



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203





Human Journals

Review Article

April 2022 Vol.:24, Issue:1

© All rights are reserved by Dr. Manju Yadav

A Review on Cholinergic Activity of Physostigmine on Devils Trumpet

	IJPPR INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH An official Publication of Human Journals	
Dr. Manju Yadav		
<i>M.O. (Ayurveda), Govt. Ayurveda Dispensary Mainpur (Mundawar) Alwar, Rajasthan, India.</i>		
Submitted:	25 March 2022	
Accepted:	31 March 2022	
Published:	30 April 2022	

Keywords: Dhatura, anticholinergic syndrome, antimuscarinic, Ayurveda, Purification

ABSTRACT

Dhatura commonly known as thorn apple or jimson weed, belongs to the family. The alkaloids present in datura exert both central as well as peripheral actions. Ingestion of a small dose will stimulate central nervous system causing excitement and restlessness as it firstly stimulates the higher centres then the motor centres and further lead to depression and paralysis of medulla, the respiration is first stimulated and then depressed and the heart centre is stimulated, since the process occurs systematically over the period the vitals become unstable with the larger doses causing depression delirium coma and finally the loss of life. The anticholinergic syndrome results from competitive antagonism of acetylcholine at central and peripheral muscarinic receptors. The severity ranges from mild symptoms to life-threatening Atropine is usually an anticholinergic (antimuscarinic) drug Differential diagnoses to consider in patients with suspected anticholinergic disease. The present review focuses on a lot of descriptions available in various Ayurvedic texts, it is a wild plant having nine other species with a wide range of medicinal and pharmacological properties. In Ayurveda, it is clearly mentioned that the drug Dhatura metal must be used exclusively after purification. Purification plays a vital role in reducing the adverse effects caused during internal administration.



ijppr.humanjournals.com

INTRODUCTION

The autonomic nervous system is divided into three parts: the sympathetic, parasympathetic and enteric nervous systems. The enteric nervous system receives input from the nervous and parasympathetic nerves and cannot act on its own. The autonomic nervous system controls muscle activity (visceral and vascular), the rate and force of heart contractions, and various metabolic, endocrine and exocrine processes. The main neurotransmitters are acetylcholine and norepinephrine. Preganglionic neurons are cholinergic. Although excitatory muscarinic acetylcholine receptors are also present in postganglionic cells, ganglion transmission occurs via nicotinic acetylcholine receptors. Postganglionic parasympathetic neurons are cholinergic, most postganglionic sympathetic neurons are noradrenergic, and a few are cholinergic (like sweat glands).

Cholinimimetic drugs are divided into two direct-acting drugs and indirect drugs. Direct agents bind and activate muscarinic and/or nicotinic receptors, while indirect agents inhibit acetylcholinesterase, which hydrolyses acetylcholine. Therefore, the concentration of acetylcholine at the synaptic cleft and neural effector junctions increases and stimulates the receptors.

Most cholinomimetic poisonings produce direct symptoms within 30 to 60 minutes after ingestion. Common symptoms include salivation, lacrimation, nausea, vomiting, headache, visual disturbances, diarrhoea, bradycardia, and hypotension. Similar effects can be seen with organophosphate and carbamate insecticides. Bradycardia, hypotension, and syncope are more common in organophosphate poisoning. Alkaloids are plant metabolites with alkali-like chemical and chemical activity and nitrogen-containing ring structure. Since ancient times, people have used plants containing alkaloids for medicinal and recreational purposes¹. There are some medically important alkaloids such as opioids. The three main pharmacological groups of amines alkaloid² are anticholinergic tropane alkaloids (also known as bicyclic alkaloids or belladonna alkaloids), hallucinogenic alkaloid amines, and excitatory alkaloid amines.

Plants containing the tropane alkaloids scopolamine, hyoscyamine and atropine include:

1. *Hyoscyamus niger* (henbane)
2. *Datura* species (jimson weed, angel's trumpet, thorn apple)

3. *Mandragora officinarum* (mandrake)

4. *Atropa belladonna* (deadly nightshade)

Datura belongs to the family of Solanaceae, in India. The common varieties of *Datura fastuosa* are *Datura alba* (White flowers) and *Datura niger* (Purple flowers).

DATURA

This herb is also known by the following names: Angel's Trumpet, Apple of Peru, Devil's Apple, Devil's Weed, Green Dragon, Jamestown Weed, Jimson Weed, Locoweed, Moon Lily, Stinkweed, and Thorn Apple.

Datura Metal commonly known as thorn apple or jimson weed, belonging to the family Solanaceae has frequently been employed in traditional medicine to treat a variety of ailments. It has been used as a hallucinogen combined with hallucinogens to induce hallucinations. Because of its physical and psychological effects, it can never be a serious drug of abuse and is often viewed as unpleasant, causing serious and long-lasting effects with a fatal effect³.

The seeds and flowers of *Datura* herb contains alkaloids like Hyoscyamine, Scopolamine and atropine which are highly toxic but found therapeutically essential as well. The poisonous substance (alkaloids) possesses anticholinergic effects like tachycardia, hyperthermia, mydriases etc., which can be resolve by administration of physostigmine as an antidote. Medico legally it has been found that the medicine is being used as a stupefying agent mixed in Prasad by the robbers for robbery, kidnapping, and also as homicidal as well as suicidal.

Angel's trumpet is a deciduous, bushy, soft herbaceous perennial plant in the nightshade family (Solanaceae), usually grown as an annual. It grows 3 to 4 feet tall and wide and is native from Columbia to Texas, where it is usually found in sunny, disturbed areas and sandy waters. Angel's trumpet tolerates average soil but prefers rich, moist, well-drained soil and full sun to partial shade. It will tolerate alkaline or sandy soil but does not do well in full shade. It is winter hardy to USDA Zone 9 to 10. Most plantings of angel's trumpet are nursery plants; however, it can be started indoors from seeds about 6 to 8 weeks before the last spring frost and set plants out after that date. Plants tend to sprawl and should be spaced about 3 feet apart or staked and supported. Deadheading flowers is not necessary, but self-seeding may occur if the plants are not deadheaded. Seeds can be collected and saved for planting in the

following spring. Container plants can be cut back and overwintered indoors in a sunny window. The large flowers are shaped like trumpets (hence the common name), are slow to develop and bloom, and have an exotic fragrance; however, the bruised leaves also give off an odour that some consider unpleasant. Each flower unravels in the evening from an unusual cigar-shaped flower bud and fades by noon the following day. All parts of the plant are highly toxic if consumed. The species of *Datura* are sometimes confused with those of *Brugmansia* (also called angel's trumpet), but *Datura* flowers face upward, whereas *Brugmansia* flowers are pendulous. Angel's trumpet is perfect for a nighttime garden. It grows well in a container on a patio or planted as a specimen or border in a bed.

Mode of action

The alkaloids present in *datura* exert both central as well as peripheral actions. Ingestion of small dose will stimulate 13 central nervous systems causing excitement and restlessness as it firstly stimulates the higher centres and then the motor centres and further lead to depression and paralysis of medulla, the respiration is first stimulated and then depressed and the heart centre is stimulated, since the process occurs systematically over the period of time the vitals become unstable with the larger doses causing depression delirium coma and finally the loss of life. Its peripheral effects are due to blockage of cholinergic fibres with resultant parasympathetic paralysis. Therefore, they inhibit secretion of sweat, saliva, mydriasis and stimulate the heart-regulating centre.⁴ Toxicity evaluation The toxicity studies of ethanol extract of the leaves of *D. stramonium* in rats were done by Giadado et al. (2007). Two doses administered (50 and 200mg/kg) extract to the rats for 5 weeks. Parameter studies were the indices of liver and kidney function and some biochemical and haematological parameters. Feed intake, final body weight, serum AST, ALT, Bilirubin, total protein, urea and electrolyte studies were not affected by the extract administered. Serum creatinine levels were however significantly raised in rats administered with ethanol extract at the dose of 200mg/kg body weight. The biochemical and haematological parameters were also affected.

Clinical Evaluation

Series of experimental 18 including clinical trials have been conducted and an ample are still carried on over the period of time, in order to prove it therapeutically. It 8 has been demonstrated to have better pharmacological potential with a great utility and practice as folklore medicine. Though the drug is established as poisonous plant 19 in the Ayurvedic manuscript but having good therapeutic properties after Shodhan process, on Shodhana the

poisonous properties diminishes and therapeutic properties get improved so in Ayurvedic preparations we use Shuddha Datura. There are so many generic preparations available in old text to treat various diseases like gastric ulceration, rhinitis, fever, asthma, fungal infections etc. On evaluating the medicinal effects, we found that the drug proved to have wide range of actions as Antibacterial⁶, Antifungal⁷, Antioxidant⁸, Herbicidal⁹, Antiviral¹⁰, Antiasthmatic¹¹, act on organophosphorus poisoning¹² etc. therefore, the drug can be used with various combinations to cure an ample number of diseases with correct dose and formulations after purification.

Purification of Datura seeds¹³

Datura seeds are tied in a cloth to create the Potali, then soaked in milk, boiled in Dola Yantra for three hours and then washed with hot water.

Mechanism of Action

Physostigmine inhibits acetylcholinesterase, the enzyme responsible for breaking down acetylcholine. By interfering with acetylcholine metabolism, physostigmine indirectly stimulates nicotinic and muscarinic receptors, resulting in increased acetylcholine availability at synapses¹⁴.

Anticholinergic syndrome

The anticholinergic syndrome results from competitive antagonism of acetylcholine at central and peripheral muscarinic receptors. Central depression often leads to hyperactive delirium, which includes confusion, restlessness, and obsessive thoughts, which are symptoms of intoxication. Peripheral depression is different, but symptoms can include: warmth, dry skin, flushed appearance, mydriasis, tachycardia, decreased bowel control, and urinary incontinence. The severity ranges from mild symptoms to life-threatening; however, seizures, coma, and cardiac toxicity are secondary to drug use on other receptors, as many Alkaliergic drugs are active on multiple receptors/ion channels, although they cannot be ameliorated by muscarinic action. Multiple drug overdoses will make the symptoms of anticholinergic toxicity less pronounced.

Anticholinergic drugs

Atropine is usually an anticholinergic (antimuscarinic) drug Differential diagnoses to consider in patients with suspected anticholinergic disease include:

Other toxicological syndromes such as:

- Serotonin syndrome
- Neuroleptic malignant syndrome
- Malignant hyperthermia
- Salicylate toxicity

Non-toxicological causes may include:

- Encephalitis Sepsis
- Neurotrauma
- Post-ictal phenomena
- Hypoglycaemia
- Hyponatraemia
- Behavioural disturbance



Investigations

- Screening tests - 12 lead ECG, blood glucose and paracetamol concentration - in deliberate self-poisoning.
- Some cough medications may also contain paracetamol - so a concentration should be considered in these accidental ingestions as well.
- Study of salicylate concentrations if differential includes salicylate toxicity.
- Study of concentrations for specific agents if available - eg. carbamazepine

Management

- Stopover any causative agents
- Active resuscitation is infrequently required. Care should be taken to maintain the airway, breathing, and circulation.

- Hypotension should initially be relieved with a 20 ml/kg crystalloid bolus.
- Treatment of epilepsy with benzodiazepines.
- Treatment of low blood sugar.
- Treat hyperthermia with cooling measures. Antipyretics are not helpful.
- Recognition and management in a quiet environment may be sufficient for those with mild symptoms. These children often receive one-on-one care.
- Anxiety/delirium usually by titrated diazepam (0.1 mg/kg - up to 5-10 mg) IV given every 30 minutes or every 15 minutes until the child is relaxed but awake. Avoid haloperidol and droperidol, which can cause anticholinergic effects.
- Urination can be stressful. A bladder scan will show if a urinary catheter is needed.
- The use of decontamination/improved removal depends on actual exposure and should be discussed with a toxicologist.
- There is some controversy regarding the use of physostigmine, a cholinesterase inhibitor used to reduce delirium in anticholinergic syndrome. Physostigmine may be prescribed after consultation with the toxicology department.

CONCLUSION

The present review indicates that a lot of descriptions are available in various Ayurvedic texts, it is a wild plant having nine other species with wide range of medicinal and pharmacological properties. Datura seeds have hyoscyamine, fastusic acid daturanolone and many other 9 tropane alkaloids that are absorbed through the mucous membrane of GIT and respiratory tract and through skin and conjunctiva causing wide range of toxicity inside the living body. Despite being a poisonous plant, it has been found useful in various diseases like Asthma, pain, dog bite, inflammation, viral, fungal as well as bacterial infections on therapeutic evaluation. While using it for therapeutic purpose, it is necessary to purify the crude drug first. Since, In Ayurveda it is clearly mentioned that the drug datura metal 14 must be used exclusively after purification. Purification plays 20 a vital role in reducing the adverse effects caused during internal administration.

REFERENCES:

1. Sopchak CA, Stork CM, Cantor RM, Ohara EP. Central Anticholinergic Syndrome Due to Jimson Weed Physostigmine. *J Toxicol.* 1998; 36:43– 5.
2. Koulapur VV, Jirli PS, Honnugar RS, Pujar SS, Patil S. Poisoning due to datura - a rare case report. *Indian J Forensic Community Med.* 2015;2(1):64–6.
3. Gautam Biswas, *A Text Book Of Forensic Medicine And Toxicology*, edition 4th 2019;chapter 50th page no. 569
4. DR. K.S. Narayan Reddy, textbook of The essentials of forensic medicine and toxicology, Edition 28th 2009
5. Giadado A, Zainab AA, Hadiza MU, Serah DP, AnasHY, Milala MA. Toxicity Studies of Ethanol extract of theLeaves of Datura stramonium in rats, 2007.
6. Akharaiyi FC (2011). Antibacterial, Phytochemical and Antioxidant activities of Datura metel. *International Journal of Pharm Tech Research.* 3(1): 478–483.
7. Mdee LK, Masoko P, Eloff JN. The activity of extracts of seven common invasive plant species on fungal phytopathogens. *S Afr J Bot.* 2009; 75(2): 375-379
8. Akharaiyi FC (2011). Antibacterial, Phytochemical and Antioxidant activities of Datura metal. *International Journal of Pharm Tech Research.* 3(1): 478–483.
9. Javaid A, Shafique S and Shafique S (2008). Herbicidal activity of Datura metel L. Against Phalaris minor Retz. *Pak. J. Weed Sci. Res.* 14(3– 4): 209–220.
10. Singh V and Singh R (2008). Effect of Datura metal seed methanol extract and its fractions on the biology and ovipositional behaviour of *Helicoverpaarmigera*. *J Med. and Aro. Plant Sci.* 30(2): 157–163
11. Pretorius E, Marx J. Datura stramonium in asthma treatment and possible effects on prenatal development. *Environ Toxicol Pharmacol.* 2006.
12. Bania TC, Chu J, Bailes D, O'Neill M. Jimson weed extract as a protective agent in severe organophosphate toxicity. *Acad Emerg Med.* 2004; 11(4): 335-338.
13. Pandit Kashinath Shastri, Rasatarangini, Varanasi, Motilal Banarasidas Pratishthan, edition 11th, 2014, Chaturvishtarang, page 711, verse 346-348.
14. <https://go.drugbank.com/drugs/DB00981>

