiaca; Spanish: burladora; Swedish: Indisk spikklubba, Unani: Dhatura, Persian: Tatura Siddha / Tamil: Oomatthai, Karuvoomatthi Sanskrit: Dhustura [9, 10, 11]. Dhatura safed (*Datura metel* L.) belongs to the family Solanaceae, the nightshade, which includes some 2,400 species [4].

It is one of the most interesting plants with hallucinogenic properties, and despite having this reputation as one of the darker hallucinogens, it has widely been used by societies historically in both the old world and the new and continues to be today. Local findings have shown that all the different parts of the plants are, either in the fresh form or in the sun-dried powdered form, used for its psychoactive property in South Western Nigeria. Literature have also shown that *Datura metel* is one of the most commonly abused local plants all over the world. Report of Drug Abuse in Nigeria by the United Nations Office on Drugs and Crime in 2007, have been shown 0.4% use of *Datura metel* out of the various narcotic and psychotropic substances of use in Nigeria when Cannabis took the largest proportion- 28% [5, 6].

Historical Overview: *Datura metel* was first documented in Sanskrit literature. Somewhat later, the Arabic physician Avicenna touted the importance of its medicinal applications and provided the exact appropriate dosage to the Arabs, who categorized the plant as a narcotic (Avery 1959). Ingesting more than therapeutic doses, it is very dangerous and can lead to insanity or even death, so great care must be taken with its consumption. Dhatura safed (*Datura metel*) flowers are often depicted in Hindu Tantric art, usually in connection with incarnations of Shiva. Dhatura safed also appears in ancient Tibetan and Mongolian texts, which has been demonstrated that this herb was indigenous to Asia prior to the fifteenth century.

In northern India, Dhatura safed (*Datura metel*) is widely known for inebriating purposes. Smoking the plant is regarded as pleasurable and not dangerous, whereas eating or drinking considered dangerous and is generally avoided. Yogis and Sadhus, in particular, smoke the seeds and leaves together with Cannabis indica and other herbs such as *Aconitum ferox* and *Nicotiana tobbacum*. In Tibet and Mongolia, this herb is used as incense in Vajramabhairava Tantra rituals intended to make the wealthy poor and to drive out certain spirits and energies. The fruits or seeds are also used to induce insanity. In China, the white blossomed variation of *Datura metel*, alba, is considered sacred, as it is believed that glistening dewdrops rained down from the heavens onto its flowers while the Buddha was giving a sermon. In ancient China, it appears that it was a popular practice to steep the aromatic flowers of *D. metel* in a wine before consumption. In Africa, *Datura metel* is used for criminal activities and in initiations. The seeds are used to poison victims so that they can be robbed. Seeds are added to the locally brewed beer to potentiate its effects [12, 13].

Pharmacognostical Properties: [10, 14, 15]

- *Datura metel* is a coarse, erect, branched, smooth or slightly hairy shrub or short-lived shrub, 0.5 to 2 meters high.
- Leaves are single, ovate to oblong-ovate, 9 to 18 centimeters long, with inequilateral base, pointed tip and irregularly and shallowly lobed margins.
- Flowers are white or nearly purple, axillary and solitary, with a large ovary. Calyx is green, about 5-8 cm long, cleft at the apex, cylindric, and divided into linear teeth. Corolla is white, about 12-16 centimeters long and the mouth about 8 centimeters in diameter, trumpet-shaped when fully opened. Stamens are 5, stigma 2-fid.
- Fruits are rounded capsules, green, about 3.5 centimeters in diameter and covered with stout, short spines, dehiscing at the apex when ripe forming an irregular suture.
- Seeds are numerous, finely pitted, closely packed, nearly smooth, and pale brown.

Distribution: In the open, waste places in and about settlements throughout the settled areas, widely found in Asia, Africa, England, India, and other tropical and subtropical regions in warm temperature regions, also cultivated also for ornamental purposes. Now pantropic in distribution [14, 15].

Parts Used: Leaves, flowers, fruits, seeds, roots, and barks. Collect newly opened flowers and sun-dry.

Properties: Bitter tasting. Considered anesthetic, anti-asthmatic, anti-spasmodic, anti-tussive, hallucinogenic, hypnotic. Leaves and seeds considered abortifacient. Plant as a whole has narcotic,

anodyne and antispasmodic properties analogous to those of belladonna [10, 11, 14]. Dried seeds are considered a more powerful soporific than the leaves. The plant has long been noted for its intoxicating and narcotic properties. An overdose causes violent narcotic poisoning. Studies have suggested anti-asthmatic, cytotoxic, antioxidant, anti-bacterial, anti-fungal, spasmogenic, anti-inflammatory, anti-gout, insecticidal, anti-fertility properties [15].

Dhatura Safed (*Datura metel* L.) in Unani Classical Literatures:

Mizaj (Temperament): Barid [4] Yabis [4] (Cold [4] Dry [4]) [16-19]

Muzir (Harmful Effects): It causes Junoon (Mania), Hizyan (Delirium), and fasad o fikr (Disturbance in cogitation) [16-19].

Musleh (Correctives): Badyan (Foeniculum vulgare), Filfil siyah (*Piper nigrum*), Ghee, Milk, shahad (Honey) [16-19].

Badal (Substitutes): Ajwain khurasani (*Hyoscyamus niger*), Afyun (*Papaver somniferum*), Shokran (Hemlok), Beek lufah (*Atropa belladonna*) [16-19].

Mikdad e khurak (Therapeutic Dose): 1-4 chawal (15- 60 mg), 30 -60- mg, 2-4 ratti (250-500 mg) [10, 20, 21].

Adulteration: Adulterants cited are the leaves of species of Xanthium (Compositae), Carthamus (Compositae), and Chenopodium (Cheno-podiaceae), which are, however, easily distinguished from the genuine drug [1].

Afa'al wa Istemal (Actions and uses) Mentioned in Unani Literatures: [16-21]

Leaves: Daf-e-Tashannuj (Anti-spasmodic), Musakkin-e-Alam (Analgesic), Mukhaddir (Anaesthetic). Used in Shaqeeqa (Migrain), Wajaul mafasil (Arthritis), Warm-e-pistan, Irqun nisha (Sciatica), Waja ul Bawaseer (painfull haemo-rrhoids), Junoon (Mania), Humma (Pyrexia), Juzam (Leprosy), Damameel, Busoor(eruptions), Kharish (Itching), Deedan e Ama'a (intestinal worms).

Fruits: Musakkin (analgesic), Muhallil (Anti-inflammatory). Used in Damameel (Boil), Busoor (Acne) *etc*.

Seeds: Habis-e-shadeed, Qabiz-e-shadeed (Astringent), Musakkin-e-dimagh (sedative), Mubahi (Aphrodisiac). Used in Nazla wa Zukam (cold and catarrah), Amraz e Dimagh(brain diseases), Sara (Epilepsy), Sahar (Insomnia), Jiryan (premature ejaculation), Waja ul Asnan(toothache), Wajaul Bawaseer (painful hemorrhoids), Zofe Bah (sexual debility).

Folkloric Uses: [12, 22-26]

- **Leaves:** Used a lot in resolutive and mitigant poultices. Smoked like stramonium in cases of dyspnea produced by asthma. Seeds and roots have the same uses; some considered the seeds to be more potent.
- **Asthma:** cut the dried leaves and stems into small slices and mix with an equal quantity of tobacco and roll into a cigarette and smoke 2 to 3 times a day.
- **Muscle Pains and Cramps Due To Rheumatism:** Boil the drug and obtain a concentrated decoction. Wash the painful parts with the warm decoction.
- **Gastric Pain:** 0.3 gm of dried material in decoction form uses.
- **Sprains, Contusions, Snakebites, Piles:** pounded fresh leaves and applied over afflicted areas.
- **Severe Cold Accompanied by Excessive Sneezing Similar to Hay Fever Symptoms:** powdered seeds (0.1 gm) in pills or loose form.
- **Psoriasis:** the oil prepared by boiling Datura seeds with sesame (linga) oil in alkaline water made from ashes of gabi. For the preparation of the alkaline water, simply dissolve the white ashes of gabi in water.
- For rheumatic swelling of the joints, lumbago, painful tumors, nodes, *etc*. the plant is applied locally as a poultice of leaves, epithem, fomentation or liniment.
- Leaves applied as an anodyne poultice**:** to inflamed breasts, or to check the excessive secretion of milk. A paste made from turmeric and datura fruit is also useful for the same.

- Leaves boiled in oil: or the oil itself is a useful application for hemorrhoids, anal fissures, and other rectal diseases associated with tenesmus.
- Juice of leaves Administered internally for the prevention of gonorrhea.
- Leaves steeped in spirits used to stimulate hair growth.
- Heated leaves applied to the spleen for intermittent fever.
- Malays used the leaves for boils, leg sores, hemorrhoids, rheumatism, swollen joints, and fish bites. Heated leaves also used enlarged spleen and swollen testicles.
- Juice of leaves dropped inside the ear for earaches.
- Salt and some amount of oil mix in a decoction of seeds induce severe vomiting and could be caused delirium.
- Oil of datura uses in apoplexy.
- Application of Paste of root with vinegar beneficial to Ascitis and inflammation.
- Due to the antispasmodic of bronchioles, fumigation of leaves prevents the Asthmatic episodes or used in chilam in place of tobacco and internally used with appropriate drugs.
- In Purulia (West Bengal) and Rajasthan, seeds use for the treatment of leprosy, leaf in guinea–worms.
- Ointment of seeds used for smallpox.
- Flowers digested in wine used as an anesthetic tincture.
- Lotion made from the flowers used for facial eruptions and feet swellings.
- In Cambodia, coconut oil is heated inside the fruit capsule, and the juice, with the oil, is squeezed into the ear.
- Plant used as an indigenous substitute for belladonna in the treatment of cataract and other eye diseases. Mydriatic potency has been reported - the watery extract of leaves is applied around the eyes, causing dilatation for two days. Also, dilatation may be achieved through an alcoholic extract of the seeds in four ounces of spirits, the tincture evaporated to dryness in a water bath, and the residue dissolved in an ounce of water.
- Roasted leaves applied to the eyes for ophthalmia.
- Powdered roots are rubbed on the gums for toothache.
- Roots used for the bites of wild dogs.
- Pill made from pounded seeds placed on decayed teeth to relieve toothaches.
- Roots boiled in milk and administered with clarified butter and treacle for insanity.
- Seeds pounded in oil used as an embrocation in rheumatism also applied to syphilitic swellings and boils.
- In Konkan, plant juice is given with fresh curds for intermittent fevers.
- In India, used for hysteria, insanity, diarrhea, asthma, skin diseases. For epilepsy, seeds of ripe fruit are burned and the smoke inhaled. Seeds used in small doses as an analgesic.
- In China, used for asthma, the dried leaves are rolled and smoked like a cigar. Dried flowers used for as anesthetic and prescribed for the treatment of asthma, cough, and convulsions.
- In Ayurvedic medicine, seeds used to treat skin rashes, ulcers, bronchitis, jaundice and diabetes
- In Brazil, used for making tea for its sedative effect. Flowers are dried and smoked as cigarettes.
- In Vietnam, dried flowers and leaves cut into small chips and smoked as cigarettes for asthma.
- In Bangladesh, leaves of *D. metel*, *Zizyphus mauritiana*, *Calotropis gigantea*, and bark of *Terminalia arjuna* are cut in pieces, boiled in water, then applied to paralyzed portions of the body 3-4 times a day and daily till cure.

Traditional Uses: There is evidence that *Datura metel* seeds have been used in ancient Indian medicine, modern Indian folk medicine, and Ayurvedic medical practices. The most common medicinal uses for Datura in these systems are for skin conditions, anxiety disorders, and respiratory ailments, along with a litany of other conditions.

The seeds are also sometimes used as a substitute for opium. In Java, the seeds are inserted into cavities or chewed to relieve dental pain. The plant is also used to treat skin diseases, colds, and anxiety in Traditional and Complementary Medicine. The plant is used to treat asthma in all regions of the world, either as smoke or incense.

The leaves and seeds of *Datura fastuosa* have been made official in the Pharmacopeia of India, and of these, a tincture, extract plaster, and poultice is directed to be made. The extract has been used successfully at the General Hospital, Madras, as a substitute for an extract of belladonna. The value of the plant as a remedy for painful syphilitic nodes, tumors, & C., is well known to many European physicians in India [12, 22, 27, 28].

Tincture Preparation: Tincture may be prepared by macerating two and a half ounces of bruised datura seeds in one pint of proof spirits, and left for seven days in a closed vessel, occasionally shaking it, and the mixture eventually pressed, filtered and measured, and sufficient spirit proof added to make one pint. The tincture induces sedative and narcotic effects similar to opium.

Leaf Extract Preparation: 100 grams of fresh leaves are crushed in a mortar to soften the leaves; add 5 litres of water to the crushed leaves and sieve after 3 days [12, 13, 22].

Others:

Hallucinogenic: Used as a ritualistic herb for its hallucinogenic effects. In Nigeria, a decoction of leaves or fruits added to drinks to achieve a "high," as a substitute for marijuana. It has been reported that the Moros intoxicated themselves with the plant before committing their massacres.

Poison: In India and Indo-China, reportedly used quite commonly with criminal intent. In China, often mixed with tea that hides the poison without raising suspicion.

Traditional Preparation: To create an inebriating beverage, equal parts of seeds and leaves of *Datura metel* and hemp flowers are added to the wine. In Asia, the leaves are often soaked in wine for inebriating effects. In Darjeeling, the seeds are used to fortify barley alcohol. They are also added to betel quids and smoked along with cannabis. In East India, women feed datura leaves to a specific species of beetle for a period of time and collect the excrement. They then mix this into the food of an unfaithful husband. In south-east Asia, the seeds are often mixed in with food or other herbs to create aphrodisiacs. In Malaysia, fifty seeds are considered a psychotropic dosage. One hundred seeds are considered dangerous and toxic. In India, 125 seeds have been reported lethal [12, 13, 22].

Therapeutic Actions and Uses: The dried leaves, flowers, and roots are used as narcotic, anti-spasmodic, anti-tussive, bronchodilator, anti-asthmatic, and as hallucinogenic. The plant was also used in a bite of mad dogs, otitis media, sores mumps pain, dropsy, anasarca, rigid thigh muscles, hemiplegia, epilepsy, convulsion, cramps, delirium, venereal diseases, syphilis, orchitis, epididymitis, and hydrocele, elephantiasis, skin diseases, hysteria, rheumatic pains, hemorrhoids, painful menstruation, skin ulcers, wounds, and burns. In Ayurveda, the plant was considered bitter, acrid, astringent, germicide, anodyne, antiseptic, anti-phlogistic, narcotic and sedative [22, 31, 32, 33].

Traditional Effects: All varieties of *Datura metel* contain psychotropic tropane alkaloids. *D. metel* contains the highest scopolamine content of the Datura genus. The entire plant also contains various withanolides (Lindequist 1992, cited in Ratsch 1998, 206).

The effects of *D. metel* vary by dosage and consumption method. When smoked in a blend with tobacco and clove oil, the effects are reported to be cheering, followed by a sleep with active dreams. In Tsongaland, the seeds are consumed, and then music is used to control the psychotropic effects, which include auditory hallucinations and powerful visions. Overdose usually results in delirium lasting for days, after which little is recalled. Criminals sometimes poison their victims with *Datura metel* seeds in order to sedate their victims and make them pliable to suggestion.

Toxicology: Datura poisoning is common in India, the seeds being usually employed; a few cases of poisoning by the leaves and root have, however, been reported. In the great majority of cases, the motive for its administration is the facilitation of theft, and when in India an individual has been first drugged and then robbed, it will usually be found that datura has been employed. A common form of theft by the aid of this poison is road robbery, and D. W. Center mentions the use in such cases of a hollow pestle, the cavity containing the seeds. Inversion of this, while pounding the masaleh or cookery, introduces the poison into the food without exciting suspicion. It rarely happens that there is any ground for suspecting homicidal intent in cases of datura poisoning; in fact, there seems to be a popular belief in this country that the drug is simply an intoxicant. As Harvey remarks, road poisoners sometimes partake with their victims of the drugged food, which they would hardly do if aware of the danger. Commonly when datura is used for criminal purposes in India, the poison is mixed with sweetmeats or food, but in exceptional has been mixed with tobacco given to the victim to smoke.

Datura is said to be used by vendors of native liquor, for the purpose of increasing its intoxicating power, the liquor being poured into a vessel that has been first filled with the smoke of the burning seeds. Suicidal poisoning by datura, if it occurs at all, is extremely rare. Accidental poisoning among children is occasionally met in India. Spices always used in Indian an intoxicant [12, 13, 22].

Phytochemical Constituents:

- Phytochemical screening of seeds yielded alkaloids, tannins, phlorotannins, cardiac glycosides, carbohydrates, flavonoids, amino acids, and phenolic compounds [30].
- A 50% ethanol eluate fraction of a macro-porous resin of the flower isolated a new compound, yangjinhualin A, and five known megastigmane sesquiterpenes [34].
- Yields tropane alkaloids such as hyoscyamine, scopolamine, anisodamine and anisodine.
- **Flowers:** Scopolamine, 0.5%; hyoscyamine, 0.04%; atropine, 0.01%.
- **Leaves:** Total alkaloid content is 0.426%, mainly as atropine and a small amount of hyoscyamine.
- Seeds contain 0.426% alkaloid, mainly hyoscyamine.
- Roots contain 0.35% hyoscyamine.
- The highest percentage of scopolamine accumulation in the root was after 16 weeks.
- The aerial parts, if compared with the root of the plant, usually accumulated relatively higher amounts of scopolamine and relatively lower amounts of atropine.
- Screening of leaves yielded alkaloids and steroids, with an absence of saponins and flavonoids. The concentration of Ca^{2+}, Mg^{2+}, Fe^{3+} and PO_3- were found to be $(4.28 \pm 0.05) \times 10^4$, 4 $(3.86 \pm 0.009) \times 10^4$, $(2.33 \pm 0.007) \times 10^4$ and $(4.65 \pm 0.06) \times 10^4$ ppm respectively [35].
- Methanol extract of whole plant isolated seven compounds *viz.*, pterodontriol B (1), disciferitriol (2), scopolamine (3), adenosine (4), thymidine (5), ilekudinoside C (6), and dioscoroside D (7) [36].
- Study of methanol extract of flowers isolated 10 new withanolides, with ametelins I-P (1-8), 1, 10-seco-withametelin B (9), and 12ß-hydroxy-1, 10-seco-withametelin B (10), together with seven known withanolides [37].
- **Mechanism of Action:** Atropine has a stimulant action on the central nervous system and depresses the nerve endings to the secretory glands and plain muscle. Hyoscine lacks the central stimulant action of atropine; its sedative properties enable it to be used in the control of motion sickness. Hyoscine hydrobromide is employed in preoperative medication, usually with papaveretum, some 30–60 min before the induction of anesthesia. Atropine and hyoscine are used to a large extent in ophthalmic practice to dilate the pupil of the eye.

Scientific Reports on Activities of *Datura Metel* L.:

- **Anti-asthmatic:** Quisumbing's compilation describes a mechanism for the plant's anti-

asthmatic effect. Asthma relief is attributed to depression or paralysis of the receptive mechanism of the parasympathetic nerves in the bronchi (a known action of solanaceous alkaloids), an effect confirmed by the relaxation produced by the alkaloidal extract from the smoke, on an isolated inter-cartilaginous portion of a bronchial ring previously contracted by pilocarpine.

When smoke is inhaled, it is possible the sticky, resinous substance may help by coating the mucosa and thus lessening the bronchial irritation. The study evaluated the potential of *Datura metel* in controlling immune response and ameliorating asthma in a mice model. Results showed potential of *D. metel* in ameliorating asthma symptoms by promoting naive T cell development and reducing activated T. cells [38].

- **Hypoglycemic / Anti-hyperglycemic:** seed powder of DM significantly produced a dose-dependent reduction of blood glucose at graded doses (25, 50, and 75 mg/kg, p.o.) when given to both normal and alloxan-induced diabetic rats [39].

- **Cytotoxic Withanolides:** Study on methanol extract of flowers of DM isolated 10 new withanolides with seven known withanolides. Compounds 1, 3, 4, and 6 exhibited cytotoxic activities against lung, gastric, and leukemia cancer cell lines [40].

- **Antimycotic:** The study has been reported the chloroform fraction of *Datura metel* to be endowed with antifungal activity against all three species of Aspergillus, *i.e., A. fumigatus*, *A. flavus* and *A. niger*. However, the cytotoxicity of the chloroform fraction was less than amphotericin B [40].

- **Anti-fungal:** Study of root and shoot extracts showed significantly suppression of growth of the target fungal pathogen, *Ascochyta rabiei*, the cause of chickpea blight diseases [41].

- **Herbicidal / Roots and Shoots:** Study for the root and shoot extracts of *Datura metel* reported towards containing herbicidal constituents in this herb that exhibited activity against *Phalaris minor* Retz., one of the most problematic weeds of wheat in Pakistan [42].

- **Toxicity Studies:** Suspensions of powdered leaf of *Datura metel* and *D. stramonium* on virgin female albino mice showed dose dependent reversible and irreversible changes. Generally, *D. metel*-treated mice showed less anatomical abnormalities than *D. stramonium*-treated mice and suggests *D. metel* could serve as a substitute for *D. stramonium* in drug development [43].

- **Antibacterial / Alkaloid:** A new antibacterial agent was isolated from *Datura metel* leaves with activity against *S. aureus*, *P. aeruginosa*, *P. mirabilis*, *S. typhi*, *B. subtilis* and *K. pneumonia*. Results support its use in phytomedicine for the treatment of asthma, cough, burns and wound healing in Nigeria [44]. Another studies have explored the antibacterial activity of methanol, n-hexane, ethyl acetate and chloroform extracts of plant species *Datura alba*. The extract from leaves, stem, roots and seeds were tested *in-vitro* against four bacterial strains by agar diffusion methods. The results suggested that leaf extracts have the highest inhibitory potential against *K. pneumoniae* and *E. coli*. The extracts from other parts showed moderate to low activities against the tested bacterial strains that reveal that the leaves of *D. alba* has the highest concentration of secondary metabolites and may prove to be an important candidate in pharmaceutical formulations against these two pathogens [45].

- **Deleterious Frontal Cortex Effect:** A study of aqueous leaf extract in adult Wistar rats caused deleterious effects on the frontal cortex of adult albino Wistar rats, with dose-depended vacuolations in the stroma of the brains of treatment group [46].

- **Sedation / Decreased Appetite:** A study of seed extract for analgesic activity showed insignificant results. The study showed a behavioral pattern of sedation and decreased appetite on the administration of the seed extract, attributed to action on u-type receptors in the CNS, which on stimulation have an

intrinsic potential to reduce the distress or the effective component of pains without any significant change in the intensity of the actual sensation. Another study revealed that 25 g/kg of methanolic crude extract induced behavioral sleep patterns (EEG) similar to that of thiopental in rats [47, 48].

- **Antimicrobial/Alkaloid:** In a study screening 17 different coastal medicinal plants for antibacterial and antifungal activity, *Datura metel* showed a wide range of antimicrobial activity against many fish pathogens. Results suggested DM can be used as a putative anti-microbial drug in the aquaculture maintenance. The antimicrobial activity of leaf, stem bark and root extracts of *D. metel* was evaluated by agar well diffusion method, against β hemo-lytic Streptococcus, *E. coli*, *P. aeruginosa*, and *S. aureus*. They were sensitive to the ethanol and aqueous leaf and stem bark extracts of *D. metel*. The root extracts of the plants had no antibacterial activity. The leaf extracts exerted potential effects on above isolates. The crude ethanol extract exhibited an inhibitory zone of more than 30 mm against P. aeruginosa. It was found that the inhibitory zones were more than 20 mm for *E. coli*, *S. aureus*, and β haemolytic Streptococcus according to previous reports. The MIC evaluated using the broth macro dilution method for these organisms was 20 mg/mL, which implied that the antimicrobial activity of the plant extracts depends on the solvent used for the extraction process [49, 50].

- **Spasmogenic:** Study of *D. metel* leaf and root extracts, scopolamine, and acetylcholine on isolated smooth muscle preparations. Leaf extract and scopolamine showed anti-spasmodic effects while the root extract and acetylcholine cause contracture in isolated rat uterus and whole rectum muscle. Results suggest a spasmogenic factor in the DM root extract [51].

- **Antioxidant:** Study the aqueous extract contained more phytochemical compounds than ethanol extracts. Antioxidant activities were higher in the plant leaf than the bark. Results suggest the plant as a natural source of antioxidants and phytochemical quality for antibacterial effectiveness [52]. Another study revealed that the extracts of the methanolic seeds exhibited the highest total phenolic content.

  At 1 mg/ml concentration, the DPPH radical scavenging activities of leaves and seeds were 66.4% and 63.3%, respectively and the inhibition percentages of ABTS radical were between 96.54% and 97.01%. Results suggest that *D. metel* extracts from both leaves and seeds could be used as potential sources of new antioxidant agents, useful in pharmaco-logical and food industries [53].

- **Anti-microbial:** Study evaluated aerial parts of *Datura metel* for antimicrobial activity against resistant pathogens of aquatic, human, and plant origin. Results showed antimicrobial property and potential for use in the treatment of infectious diseases caused by resistant pathogenic organisms [54].

- **Anesthetic / Seeds:** Study evaluated a methanolic extract of *D. metel* seeds as a potential oral anesthetic in dogs. The extract induced surgical anesthesia in dogs with recovery without complications. Results showed the seed extract to be relatively safe, inducing sleep similar to thiopentone sodium [55].

- **Anti-stress:** Withanolides from *D. fastuosa* possess anti-stress activity. When administered with diazepam, it exhibited an anxiolytic effect and inhibited the immobilization stress-induced depletion of adrenal cortisone. Adrenal cortisone help the organism to overcome annoying stimuli, but such responses can cause stress induced disorders. Detailed study of varying doses, duration, and mode of administration is essential to know the effectiveness as an anti-stress agent [56].

- **Anti-depressant Effects:** The neuropsycho-pharmacological effects of aqueous extracts of leaves and seeds of *Datura fastuosa*, were studied in rats and mice. The leaf and seed extracts at doses of 400 and 800 mg/kg increased motor activity, reduced the duration of barbituric sleeping slightly, 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 [57].

- **Flower Components / Antimicrobial:** Study of methanol extracts of *D. metel* flowers yielded four compounds. Components identified as acetic acid, trifluoro-, 2, 2-dimethylpropyl ester, 4- Trifluoroacetoxy-octane, and 1, 4-Cyclohexadiene, 1- methyl- have antimicrobial property [58].

- **Corrosion Inhibition of Mild Steel:** Study evaluated the corrosion inhibition potential of *D. metel* in acid medium on mild steel. Results showed significant corrosion inhibitive effect, probably through adsorption of phyto-constituents [59].

- **Anti-Inflammatory / Antioxidant / Leaves:** Study evaluated the *in-vitro* anti-inflammatory and antioxidant potential of leaves of *D. metel*. Results suggest considerable activity and suggests *in-vivo* studies [60].

- **Anti-Gout / Antiarthritis / Antioxidant / Leaves:** Study of a methanolic extract of *D. metel* showed more than 50% xanthine oxidase inhibitory activity *in-vitro*, comparable to standard anti-gout medicine, allopurinol. It also showed *in-vivo* hypouricemic activity against potassium oxonate-induced hyper-uricemia in mice [61].

- **Dry and Fresh Leaves Antimicrobial and Antioxidant Activity:** In a comparative study of phytochemical screening, antioxidant and antimicrobial capacities of different crude extracts from dry and fresh leaves revealed that both have a positive result for alkaloid, flavonoid, saponin and tannin compounds and all organic crude extracts from both fresh and dry leaves could be used as potential sources of new antioxidant and antimicrobial agents. Different organic solvents, including methanol, chloroform, hexane, ethyl acetate, and butanol were used to prepare the crude extracts from the fresh and dry leaves. The antioxidant activity of dry crude extracts as equivalent to DPPH (2, 2-diphenyl-1-picrylhydrazyl) was in the order of butanol > chloroform > ethyl acetate extract > methanol > hexane extract. However, the order of antioxidant activity for fresh organic crude extracts to DPPH was in the order of methanol > hexane > chloroform > ethyl acetate extract > butanol [9].

- **Anti-cancer / MCF-7 Cell Line:** Study evaluated a methanolic extract of *Datura metel* for anticancer activity against MCF-7 cell line. Results showed a leaf extract to have remarkable anticancer activity. Isolation of the compound contributing to the activity has a potential for a novel and natural phyto-medicine for the disease [62]. On evaluating the cytotoxic property of the methanolic extract of *D. metel* leaves against two isogenic human tumour cell lines, namely, HCT116 derived from human colorectal cancer and MCF 7 derived from estrogen-dependent human breast cancer cells. The cell proliferation assay was performed using tetrazolium (MTT) method. The methanolic extract exhibited significant cytotoxicity against HCT 116 cells with an IC_{50} 28.4 µg/mL. It exerted potent cytotoxicity towards MCF7 cells (IC_{50} 28.77µg/mL). That highlights the potential of *D. metel* in the treatment of breast and colorectal cancer [62].

- **Withametellins / Alkaloids / Cytotoxicity Against Cancer Cell Lines / Flowers:** MTT analysis of methanol extract of flowers yielded withametelins I-P, 12-ß-hydroxy-1, 10-seco-withametelin B and 1, 10-seco-withmetelin B. Withametelins I, K, L, and N exhibited cytotoxic activities against A549 (lung), BGC-823 (gastric) and K562 (leukemia) cancer cell lines, with IC_{50} ranging from 0.05 to 3.5 µM. Withamilin J exhibited moderate cytotoxicity against BGC-823 and K 562 [63].

- **Bio-pesticidal:** The study evaluated solvent extracts of *Datura metel* against larvae of gram pod-borer *Heicoverpa armigera*. The most active was the ethyl acetate fraction of the leaf extract, with a significant potential for use as a bio-pesticide for the control of destructive polyphagous agricultural pest-*H. Armigera* [64].

- **Insecticide / Leaves / Red Ants and Grasshoppers:** The study evaluated the leaf of *Datura metel* for acute toxicity at varying

concentrations on grasshoppers and red ants. The study showed a statistically significant dose-dependent decrease in the survival rate and an increase in the percentage mortality of red ants and grasshoppers in the presence of *Datura metel* (see constituents above) [35].

- **Antifertility / Seeds:** Study evaluated crude acetone extracts of seeds of *Datura metel* in female albino mouse for anti-fertility activity. A 2% seeds extract caused anti-implantation activity, and suggests a potential good source of anti-fertility compounds with minimal side effects after testing in human models [65].

- **Mineral Composition / Phytomonitor Potential:** The study evaluated the mineral compositions of leaf, seed, and flower of D. metal. Results yielded 12 elements, including Cu, Co, Ni, Mn, Zn, Fe, Na, K, Ca, Mg, P, and Al. Leaves were minerally richer than seed and flower counterparts. *Datura metel* was found tolerant for Co and Ni and may be used as phytomonitor for these elements in the soil [66].

- **Acetylcholinesterase Inhibitory Property / Withanolides:** The study showed the acetyl-cholnesterase inhibitory properties of *Datura metel* is due to the presence of withanolides. The methanolic extracts showed more significant dose-dependent inhibition of acetylcholinesterase [67].

- **Anti-termite / Datura:** The study evaluated the efficacy of extracts from *Datura metel*, local soap, and garlic in the management of Macrotermes belicosus. The synthetic insecticide, chlorpyrifos 0.1%, was used as control. In the laboratory, all the treatments had 75% - 100% repellence value with 100% mean insect mortality. On the field, only *D. metel* and chlorpyrifos were effective in preventing upsurge and rebuilding of termitaria. Results suggest an eco-friendly botanical potential for the management of termites in the field. (See leaf extract preparation above) [68].

- **Hallucinogenic / Seeds:** Study evaluated the hallucinogenic effect of aqueous seed extract of *D. metel* in male Wistar rats. Treated groups exhibited some behavioral changes: restlessness, aggressiveness, agitation, and disorientation, with a significant decrease in food and water intake. Results validate the action of *D. metel* on the central and peripheral nervous systems. The hallucinogenic effect may be due to the presence of the alkaloid scopolamine [69].

- **Neuro-Toxicological Effects / Leaves:** Use of leaves has been reported to cause adverse alteration in behavior. The study evaluated the acute neuro-toxicological effects of aqueous-methanol extracts of *D. metel* on total locomotive activity, motor coordination, and spatial memory in Y-maze in mice. The leaves extract caused neuro-toxicological effects in mice characterized by sedation and hypo-kinesia motor coordination impairment and disruption of short-term memory. The oral LD_{50} was greater than 2000 mg/kbw [70].

- **Effects on Visual System:** By oral administration of *Datura metel* on the visual system, as marker of toxicity using neurohisto-chemical it has been revealed that on the visual system of male Wistar rats caused neuro-degeneration of the occipital cortex, right lateral geniculate nucleus and right superior colliculus that are all indicative of necrotic process in the tissues with the involvement of lysosomal destruction. *Datura metel* is seen from the research work to be neurotoxic to the visual system in male Wistar rats [71].

- **Effects on Medial Prefrontal Cortex Histology:** The activity of ethanolic seed extract of *Datura metel* on Nissl substances, astrocytes, axonal and neuronal integrity of the medial prefrontal cortex was studied in rats. Extract was given 100 and 200 mg/kg b.w. 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 b.w. and 200 mg/kg b.w. 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 [72].

- **Nephrotoxic Effect:** Phytochemical screening and effect of *Datura metel* aqueous seed extract was evaluated in albino rats revealed the presence of phytochemicals which attributed the plant to its effects on the functional ability of the kidney as revealed by alterations in the kidney function parameters analyzed. Aqueous seed extract of *Datura metel* may suggest that there may be possible kidney damage that has occurred. Kidney function parameters are valuable tools for assessing the integrity of various parts of the kidney. The level of creatinine, electrolytes, urea and serum total protein could also provide significant information regarding the influence of a drug/compound/extract on the glomerular and tubular region of the kidney. The study therefore, revealed possible compromised in tubular and glomerular function leading to renal dysfunction following administration of *Datura metel* aqueous seed extract in rats and may have some nephrotoxic effect on the basic functions of the kidney investigated [73].

- **Effects on Kidney:** Effects of ethanolic extracts of leaf, seed and fruit of *Datura metel* on kidney function of male albino rats was investigated which indicate that the extracts mildly altered most of the biochemical parameters used in assessing kidney function as evaluated and showed its interference in kidney function. the histoarchitecture of the kidney of the animals show glomerular extrusion and collapse with resultant increased urinary space, dilated tubules, vacuolations in the epithelial lining of some of the tubules in the medulla and inflammatory cellular infiltration at some peritubular regions which shows that some parts of *Datura metel* possess mild negative effects, while some parts (in specific concentrations) could regulate the kidney function of male albino rats. This calls for caution in the use of this plant parts and therefore suggests that the use of this plant parts should be based strictly on pharmacological need [74].

- **Prenatal Exposure Effects:** During the prenatal stages the ethanolic extract of *D. metel* leaves can be used as a contraceptive because there is no signs of pregnancy in rats that were given 500 mg/kg body weight from the day of fertilization to parturition. It can also be used as an abortive drug when used in early period of gestation as it caused abortion in rats that were given 500 mg/kg body weight for the last 2 weeks of gestation period (821st day of gestation). It should be avoided in the late period of gestation, as seen in the histological observation of tissues of litters in Group C, there was retarded hippocampal development, neuronal damage and neural cell death that will affect the normal functioning of the hippocampus [75].

- **Bioefficacy against *Colletotrichum Gloeos-porioides* / Leaves:** Study Anthracnose disease caused by *Colletotrichum gloeos-porioides* is the most damaging disease causing reduction of flower set and yield losses in mango. Study evaluated the antifungal activity of various extracts *Datura metel* leaves against C. gloeosporioides. The chloroform fraction showed the best inhibition of the fungus. GC-MS analysis identified bioactive constituents *i.e.*, n-hexadecanoic acid, phytol, octadecanoic acid, oleic acid, o-xylene and cyclohexanol [76].

- **Anti-rabies / Seed:** The study evaluated Soxhlet and cold extracts of *Datura metel* fruit and seed extract for anti-viral activity against the rabies virus. *In-vitro* cytotoxicity assay was done using 3-(4, 5-dimethyl- thiazolyl-2)-2, 5-diphenyltetrazolium bromide assay. The Datura seed extract showed potential *in-vitro* antirabies activity. The study suggests further screening for *in-vivo* activity against rabies virus in a murine model [77].

- **Toxicity / Poisoning:** All plant parts are poisonous. It contains tropanic alkaloids in varying concentrations, mostly parasym-patholytic.

- Even a small dose is very poisonous because of the toxic tropane alkaloid or the presence of anticholinergic substances (scopolamine, hyoscyamine, and atropine), which can cause neural toxicity.

- In the Bicol area, reports of abuse by smoking an herbal cigarette of dried leaves and lightly fried seeds resulted in permanent mental and behavioral problems.

- **Common Side Effects:** Tachycardia (fast heart beat), a slight increase in blood pressure, dryness of the mouth and eyes, sedation.
- Early symptoms of poisoning are dilatation of the pupil, drowsiness, general weakness, with varying degrees of hallucinations.
- At toxic levels, tropanic alkaloids can cause hallucinations, delirium, mental confusion, coma, and death.
- Excessive doses can cause hallucinations, severe intoxication, and death. The window of the toxic and medicinal dose is quite small.
- With medium doses, recovery can occur in 12 to 24 h, however, with loss of memory and confusion that may last for days [35, 70, 71, 72].

CONCLUSION: Medicinal plants are becoming the most indispensable aspect of global health care, they are important for pharmacological research and drug development, not only when bioactive phytocompounds are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds. The present review gives brief information about the active constituents along with scientifically claimed medicinal and traditional uses of different parts of *Datura metel* for various human ailments, when applied both locally and through oral administration. The plant shows various types of activities such as analgesic, anti-inflammatory, anti-viral, and anti-diarrheal that may be due to the presence of the active chemical constituents. On the other hand, this plant has been used for several purposes and in several ways especially for its psychoactive activities, thus making the plant parts to be abused by the youths who are more prone to dangers of smoking and drug abuse. So, this plant should only be used therapeutically under the care of knowledgeable health care professionals. The adverse effects can be extremely severe and detrimental. Therefore, even in light of its many beneficial effects, the risk-benefit ratio should be always taken into consideration before using it.

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