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Silvics, phytochemistry and ethnopharmacy of endangered poison nut tree (*Strychnos nux-vomica* L.): A review

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Abstract

Strychnos nux-vomica L. (loganiaceae) is a well known drug plant in classical medicines. The species is pantropical and commonly observed in moist deciduous and semi evergreen forests. It contains poisonous alkaloids strychnine and brucine which are extensively used in many formulations with great therapeutic significance. Leaves, bark, root, fruits contain alkaloid of medicinal importance but seed is official in Ayurveda and other pharmacopoeias. After adopting suitable purification process, seeds of nux-vomica are used as an ingredient of many compound formulations in Ayurveda, Unani and Homeopathy systems of medicines. Often seeds are used for treating debility, paralysis, dyspepsia, dysentery, chronic rheumatism, weakness of limbs, sexual weakness, colic, intermittent fever, malarial fever & hysteria etc. It is also used as rodenticide, piscicide and pesticide in agriculture. Unscientific and overexploitation of seed along with loss of habitat put this drug plant under threat list. In this review an effort has been made to elucidate the morphophenology, nursery techniques, silvicultural management, pharmacognostic authenticity of crude drug, scientifically validated therapeutic uses in a lieu to assist further research in chemical screening of elite genotypes, developing agrotechniques of cultivation, varietal development, by-products extraction thereby protecting it from extinction.

Keywords: *Strychnos nux-vomica*, morphophenology, nursery techniques, silvicultural management, ethnopharmacy, Pharmacognosy, Strychnine, Brucine

1. Introduction

The pantropical genus *Strychnos* L. is well known as a source of poisonous alkaloid strychnine. It comprises 200 species of which about 75 species are found in Africa, 73 species in America and 44 species in Asia^[1]. Five species of genus *Strychnos* are endemic to South India and Andaman Islands^[2]. *Strychnos nux-vomica* L. commonly known as Kupilu/ Poison nut/ Strychnine tree/ Quaker button is a promising drug plant of many traditional systems of medicine including Unani, Ayurveda, Tibetan, Chinese and Homeopathy^[3, 4, 5]. It is cultivated commercially in United States, European Union, Fujian, Guangdong, Guangxi, Hainan, North Australia, Taiwan, and throughout tropical Asia^[6].

Almost all part of this tree contains alkaloids of medicinal importance but seed is official in many pharmacopoeia. The Ayurvedic Pharmacopoeia of India recommends detoxified seeds for ailment of paralysis, facial paralysis, sciatica and impotency^[3]. The root bark is useful in cholera, snakebite and intermittent fever. The leaves are applied as poultice in the treatment of chronic wounds and ulcers^[7]. The pulp of the ripe fruit is used in treating paralytic affections of palms and foot^[8]. The seeds are bitter and used as aphrodisiac, appetizer, anti-periodic, digestive, purgative, and stimulant^[9]. They are applied in the treatment of anemia, lumbago, asthma, bronchitis, constipation, diabetes, malarial fever, skin disease, paralysis, muscle weakness, emphysema, colic, insomnia, nervous debility, dyspepsia, diarrhoea, hysteria, mental emotions, epilepsy, chronic constipation, gout, chronic rheumatism, hydrophobia and spermatorrhoea^[1, 10, 11, 12]. Pharmacologically the drug plant has been tested on animals for its antifungal, antibacterial, antioxidant, anti-inflammation, anticancerous, antidiabetic, neuropharmacological properties as well as for the specific actions on gastrointestinal, bone cells and cardiovascular systems^[13, 14]. Apart from medicinal use Kupilu have also been used as rodenticide, avicide^[15], insecticide^[16, 17], Nematicide^[18] and Piscicide^[19].

The present review provides elucidative information on morphophenology, ethnopharmacy, propagation techniques, silvicultural management, post harvest management, photochemistry and pharmacology in a lieu to assist further research in chemical screening of elite genotypes, developing agrotechniques of cultivation, varietal development, byproduct extraction, and thereby protecting this prized drug plant from extinction.

Botanical classification

Kingdom	: Plantae
Division	: Magnoliophyta
Class	: Magnoliopsida
Order	: Gentianales
Family	: Loganiaceae
Genus	: Strychnos
Species	: Nux-vomica

Morphology

Strychnos nux-vomica is a medium sized deciduous tree. The trunk is tall, thick, straight and cylindrical covered with yellowish-grey to dark grey, smooth and thin barks. Wood is dense, hard white and close grained. Wood Character Changes with season. Spring favours formation of more tracheary elements and widen rays. Summer initiates the formation of longer rays and broader parenchymatous bands [20].

Branches are irregular and covered with smooth ash colored bark and shiny dark green young shoots. Leaves are broad, opposite, simple and entire, smooth, short-stalked, blade orbicular to broadly elliptical or ovate, base rounded to cordate, apex shortly acuminate or acute, glabrous and shiny above, minutely hairy especially on veins beneath, 3–5-veined from the base. Inflorescence is terminal cymes, many-flowered and appears with young leaves at the end of branchlets or on axillary shoots. Flowers hermaphrodite, actinomorphic, homogamous, greenish-white colored, small in size, nectariferous, funnel-shaped and emits unpleasant odour. Flower are pentamerous; calyx lobes ovate, outside densely hairy. corolla with a slender tube of 1 cm long, abruptly widening at the throat, outside glabrous, having pubescence at base, lobes narrowly ovate, of 3 mm long, margin thickened and minutely hairy, greenish white to white; stamens inserted at the mouth of the corolla tube exerted altering with corolla lobes. Anthers pale cream in color, ditheous, introrse and dehisce longitudinally. Ovary is superior, ovoid, glabrous, bicarpellary with axile placentation. The style is filiform, glabrous and as long as the corolla tube, stigma capitates (head-shaped). Fruit is a globose, indehiscent berry with a smooth and hard shell. The fruit is full of soft, white, fleshy and jelly-like pulp containing 1-3 seeds. Seeds are lens-shaped to orbicular or ellipsoid, covered with dense

silky hairs radiating from the centre, and giving a characteristic shine to the seed. One side of seed is concave and the other convex with a small depression in the centre of each side. Endosperm is very hard, dark grey in color, odourless and bitter in taste containing small embryo [21, 22, 23].

Phenology

The plant is deciduous in nature with leaf fall occurring in the cold season, mostly in December and January. New shiny leaves unfolds at the advent of summer season (1st week of February), followed by flowering initiation. Blooming progress through March and terminates at the end of April with peak of 30 days between mid February to mid March. Fruits take about 10-11 months for maturing and 3-4 fully matured seeds per fruit are common. Fruits attain orange red colour on ripening. Fruit shedding occurs immediately. The seeding was moderate in occurrence and dispersed by vertebrates (mammals and birds). The pulp of the fruit is eaten by monkeys (Bonnet Macaque), bats (fruit bats), rhinoceros hornbills, parakeets and other birds [24, 25]. Germination percentage is low, but sprouted seedlings showed very good withstanding capacity in the shaded condition and even though its growth rate is slow, most of them established well [26].

Ecology

ccS. Nux-vomica is native to tropical and subtropical regions of South East Asia and Australia [27]. In India it is commonly observed in moist deciduous and semi evergreen forests of West Bengal, Bihar, Maharashtra, Odisha, Central and South India up to altitude of 500m [28]. Also, observed in plains, shifting cultivation areas, degraded hillocks and up lands in 03, 06, 07, 08, 09, 12, 13, 18, 19 Agro-ecological regions of India [29] (Fig 1). In its natural habitat *Strychnos nux-vomica* occurs at the edges of dense forest, on river banks and along the shores. It is an emergent tree in mature and "undisturbed" forests and thought to be the transition stage of the succession between the pioneers and the "climax" forest. Under favourable climatic condition seedlings can get established in a wide variety of soils ranging from loamy or loamy-sandy soil, lateritic and clayey loam soils but growth is very slow [21].

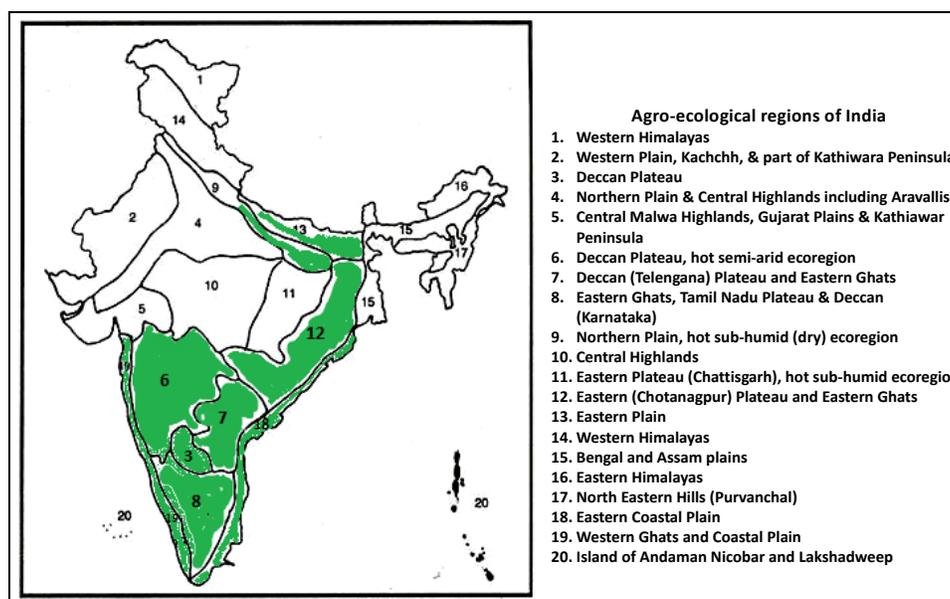


Fig 1: Distribution of *S. nux vomica* in Agro-ecological Regions of India

Status of the plant

The species is in high demand for its therapeutic values and there is acute shortage of seeds. Often seeds are collected unscientifically by lopping its branches or cutting down the trees. Young saplings are cut for fire wood by local dwellers. Poor regeneration coupled with habitat loss and heavy trading of seeds compelling this poison plant to restrict in few areas. Presently this species is sparsely observed in the forests and has been included in the list of rare endangered tree (RET) category^[30].

Propagation

S. nux-vomica is a potential medicinal plant for cultivation in Deccan and peninsular India^[31]. It can be propagated through seed and vegetative methods but reproduction through seed is more assertive^[32].

I). Propagation through Seed

Ripe berries are collected from trees during March-April. The seeds are removed from the fleshy pericarp, cleaned, dried and sorted. 750-800 seeds weigh one kilogram. Seed is orthodox and mesobiotic in nature^[33]. Seeds are desiccation tolerant, dry seed (10% moisture content) can be hermitically stored at ambient temperature for 30 weeks without losing their viability. Seeds exhibit physiological dormancy and hence slow and erratic germination (10% germination) is recorded from freshly harvested seeds^[34]. Dormancy can be removed (after-ripening) by storing seeds with 10% moisture content at ambient temperature for 30 weeks or by treating with hormones gibberellic acid (GA₃) or indole butyric acid (IBA). Treating seeds with gibberellic acid (Soaking seeds in 500 ppm gibberellic acid (GA₃) for 24 h), incubation of seeds at 40 °C for 3 days and alternate water soaking (16 h) and drying (8 h) for 14 days, the germination can be improved up to 32%. But 92 percentage of seed germination can be achieved by using after ripened seeds. Growth of seedlings is very slow but it can be improved by using medium sized polythene bags containing pot mixture of farm yard manure (FYM), soil and sand in ratio of 1:1:1^[30].

II). Propagation through vegetative methods

Macro-propagation through cuttings and root suckers is suitable^[35]. Semi-hardwood cuttings are prepared in early summer and kept under moist conditions after treating with rooting hormones. Rooting percentage is quite low, often less than 25%. Root suckers from mother plant are pricked out and transplanted in polybags for eventual planting out^[36].

Micro-propagation/ clonal propagation of kupilu can be successfully done through shoot proliferation and hypocotyl culture in suitable media. For shoot proliferation, nodal explants excised from healthy mature trees are cultured on Murashige and Skoog medium with various additions. IAA and NAA were the most suitable growth regulators, both promoting shoot and root formation^[37].

For hypocotyl culture seeds were germinated in MS medium supplemented with 1000ppm gibberellic acid (GA₃) under dark condition. Hypocotyls segments of 3mm size are cultured in MS medium with various additions and maintained at 25±1°C with 16 hr illumination at fluorescent light. Kinetin is most suitable for shoot formation and NAA is best for root formation^[38].

Silvicultural management

S. nux-vomica prefers grows well on laterite, sandy, and alluvial soils under dry or humid tropical climatic conditions. Container raised one year old seedlings are planted during

onset of monsoon. 400 trees per hectare are recommended. Fruiting starts after 15-20 years of planting. The yield of kupilu seed is proportionate to the size of the tree. Coppicing or pollarding of trees reduces the size of the tree and causes a loss in seed production which is never likely to be made up. Pruning has the same effect but to a lesser degree. Coppicing very young trees may result ultimately in their acquiring crowns of fuller spread than if they were left to grow naturally, but trees tend to develop spreading crowns as soon as height growth starts falling off. Artificial measures to promote crown spread are therefore not likely to be worthwhile. Plant is normally free of pest and diseases but in few instances leaf spot disease caused by *Colletotrichum gloeosporioides* is being reported^[39]. The yield of seed from individual trees fluctuates remarkably from year to year. Drought or fire, especially the latter, causes a subsequent drop in yield^[40].

Post harvest management

The orange-light red colour of fruit indicates maturity. Matured fruits are manually collected, fleshy pericarp was removed, washed properly and shade dried up to 10 % moisture content. Seeds are then graded according to size. Seeds of light weight and those float on the surface of water are discarded. Storage does not affect the total alkaloid content of seeds particularly strychnine and brucine. Processed mature seeds can be stored in gunny bags at ambient temperature in the usual way for a long time or till preparation of tincture^[41].

Pharmacognostical characters of crude Drug

Adulteration either intentional or unintentional reduces potency of the drug. Heavy demand coupled with extreme scarcity of raw material leads to intentional adulteration. *Strychnos nux-vomica* is known to be substituted/ adulterated with *Strychnos nux-blanda* and *Strychnos potatorum*^[42]. Macroscopic and anatomical observations along with chemical analysis are some features used for judging the purity and authenticity of crude drugs^[43]. The macro and microscopic observations along with analytical parameters of seeds of *nux-vomica* may helpful in judging the authenticity of crude drug.

Macroscopical characters of seed

Nux vomica seeds are extremely hard and greenish-grey in colour, disc shaped, 10–30 mm diameter and 4–6 mm thick, nearly flat, umbonate, somewhat oval in outline. The edge is rounded or acute. The testa is covered with silky, closely appressed, radiating unicellular lignified trichomes. In the centre of one of the flattened sides is a distinct hilum and a small prominence on the circumference marks the position of the micropyle, which is joined to the hilum by a radial ridge. The small embryo with two cordate cotyledons and a cylindrical radicle, the latter directed towards the micropyle, will be seen embedded in a grey, horny endosperm. In the centre of the seed is a slit-like cavity. The seeds are odourless when dry; but if soaked in water and left for a day or two, they develop a very unpleasant odour. Seeds are acrid, very bitter in taste^[44].

Microscopical characters of seed

Study of radial section of seed shows a very thin testa consisting of collapsed parenchyma and trichomes. The trichomes have thick walled base with slit like pits and interlocked with each other. Upper Portion of hair is almost set in right angle to the bases and all radiate towards the

margin of the seed, giving testa its silky appearance. The endosperm consists of large, non-lignified thick-walled cells [44, 45].

Characteristics of powdered raw drug

Thick-walled endosperm cells containing plasmodesma and oil globules, small aleurone grains, fragments of strongly lignified non-glandular hairs, parts of trichomes like apex, rod, and testa are microscopic botanical characters for authenticity of crude powdered drug [46, 11].

Analytical Parameters

Apart from macro and microscopic parameters other physical parameters like total ash, acid soluble ash, water soluble ash, swelling index, extractive values, fluorescence analysis etc. helps in judging the authenticity of powdered drugs [47]. Fluorescence analysis of seed powder showed green colour only in long ultra violet radiations. Other analytical parameters are given in table-1.

Table 1: Analytical parameters of *S. nux-vomica* seed powder

Parameters	Value	Reference
Total ash	4.23 ± 0.25 % w/w	[11]
Acid-insoluble ash	3.06 ± 0.05% w/w	
Water-soluble ash	0.93 ± 0.05% w/w	
Loss on drying	7.83 ± 0.28% w/w	
Swelling index	53.33 ± 11.54% v/v	
Extractive value in water	8.4 ± 0.36 %w/w	
Extractive value in ethanol	2.2 ± 0.15 %w/w	

Ethnopharmacy

Kupilu is used in folk medicines for alleviating many disorders. Perusal of classic and modern literatures reveals a wide range of therapeutic utility of almost every plant parts which are summarised below [48, 49, 50].

Leaves: Cures wounds or ulcers (cases where maggots have formed) when applied as poultice.

Flowers: Antibacterial and antioxidant

Fruits: Alleviates urinary disorder, Constipation (ripe fruits), diseases due to impure blood and paralytic affliction of paws and feet.

Seeds: Used in cholera; diabetes; emotional disorders, hysteria; epilepsy; intermittent fevers; gout, rheumatism, hydrophobia; impotence; insomnia; paralytic and neuralgic afflictions; prolapsed rectum;

antidote to alcoholism; beneficial in general exhaustion; opium poisoning; retention or nocturnal incontinence of urine; spermatorrhoea; given in combination with carminatives and antacids in dyspepsia and vomiting.

Bark: Useful in cholera and acute dysentery.

Wood: Fresh wood juice is reported to be a popular remedy for dysentery, fever, cholera and dyspepsia.

Root: Useful in cholera and intermittent fevers, applied externally for the management of snakebite and as an emetic.

Different compound formulations of Kupilu as ingredient are prescribed in different classical pharmacopoeias for the treatment of various diseases. Ayurvedic formulations include Agnitundi rasa, Shulaharana yoga, Kupilubeejadi kwatha, Krimimudgara rasa, Kitmarda rasa, Krimighatini gutika, Mahavisagarbha tailam, Visatindukadi tailam, Visatindukadilepa etc. Unani system of medicine advocates compound formulations like Habkhas, Roghankuchla, Majunizaraqi etc. as nervine tonic and for curing different body ailments. Nuxvomica is also one of the foremost and frequently used homeopathic remedies, particularly for acute conditions. Homeopaths prescribe this drug for hangovers, back pain, digestive issues, headaches, allergies, colds, flu, emotional stress, constipation, menstrual issues, and haemorrhoids [49, 51]. Meganadha thailam is a popular medicated oil formulation in Siddha system of medicines prescribed for skin diseases and rheumatic disorders [52].

Phytoconstituents

Seed of nux-vomica is the official part in classical pharmacopoeias. It is rich in alkaloids, flavonoids, tannins and triterpenoids, glycosides, lignins and steroids [53]. More than 90 chemical compounds have been isolated from different parts of nux vomica but strychnine and brucine are the principal toxic alkaloids. They occur not only in the seeds but also in roots, wood, bark, fruit pulp and hard fruit shells (Fig. 2) [54]. Indian nux-vomica seeds contain 2.6 to 3% of total alkaloids approximately, of which 1.25 to 2.5% is strychnine and 1.5 to 1.7% is brucine. The seeds additionally contain chlorogenic acid, a glycoside (loganin), and 3% of fixed oil [49]. A number of minor alkaloids of medicinal importance are also recorded and are as follows (Table-2):

Table 2: Phytochemicals in different parts of *S. nux-vomica*

Plant part	Phytochemicals	References
Leaves	Strychnine, Brucine, α & β - Colubrine, Vomisine, N-methyl pseudostrychnine, Kaempferol-7-glucoside, 7-Hydroxy coumarin, Quercetin-3-rhamnoside, Kaempferol-3-rutinoside, and Rutin.	[26, 55]
Stem Bark	Brucine, Strychnine, Mavacurine. α & β - Colubrine, Loganin, Longicaudatine, Strychnochrysin, Vomisine, Strychnoflavine, Demethoxyguiaflavine, N-methyl-longicaudatine, Pseudobrucine, Pseudostrychnine, 16-hydroxycolubrine, Caffeic acid ester, Fatty acids and Sucrose	[56, 57, 58]
Root	C-mavacurine, Strychnochrysin	[59, 60]
Flower	Strychnine, Brucine, Vomisine, Icajine and Novacine	[61]
Fruit	Strychnine, Colubrine, Brucine, Pseudostrychnine, Pseudobrucine, Strychnine N-oxide, Brucine N-oxide, Icajine, Vomisine, etc. Iridoids: Loganin, Loganic acid, Deoxyloganin, Ketologanin, Secologanin, Glycosides: Salidroside and Cuchiloside	[62]
Seeds	Strychnine, Brucine, Brucine-N-oxide, Strychnine-N-oxide, Loganic acid; 4-N-hydroxymethyl strychnidin-17-acetic acid, 10, 11-dimethoxy-4-N-hydroxymethyl strychnidin-17-acetic acid; Stryvomisine, Stryvomitine, Isopseudostrychnine, 5-Oxobrucine, 5-Oxopseudostrychnine, 11-hydroxyl-icajine, 10-hydroxyl-icajine; Deoxy-strychnine-chloromethochloride, β -colubrinechloromethochloride, α -colubrine-chloromethochloride; Pseudostrychnine, Pseudobrucine, Secoxyloganin, Caffeic acid, <i>p</i> -hydroxybenzoic acid, <i>p</i> -hydroxyphenylacetic acid, Uvaol, Stigmasta-7,22,25-triene-3-ol, Lupeol, 11- <i>oxo</i> - α -amyryn palmitate, Catechol, Maltol, Adenosine; Igasuric acid, Loganin; β -colubrine, Icajine, 16-Hydroxy- α -colubrine, Vomisine, Novacine, Pseudostrychnine, Pseudo brucine, Isostrychnine, Isobrucine, Isobrucine-N-oxide, Isostrychnine-N-oxide, 2-Hydroxy-3-methoxystrychnine; 3-methoxy icajine, 15-hydroxy strychnine, Isobrucine, Isobrucine N-oxide, Isostrychnine N-oxide, 2 hydroxy-3-methoxy strychnine.	[63, 64, 65, 66, 13, 67, 68, 26]

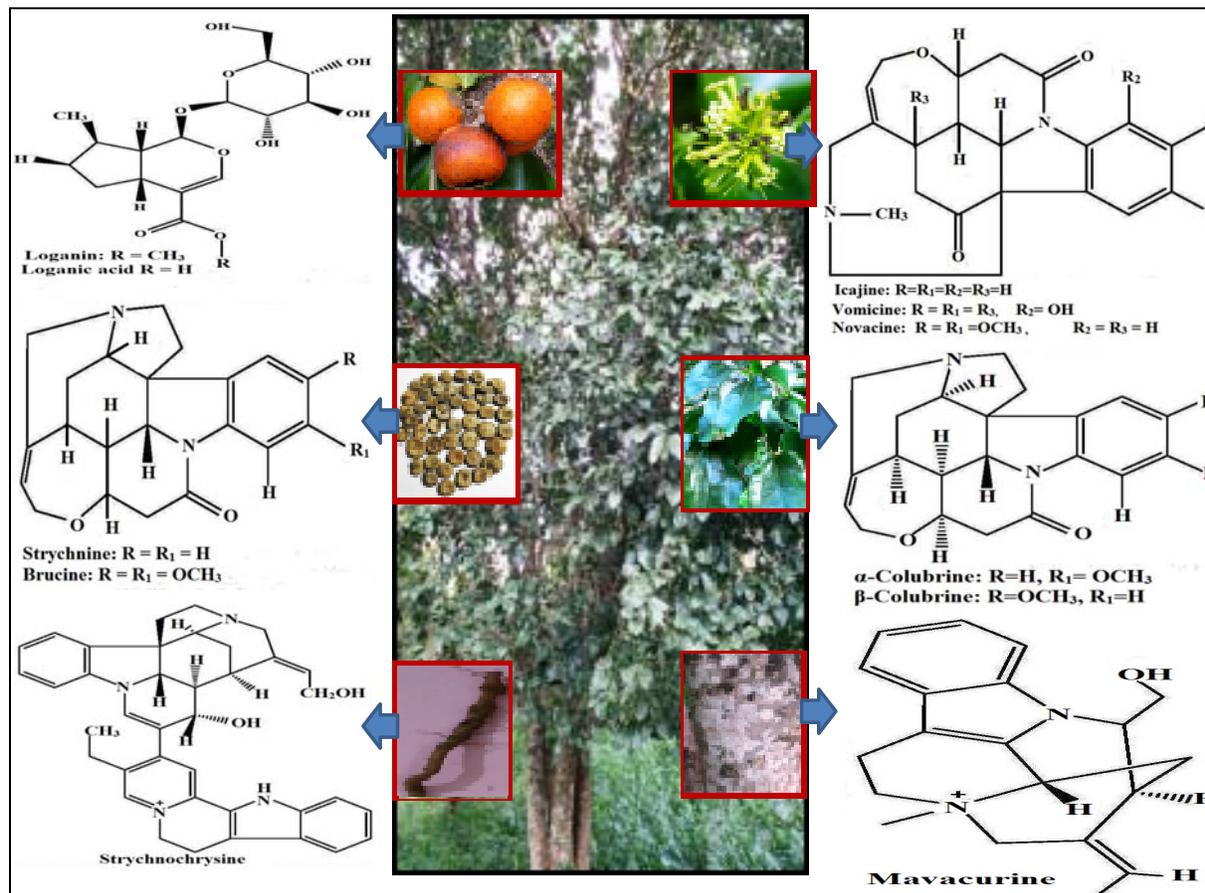


Fig 2: Phytochemicals in different plant parts of *S. nux-vomica* L.

Detoxification of *Strychnos* seeds

Processing/detoxification of *nux-vomica* seeds are very essential before its therapeutic use. Use of different factors like cow's urine, milk, ghee (purified butter), Kanji (sour gruel), castor oil, ginger juice, sand, vinegar etc. for processing are described lucidly in different pharmacopoeias (Table-3) [69, 70]. Every purification process directs towards

reducing the levels of alkaloids and has some therapeutic rationale. On heat treatment the content of major alkaloids strychnine and brucine declines with the increase in the proportion of isostrychnine, isobrucine, strychnine N-oxide and brucine N-oxide. This change in alkaloid content renders *nux-vomica* to be used as a drug [71, 72].

Table-3: various methods of purification of *S. nux-vomica* [5, 73]

Systems of medicine	Method of Detoxification
Ayurveda	<ul style="list-style-type: none"> Frying in cow's ghee (clarified butter) until brownish red Tying in a cotton cloth and placing it in a vessel of boiling cow's milk for three hours Soaking the seeds for seven days in cow's urine Dipping the seeds in Kanji (sour gruel) Parching in a sand bath (about 240°C) for three minutes
Unani medicine	<ul style="list-style-type: none"> Burying the seeds in yellow clay for 10 days and then boiling them in cow's milk. Soaking the seeds for seven days in cow's milk and then peeling the seeds Frying in cow's ghee (clarified butter) until brownish red
Chinese traditional medicine	<ul style="list-style-type: none"> Submerging in urine from healthy children Treating via licorice decoction Frying in oil bath (about 240°C) for three minutes Parching in a sand bath (about 240°C) for three minutes Treating with vinegar
Iranian traditional medicine	<ul style="list-style-type: none"> Soaking the seeds for seven days in cow's milk, peeling the seeds, and then boiling them in the milk

Pharmacological activities

Strychnos nux-vomica is a potent drug plant in traditional systems of medicine and used for ailment of various disorders. The concentration of deadly poisonous constituents can be decreased significantly by adopting a suitable detoxification method warranted for a particular therapeutic use. Scientific validation of many ayurvedic therapeutic

claims like analgesic and anti-inflammatory properties, anticancer and anti-tumor activity, antioxidant, anticonvulsant, antiemetic, antiallergic, antialcoholic and immunomodulatory property increases the importance of this poison plant in modern medicines. Detailed mode of action of different plant part extract is given in Table 3.

Table 3: Scientifically validated therapeutic uses of *S. nux-vomica*

Pharmacological Property	Plant part/ extract	Action/ effect	Reference
Anticancerous	Aqueous seed extract	G2/M phase arrest and apoptosis in AGS gastric carcinoma cells	[74]
	Root extract	Anti-proliferative and cytotoxic activity in a dose and time dependent manner on human Multiple myeloma (MM)-cell line, RPMI 8226, through apoptosis and disruption of mitochondrial membrane	[75]
	Aqueous methanolic leaf extract	Cytotoxic to human epidermoid larynx carcinoma (Hep-2), breast carcinoma (MCF-7) and colon carcinoma cell lines	[55]
Anti-tumor	Major alkaloids from Seed extract	Inhibits human hepatoma cell line-SMMC-7721 (HepG2) proliferation. Apoptosis (by brucine) via participation of caspase-3 and cyclooxygenase-2. Mitochondrial membrane depolarization through Ca ²⁺ and Bcl-2 mediated pathway	[76, 77, 78, 79]
Antioxidant	Leaf extract	Scavenging of enzymatic and non-enzymatic free radicals	[80, 81]
	Alcoholic seed extract	Inhibition of lipid peroxidation in a dose dependent manner (FeSO ₄ induced lipid peroxidation was inhibited through chelation of Fe ⁺⁺ /Fe ⁺⁺⁺ ion in the system)	[82]
Anticonvulsant/ Neuropharmacological activity	Ethanollic seed extract	Reduction of spontaneous motor activity (SMA) and inhibition of catalepsy	[83, 14]
Antiamnesic activity	Loganin	Inhibits the acetylcholinesterase activity in the hippocampus and frontal cortex.	[84]
Antiallergic and immunomodulatory property	Aqueous stem extract	suppressive activity on allergen-specific IgE (Immunoglobulin E) antibody response	[85]
Antidiarrhoeal potential	Methanolic root bark extract	Reduced induction time of diarrhoea and total weight of the faeces	[86]
Anti-diabetic	Alcoholic and aqueous seed extracts	Increases uptake of glucose at tissue level, increases pancreatic beta cell function and inhibition of intestinal absorption of glucose	[7, 11]
Analgesic and anti-inflammatory	Aqueous methanolic leaf extract	Inhibitory action on the synthesis and/or release of inflammatory mediators such as PGE ₂ , TNF- α and thereby reduced pain and writhing behaviour	[87, 88, 55]
Antipyretic	Aqueous methanolic leaf extract	Dose-dependent inhibitory effect on hyperthermia. Antipyretic effect started as early as 1 h and maintained up to 5 h after the extract administration @ 400 mg/kg bw	[55]
Hepatoprotective and anticholestatic activity	Loganin from fruit extract	Dose dependant activity on the viability of the hepatocytes and the reversal of reduced parameters of bile.	[89]
Antisnake venom activity	Seed extract	Reduces snake venom induced lethal functions like haemorrhage, defibrinogenating, cardiotoxic, neurotoxic, PLA ₂ enzyme activity etc. Bears potential polyvalent snake venom antiserum properties.	[90]

Biological activities

a. Antimicrobial activity

Nux-vomica plant extracts possess anti bacterial and antifungal properties. Silver nanoparticles (SNPs) from *strychnos nux-vomica* (prepared by heating the mixture of 10 ml aqueous seed extract with 90 ml of 1 mM aqueous of Ag(NO₃)₂ at 60-800C for 20 min) is used by the ethnic groups of Kurnool district, Andhra Pradesh, to treat leucoderma. Phytochemical screening of this drug by Subbaiah and Savithamma [53] showed the presence of alkaloids, flavonoids, tannins and triterpenoids, glycosides, lignins, steroids. SNPs have good antimicrobial activity against different microorganisms *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhi* species of bacteria and *Paecilomyces varioti*, *Pencillium rubrum* and *Aspergillus flavus* species of fungi.

Methanolic extract of *Strychnos nux vomica* flowers bears antibacterial properties and can be used to treat against infections caused by *Candida albicans*, *Klebsiella pneumonia* etc. High radical scavenging activity against the synthetic DPPH (2, 2-diphenyl-1-picryl-hidrazila) infers its high antioxidant activity [48].

b. Rodenticide Properties

Alkaloid strychnine from seed extract of nux-vomica was used for the eradication of rodents during early nineties in United States and other European countries. Sometime used for killing stray dogs, cats, crows and other vermins. it was

banned after 2006 because of absence of health and safety data. Currently, strychnine is registered for use only below ground as a bait application to control pocket gophers in America [91].

c. Insecticidal and nematocidal properties

Seed, leaf and stem extract possess insecticide and nematocidal properties. Ethyl acetate leaf extract at 200 ppm is lethal to third instar larvae of Mosquito *Culex quinquefasciatus*; a vector for *Wuchereria bancrofti* responsible for filariasis. The toxicity level showed LC₅₀ value of 222.28 and 146.99 ppm after 24 and 48 hours respectively (Arivoli and Tennyson (2012). Thambi and cherian [92] reported toxicity of ethyl acetate leaf extract at 500 ppm to rice weevil *Sitophilus oryzae* L. 100% mortality was observed after 72 hours. The acetone extract of dried stem is also toxic against polyphagous beetles. Seed extract possesses larvicidal properties against the fourth instar larvae of the yellow fever mosquito *Aedes aegypti* (Arivoli and Tennyson 2012). Hexane extract of seeds at 2 percent reduces the feeding activity (to 70.57 %) of polyphagous pest *Helicoverpa armigera* [16]. Aqueous leaf extract possesses nematocidal properties against the burrowing nematode, *Radopholus similis* at 200ppm [93].

Acute and sub-acute toxicity studies

Strychnine and brucine the most abundant alkaloids of nux vomica are highly toxic to humans and animals [91]. Both

compounds are neurotoxic and competitive antagonist of the glycine receptors in the vertebrate central nervous system. Lethal doses of strychnine induce convulsions of the central nervous system and death through respiratory or spinal paralysis or cardiac arrest. The common cause of death is respiratory failure^[88]. The lethal dose of strychnine was found to be 30-120 mg for an adult individual and 15 mg for a child^[91]. Brucine is poisonous but its toxic effects are only one eighth of that of strychnine. Lethal concentration causes life threatening complications like rhabdomyolysis and acute renal failure. The lethal dose of Brucine for an adult individual is 1000mg^[8, 62]. Excess dose of nux-vomica causes convulsions and tetanus like symptoms. Symptoms includes chest discomfort, contractions of all limb muscles, carp pedal spasm, muscle pain, numbness, hyperventilation, confusion, nystagmus (rapid movement of the eyes), knee-jerks, tiredness and seizures^[27]. Complications consist of hyperthermia, renal failure and rhabdomyolysis.

Conclusion

S. nux-vomica possesses alkaloids of poisonous nature but it is a promising drug plant in many classical and modern medicines. Few medicinal actions like anticancerous, antioxidant, antimicrobial, analgesic and anti-inflammatory, anti-diarrhoeal, wound-healing and neuropharmacological properties are evaluated against animals. There is a vast scope for clinical trials, investigation in the field of medicinal and pharmaceutical sciences for holistic applications of this plant. Most of the seeds are collected from forests unscientifically. Scarcity of seeds, illicit felling for firewood and habitat loss is responsible for making it endangered. Genotypic evaluation for elite genotypes of pharmaceutical importance, breeding for early fruiting varieties and development of agrotechniques of cultivation are also some areas needs attentions which will be helpful for commercial cultivation and conservation of this drug plant from extinction.

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