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Datura Metel: A Comprehensive Review Of Its Ethnomedicinal Uses, Chemical Composition, And Pharmacological Applications

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Abstract

Datura metel, an herbaceous perennial widely distributed in tropical countries, has a rich history of traditional uses in ethnomedicine with diverse chemical compounds. Recognized for its medicinal properties, it has been traditionally utilized as a hallucinogenic, narcotic, anti-tussive, antispasmodic, bronchodilator, and anti-asthmatic agent. Its applications extend to addressing various conditions such as epilepsy, diarrhea, hysteria, skin diseases, rheumatic pains, painful menstruation, hemorrhoids, wounds, burns, and skin ulcers. In Ayurveda, *D. metel* is acknowledged as an astringent, bitter, germicide, acrid, anti-phlogistic, anodyne, narcotic, antiseptic, and sedative medicinal plant, playing a significant role in traditional medicine. The review emphasis traditional uses, chemical composition, and diverse medicinal applications of *D. metel*, providing valuable insights into its potential pharmacological relevance.

Keywords: Datura metel, phytochemicals, Traditional medicines, pharmacological activities

1. Introduction

Medicinal plants, with their abundant bioactive compounds, play a pivotal role in pharmaceutical research, serving as a crucial bridge between traditional healing practices and the development of modern drugs. Their rich array of beneficial components underscores their significance in advancing healthcare solutions (Saboon et al., 2019, Adedokun et al., 2023). One such plant species is *Datura* spp., a flowering medicinal herb that pertains to the Solanaceae family a globally cultivated plant recognized by names such as Indian thornapple, Hindu *Datura*, and metel, has firmly established its presence in Europe, Asia, America, South Africa, and various tropical and subtropical regions (Sharma et al., 2021). *Datura* spp. boasts captivating beauty with its large, trumpet-shaped flowers that display a spectrum of colors, making it a highly sought-after ornamental plant in warmer climates. This shrub-like annual or short- lived, shrubby perennial harbors a potent cocktail of tropane alkaloids, including scopolamine and hyoscyamine. Consequently, all parts of the plant are highly poisonous if ingested. The consumption of any portion of the *Datura* plant can lead to severe anticholinergic effects, causing toxicity. Notably, the entire plant possesses some level of toxicity, with the seeds identified as the most toxic. Furthermore, neither drying out nor boiling the plant eliminates its toxic properties (Firdaus et al., 2020; Monira and Munan, 2012).

2. Vernacular names

In Bengali, *Datura metel* L. is known as ”Dhutura” Inter- nationally, the plant is recognized by various names, such as tatura, jozmashel, and jozmathel in Arabic; yang jinhua in Chi- nese; and purple thorn- hoary ,thorn-apple, Hindu thorn-apple, and horn-of-plenty in English. Additionally, it is referred to as sadadhatura in Hindi, huindogmalpul in Korean, burbiaca in Portuguese, burladora in Spanish, and indisk spikklubba in Swedish (Al-Snafi, 2017).

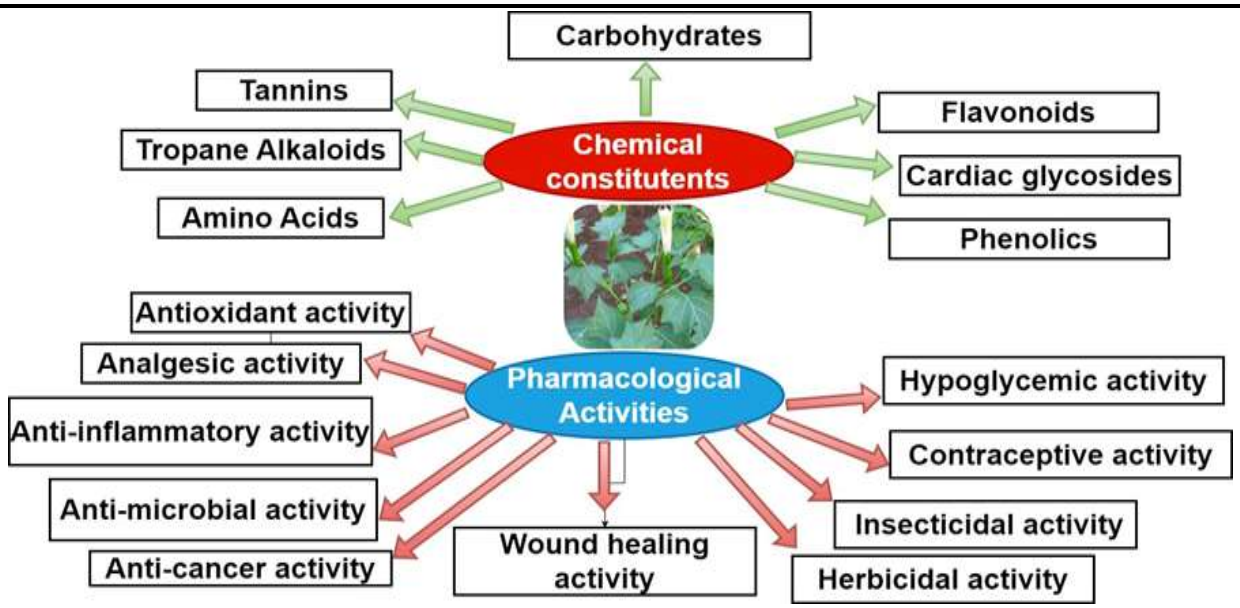

Figure 1: Graphical representation of chemical constituents and pharmacological activities of *D. metel*

3. Botanical Description

D. metel, a perennial herbaceous plant, branches out to ap- proximately 1.5 m in height. Its leaves are alternately arranged, dark green, shallowly lobed, and broadly ovate. Measuring around 10–20 cm in length and 5–18 cm in breadth, the leaves are petiolate with simple blades and sinuate or completely den- tate margins, covered in soft, short greyish hairs. The large, single, trumpet-shaped flowers, positioned in leaf axils or branch forks, showcase a delightful fragrance and a spectrum of colors, ranging from white to yellow and light to dark purple. These flowers contrast with the glandular or simple hair structures of the plant. The egg-shaped fruit is capsulated with short spines, measuring 5 cm in diameter, and typically exhibits irregular dehiscence with four valves. The dry capsule is unarmed and enclosed by remnants of the persistent calyx.*Datura* plants, including *D. metel*, are characterized by laterally compressed seeds with a curved embryo and generally possess 12 pairs of chromosomes (Islam et al., 2023, Monira and Munan, 2012).

Figure 2: Different parts of *D. metel* including (a) Flower, (b) Fruit, and (c) Seeds

4. Traditional Uses and Therapeutic Significance

D. metel, a plant traditionally employed in the treatment of asthma, convulsions, pain, and rheumatism, also possesses hypolipidemic properties (Pan et al., 2007; Arowora et al., 2016). Abundant in phenolic compounds, alkaloids, glycosides, triterpenes, and flavonoids, *D. metel* is a botanical reservoir of di- verse bioactive constituents (Jakabova´ et al., 2012). Believed to have originated in the Americas, *D. metel* is

extensively cultivated in tropical and subtropical regions, primarily valued for its aesthetically pleasing flowers (Glotter et al., 1973). The plant influence extends to East Asia, including India, where it holds significance in traditional Bangladeshi herbal medicine (Monira and Munan, 2012). In Ayurvedic medicine, it is utilized for analgesic, antiepileptic, anti-inflammatory, antioxidant, antiulcer, and protective properties against organophosphate pesticide effects Lawal et al.,2023; Sharma et al., 2021). Traditional Chinese Medicine in- corporates the flowers of *D. metel*, known as baimantuoluo, for addressing skin inflammation and Psoriasis (Su et al., 2017). Ayurvedic medicine further employs *D. metel* seeds to treat conditions such as skin rashes, ulcers, bronchitis, jaundice, and diabetes (Firdaus et al., 2020). In Brazil, the seeds are utilized to prepare a tea with sedative properties, and the dried flowers are smoked as cigarettes (Monira and Munan, 2012). The diverse applications of *D. metel* in various traditional medicinal practices highlight its significance and therapeutic versatility.

5. Chemical constituents

Phytochemical analysis of various parts of *D. metel* revealed the presence of diverse bioactive compounds. Seeds exhibited the presence of alkaloids, tannins, phlorotannins, cardiac glycosides, carbohydrates, flavonoids, amino acids, and phe nolic compounds, with a predominant alkaloid identified as hyoscyamine. Flowers contained scopolamine, hyoscyamine, atropine, yangjinhualin A, and megastigmane sesquiterpenes, including anisodamine and anisodine. Leaves contained atropine and hyoscyamine, while roots exhibited hyoscyamine and scopolamine (Afsharypuor et al., 1995). A comprehensive chemical investigation of the acidic methanol extract of the whole plant led to the isolation of seven compounds: pterodontriol B, disciferitriol, scopolamine, adenosine, thymidine, ilekudinoside C, and dioscoroside D (Mai et al., 2017). Tropane alkaloids, namely atropine, hyoscyamine, and scopolamine, were found throughout the plant, primarily concentrated in the leaves and seeds, and are known for their toxic properties. These alkaloids inhibit both central and peripheral muscarinic neurotransmission, resulting in the manifestation of anticholinergic syndrome (Adamse et al., 2014). Furthermore, a novel withanolide, daturilin, was isolated from the alcohol- soluble extract of fresh *D. metel* leaves. Its structure was identi- fied as 1-oxo-21,24S-epoxy-(20S,22S)-witha-2,5,25-trienolide Siddiqui et al. (1987). Additionally, the methanol extract of *D. metel* flowers yielded new withanolides, named withame- telins IP, 1,10-seco-withametelin B, and 12-hydroxy-1,10-seco-withametelin B (Pan et al., 2007). From the aerial parts of *D. metel*, three new withanolide glycosides named *Datura*metelins H–J, *Datura*taturin A, and 7,27-dihydroxy-1- oxowitha-2,5,24-trienolide were isolated from the methanol ex- tract (Ma et al., 2006). From an acidic methanol whole plant extract, five metelosides (A–E) and four known compounds were isolated, indicating the complexity of the chemical composition of *D. metel*. Additionally, seven glycosides, identified as daturglycosides 1–7, were isolated from the leaves of D. metel (Tan et al., 2020). Further chemical exploration of *D. metel* seeds led to the isolation of three new compounds, including a sesquiterpenoid and aliphatic glycoside, from an ethanol extract (Liu et al., 2020). Moreover, a novel phenolic glycoside, methyl 3,4-dihydroxyphenylacetate-4-O-[2-O--D-apisoyl-6-O- (2-hydroxybenzoyl)]--D-glucopyranoside, was identified in the roots of *D. metel* (Qin et al., 2021). These findings underscore the rich phytochemical diversity of *D. metel*, with potential implications

for its pharmacological and toxicological properties.

6. Pharmacological Profile

6.1. Antioxidant activity

D. metel and its derived compounds have demonstrated antioxidant properties. Crude ethanol and water extracts from various parts of the herb have been found to contain alkaloids, saponins, glycosides, phenols, and flavonoids. Ethanolic ex- traction displayed a scavenging capacity between 25.51% and 3.41%, while the aqueous extraction showed values between 49.30% and 23.82% (Akharaiyi, 2011). The hydroalcoholic ex- tract of *D. metel* seeds exhibited a slightly higher antioxidant action compared to the methanolic extract, with IC50 values of 25.78 µg/mL and 28.34 µg/mL, respectively (Alam et al., 2020; Al-Snafi, 2017a). Additionally, the aqueous extract of seeds and leaves of *D. metel*, estimated at 2.5 and 1.5 mg/mL, respectively, demonstrated antioxidant activity and prolonged cardiac arrest to 35 to 37 minutes, surpassing the normal sur- vival time of 14 minutes (Mbida et al., 2022). The n-hexane extract of *D. metel* contained tocopherols, primarily gamma- tocopherol, and exhibited the ability to neutralize 40% of the DPPH radical (Ramadan et al., 2007). Bhardwaj et al. (2016) demonstrated that the hydroalcoholic extract of the seeds exhibited slightly higher antioxidant activity than the methanolic extract. Specifically, the hydroalcoholic IC_{50} value was recorded at 25.78 µg/mL. Furthermore, Studies reported that the methanolic extract of *D. metel* displayed significant *in-vitro* xanthine oxidase inhibitory activity, exceeding 50%, com- parable to the standard anti-gout medicine allopurinol (Ganesh et al., 2015). Additionally, this extract demonstrated *in-vivo* hypouricemic activity against potassium oxonate-induced hyper-uricemia in mice. Another study, the IC_{50} values of methanolic and hydroalcoholic seed extracts of *D. metel* recorded using the DPPH model indicated slightly higher antioxidant activities for the hydroalcoholic extract (IC_{50} of 25.78 µg/mL) compared to the methanolic seed extract (IC50 of 28.34 µg/mL) (Alam et al., 2021, Al-Snafi 2017).

6.2. Anti-inflammatory activity

Lawal et al. (2023) conducted an evaluation of the methanolic extract of *D. metel* for its anti-Parkinson's disease (PD) behavioral effects *in-vivo* using haloperidol-induced cataleptic mice. The study suggests that the *D. metel* extract exhibits potential anti-inflammatory properties, as evidenced by its ability to improve motor coordination in mice with in- duced inflammation. Prasathkumar et al. (2022) investigated the anti-inflammatory potential of *D. metel* leaves, along with exploring its antioxidant and wound healing capabilities. Qin et al. (2021) identified a newly isolated glycoside from *D. metel* roots, methyl 3,4-dihydroxy-phenylacetate-4-O-[2-O--D- apisoyl-6-O-(2-hydroxybenzoyl)]--D-glucopyranoside, which demonstrated anti-inflammatory activity. Imo et al. (2019) tested ethanolic extracts of *D. metel* leaf, seed, and fruit on male albino rats and found a nephroprotective effect on kidney function.

6.3. Anti-microbial activity

6.3.1. Anti-bacterial effect

The ethanolic and aqueous extracts (20 mg/mL) derived from the leaf, stem bark, and roots of *D. metel* demonstrated an- timicrobial activity against various bacterial strains, including *Streptococcus dysenteriae*, *Pseudomonas aeruginosa*, *Bacillus cereus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococ- cus aureus*, and *Streptococcus hemolytic* (Akharaiyi, 2011). The study reported zones of inhibition produced by the leaves and stem bark extracts ranging between 12 and 35 mm, while the aqueous extract exhibited zones between 10 and 22 mm, and the ethanol extract demonstrated zones between 12 and 32 mm. Notably, the ethanolic extract showed significant sup- pression of Staphylococcus aureus among the tested bacteria. Bachheti et al. (2018) observed that the seed oil of *D. metel* exhibited inhibitory effects against at least 7 bacterial strains, with the highest inhibition zones and lowest minimum inhibitory concentration (MIC) observed for strains such as *Pseudomonas aeruginosa* (18 mm) and *Lactobacillus delbrueckii* lactis (19 mm). The antibacterial response was found to be positively correlated with the concentration of the seed oil. Furthermore, Prasathkumar et al. (2022) reported a significant (p ¡ 0.05) antibacterial effect and biofilm inhibition of the methanolic extract against *Bacillus subtilis*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Escherichia coli*, with inhibition percentages of 94%, 88%, and 92%, respectively. *D. metel* leaf, stem bark, and root extracts were tested for antimicrobial activity against hemolytic *Streptococcus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* using the agar well diffusion method. The crude ethanol leaf extract showed a significant inhibitory zone of over 30 mm against *P. aeruginosa*, while inhibitory zones exceeding 20 mm were observed for *E. coli*, *S. aureus* (Sakthi et al., 2011; Akharaiyi 2011). A novel antibacterial agent, 5,7-dimethyl-6'- hydroxy-3'-phenyl-3-amine-yne sitosterol, has been isolated from *D. metel* leaves. This compound exhibits activity against a range of bacteria, including *S. aureus*, *P. aeruginosa*, *P. mirabilis*, *S. typhi*, *B. subtilis*, and *K. pneumonia*. The results suggest its potential application in phytomedicine for treating conditions such as asthma, cough, burns, and wound healing (Okwu et al., 2009).

6.3.2. Anti-fungal effect

In a study, various fractions of *D. metel*, including chloroform, hexane, methanolic, and acetone, exhibited antifun- gal activity against *Aspergillus fumigatus*, *A. niger*, and *A. flavus*. The minimum inhibitory concentration (MIC) for the chloroform fraction was determined to be 625.0 µg/mL. Additionally, a pyrrole derivative, 2-(3,4-dimethyl-2,5-dihydro-1H-pyrrol-2-yl)-10-methylethyl pentanoate, isolated from the leaves, showed activity against *A. niger*, *Candida albicans*, *A. flavus*, *C. tropicalis*, and *A. fumigatus* (MIC value: 87.5 mg/mL) (Sharma et al., 2002). The antifungal properties of *D. metel* extracts from leaves and stems were explored, with the 3.5% concentration of leaf extract inhibiting *Rizoctonia solani* by 75%, surpassing the inhibitory effect of the stem extract at the same concentration (Hanif et al., 2022). In the context of chickpea blight diseases caused by *Ascochyta rabiei*, root and shoot extracts of *D. metel* were found to significantly suppress the growth of the fungal pathogen (Shafique, 2012).

6.4. Wound Healing activity

In a study, Nithya et al. (2011) evaluated the wound healing potential of *D. metel* using an ethanolic extract in Wistar albino rats. The results indicated a substantial enhancement in the wound breaking strength in the incision wound model when treated with the extract compared to control groups. Additionally, the wounds treated with the *D. metel* extract exhibited faster epithelialization, and the rate of wound contraction showed a significant increase compared to control wounds. These findings underscore the potential wound healing properties of *D. metel*. Another study, administering *D. metel* seed extract at a dosage of 7.5 mg/kg through intraperitoneal injection to male rats, prior to their exposure to a 25 mg/kg dichlorvos injection, led to significantly prolonged survival times. Animals treated with *D. metel* exhibited an impressive extension of survival, with an additional 24 hours compared to the non-treated group (Al-Snafi, 2017). Prasathkumar et al., (2022) conducted a study to explore the wound healing efficacy of *D. metel* leaves extract. The findings revealed that the methanolic extract of *D. metel* leaves exhibits significant potential as a therapeutic agent. Its application extends beyond treating metabolic diseases to encompass the effective management of superficial chronic diabetic wounds. The findings suggest that *Datura* may offer therapeutic benefits in the context of wound healing and protection against toxicological challenges.

6.5. Herbicidal activity

Javaid et al. (2008) evaluated n-hexane, methanol, and water extracts derived from both the root and shoot, each at concentrations of 5%, 10%, and 15% (w/v), exhibited pronounced herbicidal effects against *Phalaris minor* Retz. Furthermore, the root extracts, specifically the methanol (5–15%) and n-hexane (15%) extracts, demonstrated significant inhibitory effects on germination, as well as reductions in shoot and root lengths of the *Phalaris minor* Retz samples. These observations underscore the potential herbicidal properties of the plant extracts, suggesting their efficacy in controlling the growth and development of the targeted plant species.

6.6. Insecticidal activity

The methanolic extract of *Datura* seeds exhibited efficacy against *Helicoverpa armigera*. It has a significant impact on various developmental stages of *Helicoverpa armigera*, including larval, pupal, pupation quantity, and adult emergence (Monira and Munan, 2012; Al-Snafi, 2017). In another study evaluating the effectiveness of extracts from *D. metel*, local soap, and garlic in the management of *Macrotermes belicosus*, a synthetic insecticide, chlorpyrifos at 0.1%, served as the control. In laboratory settings, all treatments demonstrated repellence values ranging from 75% to 100%, with a 100% mean insect mortality. In field conditions, only *D. metel* and chlorpyrifos proved effective in preventing the upsurge and rebuilding of termite mounds Osipitan et al. (2013). These results suggest the eco-friendly potential of botanical extracts, particularly *D. metel*, for the management of termites in agricultural settings. Kuganathan et al. (2011) demonstrated dose-dependent decrease in the survival rate and an increase in the percentage mortality among both red ants and grasshoppers exposed to *D. metel* extract (Kuganathan et al., 2011).

6.7. Anti-cancer activity

Datura species are rich sources of withanolides, a class of compounds known for their substantial anti-cancer effects (Islam et al., 2023; Akhtar et al., 2020). In another study, three newly identified glycosides named *Datura*metelins H to J, along with established compounds *Datura*taturin-A and 7,27-dihydroxy-1- oxowitha-2,5,24-trienolide, were tested against HCT-116 (human colorectal carcinoma), revealing IC_{50} values of 3.2 ± 0.2 M (unspecified whether it was for all tested compounds or specific ones). Additionally, stem and root extracts of *D. metel* demonstrated cytotoxic actions against HepG-2 (human liver cancer cells) with IC_{50} values of 341.12 and 613.88 µg/mL, respectively. The root and leaf extracts were effective against HeLa (cervical carcinoma cells) with IC_{50} values of 348.35 and 267.76 µg/mL, respectively. Methanolic extraction of *D. metel* fruits exhibited an IC50 of 3 mg/mL against the Vero cell line in an in vitro cytotoxicity assay using the MTT method (Roy et al., 2016). Furthermore, a study by Tan et al. (2020) evaluated 24 compounds from *D. metel* against Hela, Ishikawa, and MGC-803 cell lines, identifying seven compounds with significant antiproliferative actions. These findings collectively highlight the diverse cytotoxic and antiproliferative potential of compounds derived from *D. metel* against various cancer cell lines. Another study, In the MTT analysis of the methanol extract of *D. metel* flowers, compounds were identified, including withametelins I, K, L, and N demonstrated notable cytotoxic activities against A549 (lung), BGC-823 (gastric), and K562 (leukemia) cancer cell lines, with IC50 values ranging from 0.05 to 3.5 µM. Withamilin J exhibited moderate cytotoxicity against BGC-823 and K 562. These findings suggest the potential of these compounds as candidates for further exploration in cancer therapy due to their cytotoxic effects against multiple cancer cell lines (Nazeema et al., 2014). The investigation conducted by Pan et al. (2007) on a methanol extract of the flowers of *D. metel* resulted in the isolation of 10 new withanolides. Among these, withametelins I, K, L, and N demonstrated cytotoxic activities against various cancer cell lines. Specifically, they exhibited cytotoxicity against K562 (leukemia), BGC-823 (gastric), and A549 (lung) cancer cell lines, with IC_{50} values ranging from 0.05 to 3.5 µM. Withamilin J, another withanolide isolated in the study, demonstrated moderate cytotoxic activity against K562 and BGC-823, with less cytotoxicity observed against the A549 cell line. These findings highlight the poten- tial anticancer properties of the isolated withanolides from *D. metel* flowers.

6.8. Hypoglycemic effect

Hypoglycemia is the state of having blood sugar (glucose) levels that are below normal. *D. metel* seed extract showed hypoglycemic action in alloxan-stimulated diabetic rats. The seed powder of *D. metel* 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 (Murthy et al., 2004)

6.9. Contraceptive Activity

Pandiarajan et al. (2012) demonstrated antifertility effects in acetone extracts from *D. metel* seeds in female albino mice. Administration of crude seed extracts at concentrations of 0.5%, 1%, and 2% resulted in varying degrees of anti-implantation activity. Notably, the 2% seed extract demonstrated 100% anti-implantation activity, showcasing the potential of *D. metel* seeds as a source for antifertility com- pounds with minimal side effects, warranting further investigation in other human models.

6.10. Analgesic activity

The seed extract of *D. metel* showed insignificant analgesic effects. This was attributed to the action of receptors in the central nervous system (CNS). Stimulation of these receptors has an intrinsic potential to reduce distress or the effective com- ponent of pains without causing a significant change in the intensity of the actual sensation, while the seed extract did not exhibit significant analgesic effects, it had other observable effects on behavior and appetite, likely due to its interaction with specific receptors in the CNS (Wannang et al., 2009). The aqueous extracts derived from both leaves and seeds of *D. metel* exhibited notable neurological effects in rats when administered at doses of 400 and 800 mg/kg. These effects included heightened motor activity in the brain, intensified catalepsy, antagonized ptosis, and a reduction in the duration of barbiturate-induced sleep. Additionally, the extracts demonstrated antidepressant characteristics at lower doses (Al-Snafi, 2017).

7. Conclusion and future perspectives

D. metel exhibits diverse pharmacological activities, at- tributed to its active chemical constituents. However, despite its therapeutic potential, *D. metel* has been historically utilized for psychoactive purposes, rendering its plant parts susceptible to misuse, particularly among youths engaged in smoking and drug abuse. This underscores the importance of caution in its usage. The plant should only be employed therapeutically under the supervision of knowledgeable healthcare professionals due to the potential severe and detrimental adverse effects associated with its misuse. While acknowledging the manifold beneficial effects of *D. metel*. This cautionary approach is necessary to mitigate the potential dangers and ensure the safe and informed application of the plant for therapeutic purposes.

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