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A REVIEW ON PHARMACOGNOSY, PHYTOCHEMISTRY AND PHARMACOLOGICAL ACTIVITY OF DATURA INNOXIA PLANT

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ABSTRACT:

Datura innoxia a wild-growing plant of the Solanaceae family, is widely distributed and easily accessible. It contains a variety of toxic tropane alkaloids such as atropine, hyoscamine, and scopolamine. In Eastern medicine, especially in Ayurvedic medicine, Datura. innoxia has been used for curing various human ailments, including ulcers, wounds, inflammation, rheumatism and gout, sciatica, bruises and swellings, fever, asthma and bronchitis, and toothache. A few previous studies have reported on the pharmacological effects of Datura innoxia however, complete information regarding the pharmacology, toxicity, ethnobotany and phytochemistry remains unclear. Ethnomedicinally, the frequent recreational abuse of Datura innoxia has resulted in toxic syndromes. Datura innoxia in the form of paste or solution to relieve the local pain, may not have a deleterious effect; however, oral and systemic administration may lead to severe anticholinergic symptoms. For this reason, it is very important for individuals, mainly young people, to be aware of the toxic nature and potential risks associated with the use of this plant. This comprehensive review of Datura innoxia includes information on botany, phytochemistry, pharmacology, toxicology and ethnomedicinal uses.

KEYWORDS

Datura innoxia, Jimsonweed, Phytochemistry, Ethnopharmacology Traditional uses, Pharmacology.

INTRODUCTION

Plants have been widely used in the treatment of human traumas and diseases. The demand for medicinal plant is increasing constantly due to growing recognition of natural product. Herbal medicine is an important part of both traditional and modern system of medicine[1]. Dartura innoxia is a annual plant from the Solanaceae family. It is

widely well known medicinal herb. It is a wild growing flowering plant and was investigated as a local source for tropane alkaloids which contain methylated nitrogen atom and include anticholinergic drugs atropine and scopolamine from ancient civilization it was traditionally used for religious visionary purposes through out world. An extract made from the leaves is taken orally for the treatment of asthma and sinus infections, and stripped bark are applied externally to treat swellings, burns and ulcers The incidence of Datura innoxia poisoning is sporadic with a cluster of poisoning cases in the 1990s and 2000s, the United States media reported some cases occurring mostly among adolescents and young adults dying or becoming seriously ill from ingesting. Some medicinal uses of the plant are its anti-inflammatory property of all parts of the plant, stimulation of the central nervous system, respiratory decongestion, treatment of dental and skin infections, alopecia and in the treatment of toothache. It is a hallucinogenic plant that causes serious poisoning. Consumption of any part of the plant may result in a severe anticholinergic reaction that may lead to toxicity and occasionally cause diagnostic difficulties. Cases of poisoning have been reported after eating the berries. Death may occur from heart failure after ingesting 125 seeds, because the seeds contain the highest concentration and has a rapid onset of action, thus may be potentially useful as an alternative to atropine for the treatment of the muscarinic symptoms of organophosphate toxicity and some of central anticholinergic effects. The wide distribution, the strong toxicity and the potential for occurrence in foodstuffs are responsible for the numerous incidents in humans[2]. Datura genus distributes over tropical and warm temperate regions of the world. About ten species of Datura are found, of which Datura anoxia and D. innoxia are most important drug plants. Datura has long been known as a medicinal plant and as a plant hallucinogen all over the world. Pre-historic use of Datura in medicinal and ceremonial rituals could be observed in aboriginal in Indian sub-continent[3]. The therapeutic activities of most plants are due to the presence of one or more of such components like alkaloids, tannins, saponins and cardiac glycosides. The phytochemical screening revealed the presence of saponins, tannins, steroids, alkaloids, flavonoids, phenols and glycosides[4]. Atropine and scopolamine are competitive antagonists of muscarinic cholinergic receptors and are central nervous system depressants. All parts of the plant are toxic, but the highest amount of alkaloids is contained in the ripe seeds[4,5]. Many cases of accidental poisoning by Datura innoxia have been reported when these plants were eaten accidentally[6].

MORPHOLOGY

Datura innoxia is an annual plant . The stem is herbaceous, branched and glabrous or only lightly hairy. By cultivation the plant reaches a height of about one meter[23-24]. The branching stems are spreading, leafy, stout, erect, smooth and pale yellowish green in color, branching repeatedly in a forked manner. Leaves are hairy, big, simple dentate, oval glabrous, apposite veins of leaves are pale black, stalked, 4-6 inch long, ovate and pale green. The upper surface is dark and grayish-green, generally smooth, the under surface paler, and when dried, minutely wrinkled . Datura innoxia bears funnel shaped, white or purple coloured flowers, with 5 stamens and superior ovary . The average length of flower is about 3 inches. The calyx is long, tubular and somewhat a swollen below and very sharply five angled surmounted by five sharp teeth. Corolla is funnel shaped. Stem stalk is pale blue or greenish white. Seeds are black, kidney shape and flat[25-26]. Fruits are as large as walnuts and full of thorns (hence the English name “thorn apple”) . The plant is strong narcotic, but has a peculiar action on the human which

renders it very valuable as medicines. The whole plant is poisonous and the seeds are the most active; neither dying nor boiling destroys the poisonous properties. The symptoms of acute Jimsonweed poisoning included dryness of the mouth and extreme thirst, dryness of the skin, pupil dilate ion, impaired vision, urinary retention, rapid heartbeat, confusion, restlessness, hallucinations, and loss of consciousness[2].




PHYTOCHEMICALS

The major tropane alkaloids hyoscyamine and scopolamine and several minor tropane alkaloids have been identified in Datura species. Typical examples of minor alkaloids in D. stramonium are tigloidin, aposcopolamine, apoatropin, hyoscyamine N-oxide and scopolamine N-oxide17-20. 6 ditigloyloxytropane and 7-hydroxyhyoscyamine are reported for the first time in this species (Das S et al., 2012). Distribution of hyoscyamine and scopolamine in D. stromonium was studied. The production of hycyamine and scopolamine in D. stromonium has been investigated in the different plant parts, at different stages of their life cycle. The maximum contents were found in the stems and leaves of young plants, hyocyamine being always the predominate component. These compounds were included in many pharmacopieas because of their anticholinergic activities (shagal MH et al., 2012). D. stramonium contain variety of alkaloids including atropine, hyoscamine and scopolamine (ivancheva S et al., 2006). Sixty-four tropane alkaloids have been detected from D. stramonium. Two new tropane alkaloids, 3-phenylacetoxy-6, 7-epoxynortropane and 7- hydroxyapoatropine were tentatively identified. The alkaloids scopoline, 3-(hydroxyacetoxy) tropane, 3- hydroxy-6-(2-methylbutyryloxy) tropane, 3-tigloyloxy-6- hydroxytropane, 3, 7-dihydroxy-6-tigloyloxytropane, 3- tigloyloxy- 6-propionyloxytropane, 3 phenylacetoxy-6,7- epoxytropane, 3-phenylacetoxy-6-hydroxytropane, aponor scopolamine, 3, 6 -ditigloyloxytropane and 7- hydroxyhyoscyamine are reported for the first time for this species. Other alkaloids found in D. stramonium include (strahil B et al.,2006): Hygrine, 3á, 6-Ditigloyloxy- 7-hydroxytropane, 6-Hydroxyhyoscyamine, Pseudotropine, 3á-Tigloyloxytropane, Hydroxy-6-tigloyloxytropane, Phenylacetoxytropane, 3-Tigloyloxy-6-(2- methylbutyryloxy) tropane, Hyoscyamine, 3-Tigloyloxy-6-isovaleroyloxy-hydroxytropane, Scopolamine, Tropinone, Scopine, 6-Hydroxyacetoxytropane, 3,6-Diacetoxytropane, 3-Tigloxyloxy-6-acetoxytropane, 3-Tigloyloxy-2- methylbutyryloxytropane, 3á, 6-Ditiglotoxytropane, 3- Acetoxy-6-isobutyryloxytropan, 3-(2-Phenylpropionyloxy) tropane, Littorine, 6-Hydroxyapoatropine, 3, 6- Ditigloyloxy- 7-hydroxytropane, 3-Tropoyloxy-6- acetoxytropane, 3,6-Dihydroxytropane, 3- Tigloyloxytropane, 3-Tigloyloxy-6- propionyloxy-7- hydroxytropane, 3á-Apotropoyloxytropane, Aposcopolamine, 3, 6-Ditigloyloxytropane, 3-(3'- Acetoxytropoyloxy) tropane, 3á-Tigloyloxy-6- hydroxytropane, Tropine, 3-Acetoxytropane, 3-Hydroxy-6- acetoxytropane, 3-Hydroxy-6-methylbutyryloxytropane, 3- Tigloloxy-6- isobutyryloxytropane, Aponorscopolamine, 7- Hydroxyhyoscyamine, Meteloidine, 3, 6- Ditigloyloxytropane. The phytochemical analysis of the plant revealed that D. stramonium contained saponins, tannins and alkaloids and glycosides. The secondary metabolites identified in the plant materials in the study of Banso A, Adeyemo S showed antimicrobial activity. (Banso A et al., 2006).

Pharmacological activity:

Antiasthmatic activity:

Datura innoxia in asthma treatment and possible effects on prenatal development was studied. Exposure of the foetus to Datura innoxia when a mother use it for asthma, will cause a continuous release of acetylcholine, resulting in the desensitization of nicotinic receptors, this could ultimately result in permanent damage to the foetus. Therefore we conclude that this African herbal remedy should be used with caution during pregnancy[7].

Anticholinergic activity:

The alkaloids found in Datura innoxia, are organic esters used clinically as anticholinergic agents. Jimson weed has been reported as a drug of abuse and has been involved in the accidental poisoning of humans and animals. Symptoms of acute jimson weed poisoning included dryness of the mouth and extreme thirst, dryness of the skin, pupil dilation and impaired vision, urinary retention, rapid heartbeat, confusion, restlessness, hallucinations, and loss of consciousness. The anticholinergic syndrome results from the inhibition of central and peripheral muscarinic neurotransmission[8-10]. The classic anticholinergic poisoning occurs by consumption of the tropane alkaloid-containing plant .Tropane alkaloids include hyoscyamine contained in leaves, roots, seeds; hyoscine, atropine (dl-hyoscyamine) and scopolamine (l-hyoscine) found in roots. They act as competitive antagonists to peripheral and central muscarinic acetylcholine receptors leading to a general paralysis of the parasympathetic innervated organs. Acute psychosis or delirium can occur due to its effect on the central nervous system as tertiary amines can inhibit CNS receptors .Coma and seizures are rare findings but raise concerns of extreme gravity .Teenagers with intentional ingestion of the plant represent most cases of Datura stramonium poisoning reported in the literature, as they seek for its hallucinogenic and euphoric effects. The entire plant especially the foliage and seeds, is toxic due to its content of tropane alkaloids. The contained atropine, L-hyoscyamine and L-scopolamine cause anticholinergic syndrome, which results from the inhibition of central and peripheral muscarinic neurotransmission

Acaricidal, repellent and oviposition deterrent properties:

The ethanol extracts obtained from both leaf and seed in Datura innoxia (Solanaceae) were investigated for acaricidal, repellent and oviposition deterrent properties against adult two-spotted spider mites under laboratory conditions. Leaf and seed extracts, which were applied and caused 98% and 25% mortality among spider mite adults after 48 h. These results suggest that Datura innoxia extracts could be used to manage the two-spotted spider mite[11].

Antimicrobial Activity:

The methanol extracts of D. stromonium and Datura inoxia showed activity against Gram positive bacteria in a dose dependent manner. Little or no antimicrobial activity was found against Escherichia coli and Psuedomonas aeruginosa[12]. The anti-microbial activity of combined crude ethanolic extract of Datura innoxia, Terminalia arjuna and Withania somnifera in cup plate diffusion method for antibacterial and antifungal activity. The extracts were subjected to screening to detect potential antimicrobial activity against Staphylococcus aureus, Bacillus subtilus, Escherichia coli, Klebsiella pneumoniae, Micrococcus luteus and Candida albicans with compare Ciprofloxacin standard drug[13].

Anticancer activity:

An integrated approach is needed to manage cancer using the growing body of knowledge gained through scientific developments. Thousands of herbal and traditional compounds are being screened worldwide to validate their use as anti-cancerous drugs. Datura innoxia in therapeutic dose of 0.05-0.10 g was used to cure cancer. Likely un safe produce vomiting, hypertension, loss of consciousness may lead to coma but may interact with anti-cholinergic drugs[14].

Anti inflammatory activity:

Coriandrum sativum (C. sativum), Datura innoxia and Azadirachta indica (A. indica) are traditionally used in treatment of inflammation. Ethanolic extracts of fruits of C. sativum, leaves of Datura innoxia Ethanolic extracts of fruits of C. sativum, leaves of Datura innoxia and A. indica were subjected to preliminary screening for anti-inflammatory activity in albino rats. All ethanolic extracts exhibited significant anti-inflammatory activity comparable to the standard drug diclofenac sodium against carrageenan induced rat paw edema method. Among these plant A. indica showed maximum anti-inflammatory activity per hour[15].

Larvicidal and mosquito repellent activities:

Ethanolic extracts of leaves of Datura innoxia were evaluated for larvicidal and mosquito repellent activities against Anopheles stephensi and Culex quinquefasciatus. The LD_{50} values for larvicidal activity were found to be 86.25, 16.07 and 6.25 mg/L against Aedes aegypti, Anopheles stephensi and Culex quinquefasciatus respectively. The ethanolic leaves extract of D. innoxia provided complete protection time (mosquito repellency)[16].

Pesticide toxicity:

Extract of Datura innoxia was effective in countering the toxicity of the cypermethrin pesticide toxicity[17].

Antifungal activity:

Antifungal activity of a concoction brewed from Datura innoxia, Calotropis gigantea, A. indica (neem) and cow manure (T1) followed by methanol-water (70/30 v/v) extracts of Datura innoxia, Calotropis gigantea and A. indica T2 against Fusarium mangiferae. The study proved that the concoction-brewed compost T1 is effective, inexpensive, easy to prepare and constitutes a sustainable and eco-friendly approach to control floral malformation in mango when it is sprayed at bud break stage and again at fruit set stage[18].

Toxicity studies:

Toxicity studies of ethanol extract of the leaves of Datura innoxia in rats. Two doses of 50 and 200 mg/kg of the extract were administered to the rats for five weeks. Parameters studied were the indices of liver and kidney function and some biochemical and haematological parameters. Feed intake, final body weight, serum AST, ALT, billurubin, total protein, urea and the electrolyte studied were not affected by the extract administration. Serum creatinine levels were however significantly raised in the rats administered with ethanol extract at the dose of 200 mg/kg body weight. The biochemical and haematological parameters were also affected[19].

The effects of acute, subacute and chronic administration of alkaloids atropine and scopolamine, the main constituents of the active principle of Datura innoxia with toxic properties, were studied in male Albino Wistar rats. After acute i.p. administration of dose 100 mg/kg of total alkaloids to the seeds of Datura innoxia, there were no remarkable changes in general appearance and no deaths occurred in any experimental group. Twenty four hour after total alkaloids of seeds, a significant reduction in indices of liver, spleen brain and kidney function and some biochemical and haematological parameters were observed. The red blood cells, hematocrit, hemoglobin and white blood cells were significantly higher in the treated groups than the control group. Subacute study for four weeks showed no resulting mortality or signs of toxicity. In chronic study, the synthetic alkaloids administered i.p. at daily doses of 4.2 mg/kg of atropine and 1.6 mg/kg of scopolamine, did not produce death. However diarrhoea and hypoactivity were observed. The relative weight of liver was significantly less than that of the control group[20]. The effects of acute, subacute and chronic administration of alkaloids atropine and scopolamine, the main constituents of the active principle of Datura stramonium, with toxic properties, were studied in male Albino-Wistar rats. After acute i.p administration of dose 100 mg/kg (1/4 DL50) of total alkaloids to the seeds of D. stramonium, there were no remarkable changes in general appearance and no deaths occurred in any experimental group. 24 h after total alkaloids of seeds, a significant reduction in tissues (liver, spleen and brain) was observed. The red blood cells (RBC), Hematocrit (HCT), Hemoglobin (HGB) and white blood cells (WBC) were significantly higher in the treated groups than the control group. There were no statistical differences in Glutamic-oxaloacetic transaminase (GOT), Glutamic-Pyruvic Transaminase (GPT) and alkaline phosphatase (ALP) observed between groups. Histological examination of liver showed no histopathological changes. Subacute study for four weeks showed no resulting mortality or signs of toxicity. The relative weight of kidneys showed a significant decrease, however, these doses of synthetic alkaloids (5.2 mg/kg of atropine and 2.6 mg/kg

of scopolamine) produced significant increase of lungs in comparison with the control group. RBC, HBG, HCT and PLT values of control group were significantly higher than those of the treated group. The enzyme activities of GOT, GPT and ALP were significantly increased. The microscopic examination of liver showed normal conservative lobular architecture and necrotic areas. In chronic study, the synthetic alkaloids administered i.p at daily doses 4.2 mg/kg of atropine and 1.6 mg/kg of scopolamine, did not produce death, However the diarrhoea and hypoactivity were observed. The relative weight of liver was significantly less than that of the control group. The haematological analysis revealed a significant decrease in RBC, HCT, HBG and WBC and we observed manifold centrolobular necrotic areas, and blood congestion and dilated central veins in treated groups.

Biopesticide with antifungal activity:

Biopesticides (leaf extracts) obtained from eight plants (Vitex negundo, Polyathia longifolia, Vinca rosea, With ania somnifera, Lawsonia inermis, Adhotoda zylanica, Datura innoxia and Hyptis suaveolens) showed antifungal activities against the fungal pathogen (Fusarium oxysporum) of wilt of pigeon pea . Both in vivo and in vitro higher concentration of ethanolic leaf extracts of all eight plants showed complete inhibition in linear growth and sporulation in test fungi[21].

Protective agent in severe organophosphate toxicity:

Treatment of patients following an organophosphate (OP) exposure can deplete a hospital's entire supply of atropine. Given the possibility of multiple severe exposures after a terrorist attack using OP nerve agents, there exists a need for either greater atropine stores or the development of alternative antidotes. Jimsonweed (Datura innoxia) contains atropine and other anticholinergic compounds and is common and readily available. It is used recreationally for its central anticholinergic effects and is easy to be made into an extract by boiling the crushed seeds. The extract has rapid onset of effects and may be useful for treatment of OP poisoning. Pre treatment with Datura innoxia extracts significantly increases[22].

Acknowledgement

This review gives information about the bioactive constituents, pharmacological activity , along with the scientifically claimed medicinal uses of Datura innoxia. Several alkaloids, carbohydrates, fat, proteins and tannins have been tested and performed in Datura innoxia. The plant shows various types of activities such as analgesic and anti-asthamatic activity Acaricidal, repellent and oviposition deterrent properties, antimicrobial activity, anticancer activity, antiinflamatory activity, Larvicidal and mosquito repellent activities, antifungal activity, Pesticide toxicity, Anticholinergic activity, which may be due to the presence of the investigated active chemical constituents. The pharmacological studies so far have been performed in vitro and in vivo. Therefore, there is a need of investigation and quantification of phytoconstituents and pharmacological profile. Toxicology profile will provide increasing in the haematological parameters. since based on the above scientific proof , the active

constituents of datura innoxia which are hyoscine scopolamine hyosamide was formulated to treat the different ailments such as kanakasava.

Kanakasava: contains purified datura that is mainly aimed at treating and preventing of respiratory disease the formulation also provides relief from acute asthma.

Hyosamine butyl bromide: it is also known as scopolamine butyl bromide which shows the anticholinergic activity used to treat abdominal pain and different types of spasms.

Hyosine hydrobromide tablet:used in travel sickness and belongs to anticholinergic medication.

Hysoscyamine sulphate : it shows anticholinergic activity usually prescribed for treatment of colic in infants.

Scopolamine transdermals: the skin patches is used to prevent nausea and vomiting caused by motion sickness.

Scopolamine tablet: used to treat symptoms of irritable bowel syndrome and motion sickness.

Hence there are limited formulation done in datura using active constituents such as hyosine ,scopolamine ,hyosinamide further formulations and studies can be done by using the following constituents of datura Acetic-acid Plant Acetione Leaf Aconitic-acid Plant Alkaloids Fruit 4,600 ppm; leaf 2,500 - 5,100 ppm Plant 1,000 - 5,000 ppm; root 2,100 ppm; Seed 1,000 ppm; stem 2,500 - 2,600 ppm Alpha-ketoglutaric-acid Plant Apoatropine Plant Ascorbic-acid Plant Atropamine Plant Atropine Plant Atropinesterase Plant Butanol Leaf 51 Caffeic-acid Plant Capsidol Plant Citric-acid Plant 750 ppm Cuscohygrine Leaf Datugen Plant Datugenin Plant Ditigloyl-d-dehydroxytropane Plant Eo Leaf 450 ppm Esculetin Plant Ethanol Plant Fat Seed 150,000 - 300,000 ppm Ferulic-acid Plant FluroDaturatine Plant Formaldehyde Plant Formic-acid Plant Fumaric-acid Plant Galactose Leaf Glucose Leaf Glycolic acid Plant HomofluroDaturatine Plant Hyoscine Leaf550 - 2,500 ppm; seed 1,200 - 5,000 ppm Hyoscyamine Seed 80 - 490 ppm Isobutyraldehyde Plant Lactic- acid Plant Lignoceric-acid Plant Linoleic-acid Seed 22,500 - 45,000 ppm Malic acid Plant 2,120 ppm Meteloidine Leaf Methanol Leaf Neochlorogenic-acid Plant Nicotine Plant Oleic-acid Seed 93,000 - 186,000 ppm Palmitic-acid Seed 15,000-30,000ppm Potassium-nitrate Plant Propionaldehyde Plant Protein Seed 140,000-194000ppm Putrescine Plant Rutin Plant Scopin Plant 52 Scopol Seed5 3-3050 Scopoletin Plant Scopolin Plant Sitosterol Seed Sophorose Leaf Stearic-acid Plant Succinic-acid Plant Tannin Plant 70,000 Tigloylmeteloidin Plant 5-25ppm Umbelliferone Plant Vitastramonolide Plant.

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