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KUCHALA; A MIRACLE REMEDY OR POISON NUT - A REVIEW

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ABSTRACT

Strychnos nux-vomica, commonly known as *kuchala*, (*Loganiaceae*-Family) is a widely distributed poisonous plant but it is used in many medicinal preparations of ayurveda and other allied medicinal pathies. It is included in *Surasadi Gana* in *Sushruta* , *Amradi Phala Varga* in *Bhavaprakash* and *Vishatindukadi Varga* in *Nighantu Adarsh*. The traditional medicinal component is its seed, called *nux-vomica*. *Kuchala* is well known for its anti-phlegmatic effect, nerve tonic and stimulant properties which makes it an important drug in treatment of insomnia, epilepsy, paralysis, nocturnal incontinence of urine, impotence etc. Many compounds including alkaloids, flavonoid glycosides, triterpenoids, steroids and organic acids have been isolated and identified from *Strychnos nux-vomica*. These compounds have analgesic, anti-inflammatory, anti-tumor, antimicrobial effect and regulates the immune function. Strychnine, the principal toxic compound is used in medicine as a stimulant & also as a rodenticidal agent.

KEYWORDS: *Kuchala, Nux-vomica, Ayurveda,* Insomnia, Strychnine.

INTRODUCTION

Kuchala a widely used ayurvedic drug classified under *upvisha varga*.[1] It is cited in the treatises of Ayurveda that the *Visha* (poison) becomes *Amruta* (nectar) after logical administration. It has been stated categorically that strong poisons could be the best medicine, if it is used after proper detoxification *(shodhana*) in proper therapeutic dose and formulation.

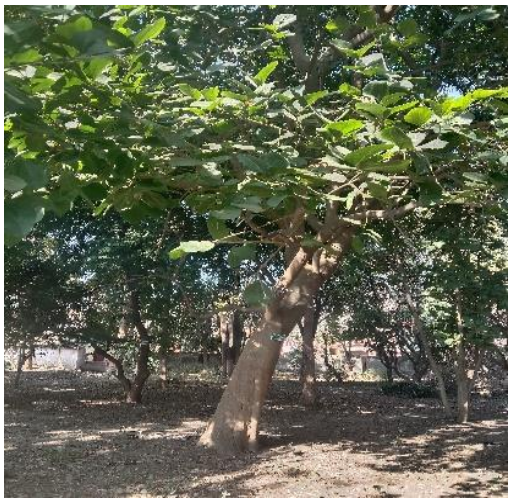
On the contrary, a good medicine may affect adversely unless it is used for proper person in proper dose.[2] Common names of *kuchala* are Nux-vomica, poison nut, snakewood, dog button.[3] Other synonyms of *kuchala* include *Kupeelu, Kakatundika, Kakapiluka, vishatinduka.*[4]

Table 1: Ayurvedic Properties of *Kuchala.*[1]

GUNA	*RAS*	*VIPAKA*	*VIRYA*	*KARMA*
Laghu	*Kshaya Tikta Katu*	*Katu*	*Ushna*	*Kaphavatahara, Grahi, Deepan, Pachan, Shothhara, Vednasthapna, Vajikarana*

Modern toxicology has classified *Strychnos nux-vomica* as a Neurotic Spinal Excitant poison.[5] This is a medium-sized evergreen tree with a short thick trunk. The wood is dense, hard white, and close-grained. The leaves are about 10 cm long and 7.6 cm wide with an opposite arrangement, short stalked, are oval shaped with shiny coat and are smooth on both sides.[6]

The young shoots are deep green in colour. The branches are shiny and deep green in colour.[7] The flowers are small, funnel shape with a pale green colour.[6] Fruits are about equal to or more than 140 gm that possesses smooth and hard shell during the early stage and when ripened it has a mild shade orange colour.[7] The ripe fruit contains seeds which are poisonous, flat, circular discs, 2.5 × 0.6 cm, dark grey in colour completely covered with hairs radiating from the center of the sides. Unbroken seed produce no poisonous effect until its pericarp dissolves.[6]



Distribution

It is found throughout tropical India up to an altitude of 360 m, in Uttar Pradesh, Bihar, Orissa, Coromandel Coast, Andhra Pradesh and Karnataka. It is most common in the forests along the western coast.[8]

Table 2: Phytochemical constituents & therapeutic uses of different parts of *Kuchala.*

S.NO.	PART	CHEMICAL CONSTITUENTS[9]	USES
1.	SEED	Strychnine (1.25-1.5%), brucine (1.7%) pseudostrychnine , pseudobrucine, β-colubrine, 15-hydroxystrychnine, 15-acetoxystrychnine etc.	Anti-diarrhoeal, tonic, diabetes, rheumatism, insomnia, paralytic and neuralgic afflictions prolapsed rectum, general exhaustion, retention or nocturnal incontinence of urine, spermatorrhoea.[10]
2.	FRUIT	Strychnine, 4-hydroxystrychnine, pseudobrucine, strychnine N-oxide, N-methyl-sec-pseudo *β*-colubrine.	Urinary disorders, in diseases due to impure blood.[11]
3.	BARK	Brucine, strychnine, α-colubrine, mavacurine, vomicine, caffeic acid ester, novacine.	Cholera, acute dysentery, intermittent fevers, epilepsy.[12]
4.	LEAVES	Kaempferol-7-O-β-D-glucopyranoside, umbelliferone , quercetin-3-rhamnoside, kaempferol-3-O-rutinoside, rutin	Wounds or ulcers as poultice more especially in those cases when maggots have formed.[13]

PRINCIPAL CHEMICAL CONSTITUENTS OF KUCHALA

Strychnine and Brucine are considered to be the major bioactive & principal toxic compounds.[14]

STRYCHNINE: $C_{21}H_{22}N_2O_2$, this violently poisonous alkaloid is crystalline, slightly soluble in cold water. Strychnine is a strong convulsing agent & terrible tetanic poison, affecting the cerebrospinal system. The muscles and nerves being scarcely altered with congestion of brain spinal cord, lungs, stomach may be there.

Fatal Dose: As low as 4 grain or 1.5–2mg/kg. Indeed, it is recorded that a grain killed a two-year old child in four hours, while 8 grain killed a man in twenty minutes.[15]According to a study of Gosselin et al., 1984 strychnine has been placed in toxicity category, indicating the greatest degree of acute toxicity, for oral and ocular effects.[16]The differential diagnosis includes pathological conditions such as epilepsy, tetanus, meningitis, rabies, phenothiazine overdose, exposure to chlorinated hydrocarbons, organophosphates or other substances that

may cause myoclonus or seizures.[17,18]Strychnine is over 10 times more potent than brucine.[19]

BRUCINE: ($C_{23}H_{26}N_2O_4$) Brucine is very bitter, freely soluble in cold alcohol.[15]It absorbed much slower & decidedly less dangerous than strychnine. The treatment for brucine poisoning is same as for strychnine.[20]A study of Li et al., 2018; Qin et al., 2018 showed that brucine is usually used as an anti-inflammatory & an analgesic. It has also anti-tumor effect on various tumors. In a study Li et al., 2012 reported that in bone metastasis of nude mice model with breast cancer, brucine might inhibit tumor angiogenesis, growth, and bone metastasis. Shi et al., 2018 established that brucine could inhibit the growth and migration of colorectal cancer cells LoVo.[21]

Signs and Symptoms

Signs and symptoms can be observed within 15-30 min. of ingestion which are as follows:

- Bitter taste in mouth.
- Choking sensation in throat and stiffness of the neck and face.
- Cyanosed face, anxious look, prominent eyeballs with dilated pupils.
- Mouth is filled with bloodstained froth.
- Restlessness, increased rigidity of muscles and muscular twitching.
- **Convulsions:** Any sensory stimulus (pain, touch or noise) may produce violent muscular spasm. Initially clonic but eventually becomes tonic and affects all the muscles at the same time.
- Contraction of the jaw and facial muscles with the corners of the mouth drawn leads to a condition known as **Risus Sardonicus**.
- Convulsions are most marked in anti-gravity muscles resulting in hyperextension **(opisthotonus)**. Sometimes, the spasm of the abdominal muscles may lead to forward bending or the sideways of the body either **emprosthotonus** or **pleurosthotonus**.
- Death occurs due to medullary asphyxia or spasm of respiratory muscles.

Management

- Maintain clear airway and adequate ventilation.
- Convulsions Control:

✓ Dark room without disturbance and noise.

✓ Benzodiazepines remain the first-line of treatment. Diazepam 0.1-0.5mg/kg IV slowly.

- ✓ If ineffective, general anesthetics and/or muscle relaxants, like gallamine should be given.
- If there are no convulsions, gastric lavage with $KMnO_4$ may be done cautiously. Activated charcoal is administered to adsorb strychnine and to reduce its absorption after 1 hour of ingestion.
- Rest symptomatic treatment.

Autopsy Findings

- Early onset and disappearance of rigor mortis.
- In the muscles, the extravasated blood may be observed.
- Viscera are congested.
- Postmortem caloricity.
- Dilated pupils.

Samples to be preserved at autopsy

- Blood (Blood levels in the range of 0.1 to 0.3 mg/100ml are generally lethal).[23]
- Routine viscera
- Spinal cord

Forensic Significance of Plant

- One of the most deadly poisons.
- Death is usually accidental due to overdose, quack remedies and poison mistaken for some other harmless drug, or in children eating the seeds.
- It is used as an aphrodisiac, as cattle and arrow poison and to kill dogs and rats.[22]

PART USED: - Seed (mostly used) & root bark (rarely). It should be purified before using for medicinal purposes.[24]

FATAL DOSE: 1-2 crushed seeds or 50 mg-100 mg of strychnine.

FATAL PERIOD: 1-2 hours.[25]

Kuchala Shodhan

Specific methods for purification described in different textbooks of Ayurveda are given below:

a. Seeds are soaked in *kanji* (Acidic fermented medicated water) for three days. After three days its outer covering is removed by scraping with knife and left under sunlight to dry. Make a powder of completely dried seeds and store in air tight container.[27]

b. Seeds fried in *goghrtia* on slow heat. After completely frying process their skin separates. Skinless seeds are powdered & stored.[27]

c. Seeds soaked into *gomutra* for three[26] or seven days with changing *gomutra* daily.[1] After seven days seeds will be scraped to remove outer cover and kept under *swedana* in cow milk for three days. Then these seeds will fried in *goghrita* for therapeutic use.[28]

FORMULATIONS OF *KUCHALA*

- *Krimighatini gutika*[29]
- *Agnitundi rasa*[30]
- *Visatindukadi tailam*[31]
- *Shulaharana yoga*[32]
- *Kupilubeejadi kwatha*[33]
- *Navajeevanrasa*[1]
- *Laxmivilasarasa*[1]

In vivo *and* In vitro study for pharmacological effects of *nux-vomica*

- **Antioxidant**

The ethanol extract of *nux-vomica* seeds dose dependently inhibited the $FeSO_4$-induced lipid peroxidation through the chelation of Fe++/Fe+++ ions.[34] In further studies, Chitra et al. established that the methanol extract of seeds reduced lipid peroxidation and increased the levels of antioxidant enzymes in the liver of alloxan-induced diabetic rats.[35]

- **Antinociceptive**

In recent studies, oral administration of hydro-methanolic leaves extract in dose of 400 mg/kg showed highest analgesic potential which was comparable to diclofenac (100 mg/kg) in various animal models due to the presence of strychnine, brucine, brucine N-oxide in association with analgesic flavonoid compounds in leaves.[36]

- **Anti-inflammatory**

Mitra et al. reported the significant anti-inflammatory activity of raw and purified seed extract of this plant against formaldehyde induced hind paw edema in rats.[37] In a study, the modified total alkaloid fraction (MTAF) of *nux-vomica* seeds extract with a low strychnine content showed 1.8 times higher anti-inflammatory potential than that of total alkaloid fraction (TAF) at the dosage of 1 mg/kg body weight against xylene-induced ear edema in

rats.[38,39] Alkaloids of nux vomica seeds such as strychnine, brucine and brucine N-oxide were reported as primary active compounds responsible for significant anti-inflammatory activity.[38,40]

- **Antimicrobial**

Gnanavel et al. reported that the n-butanol extract of leaves showed strong inhibitory potential against some pathogenic bacterial (*S. aureus, K. pneumonia, B. subtilis*) and fungal (*Aspergillus terreus, A. flavus* and *A. niger*) strains.**[41]** It has been also reported that the *nux-vomica* dilution 200C showed strong antiviral potential against Chicken Embryo Virus of fowls.[42]

- **Anticancer**

In vitro study by Eldahshan and Abdel-Daim revealed that the methanolic leaves extract of *nux-vomica* exhibited potent anti-proliferative activity against human epidermoid larynx, breast and colon carcinoma cells with IC50 value of 17.8, 36.3 and 41.2 µg/ml, respectively.[36] The aqueous extract of *nux-vomica* roots have also been showed anti-proliferative activity against human multiple myeloma cell lines with IC50 value of 11 mg/ml.[43,44] In vivo and in vitro studies showed that the brucine suppressed VEGF induced tumor angiogenesis via inhibiting VEGFR2 signaling pathway.[45,46]

- **Antipyretic**

Antipyretic activity of *nux-vomica* leaves extract against yeast induced pyrexia in rats was studied by Eldahshan and Abdel-Daim. The methanolic leaves extract showed dose dependent antipyretic activity however higher dose of extract (400 mg/kg) showed comparable efficacy as compare to the standard drug, paracetamol (150 mg/kg).[36]

- **Gastroprotective**

In Ayurvedic as well as in homeopathic medicines various forms of *nux-vomica* seeds extract are often clinically used as important remedy for gastritis, gastric ulcers, atony and relaxation of the stomach and bowels. Recent investigation with highly diluted form of *nux-vomica* seeds extract (10c) prepared in ethanol was found to reduce *Helicobacter pylori* induced up-regulation of HB-EGF gene expression in KATO-III cells even in dilutions beyond Avogadro's number.[47]

- **Neuropharmacological**

Studies showed that the sub-convulsive dose of processed seed extract (125 mg/kg) significantly inhibited the pentylenetetrazole-induced convulsions and potentiated barbiturate induced hypnosis in animals and the facts are indicative of CNS depressant action of processed seed extract of *nux-vomica*.[48] Further, the brucine was found to allosteric enhancers of acetylcholine binding to the muscarinic 1 receptor by 2-fold.[49]

- **Anti-snake Venom**

Anti-snake venom potential of *nux-vomica* seeds extract was evaluated by Chatterjee et al. In low doses, *nux-vomica* seeds extract was found to effectively neutralized *Daboia russelii* venom induced lethal, haemorrhage, defibrinogenation, phospholipase A2 (PLA2) enzyme activity and *Naja kaouthia* venom induced lethal, cardiotoxicity, neurotoxicity & PLA2 enzyme activity.[50]

- **Anti-alcoholic**

Different dilutions (30C, 200C and 1000C) of *nux-vomica* were reported to exhibit anti alcoholic effect in mice. Administration of all three potencies of *nux-vomica* restored ethanol-induced loss of righting reflex in mice more quickly than the controls.[51] Despite, other in vivo studies on toads and mice revealed that the *nux-vomica* dilution 30C and 200C significantly reduced ethanol induced sleep time.[52-54]

Clinical Studies

- **Effect on rhinitis**

In an open, multicenter clinical trial in children with acute rhinitis has demonstrated the usefulness of homeopathic *nux-vomica* dilution (potency) in the treatment of acute rhinitis. The *nux-vomica* 6C dilution was applied in 109 children with acute rhinitis. Among them, 79.82% of children were completely cured and 14.68% of children were remarkably improved, while 5.50% of children improved moderately within 7 days of trail period.[55]

- **Effect on sinusitis**

Observational study was carried out to determine effectiveness of *nux-vomica* dilutions (potencies) in acute and/or chronic, frontal, fronto-maxillary, sphenoidal, ethmoidal and maxillary sinusitis. *Nux-vomica* 30C, 200C and 1000C dilutions were applied on 16 different sinusitis cases and these dilutions were found to be useful in 14 different sinusitis patients in relieving sinusitis indications.[56]

- **Effect on insomnia**

The high dilutions of *nux-vomica* extract are known to be clinically useful for the treatment of insomnia. A clinical study on 10 human subjects showed that the *nux-vomica* dilutions (3C and 15C) significantly lowered the serum cortisol levels in 38% patients.[57]

DISCUSSION

Kuchala is a well known spinal poison though it is important part of Ayurvedic pharmacopeia. Rastrangini described about the shodhan process of *kuchala* so that shodhit *kuchala* can get used in number of medicinal formulations as it is a basic ingredient of many ayurvedic formulations. Strychnine stimulates all the parts of central nervous system specially anterior horn cells of spinal cord causing greatly increased reflex excitability causes generalized contraction of the muscles. It has been documented that compounds of *Strychnos nux-vomica* have antioxidant, anticancer, gastroprotective, anti-alcoholic & many other pharmacological effects.

CONCLUSION

Though *kuchala* is taken into account as poison nut but after the specific purification method it works as a miracle remedy. The data indicates that *kuchala* is effective in rhinitis, sinusitis, insomnia and nocturnal incontinence of urine. For quick action, visha dravyas like *kuchala* are used in various medicinal formulations as they get spread rapidly in body due to their *Ushna, Teekshna, Ashukaritwa* properties.

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