



## PHARMACOLOGICAL PROFILE OF POISONOUS HERB, KUPEELU (STRYCHNUS NUX VOMICA LINN.) - A SYSTEMATIC REVIEW

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**ABSTRACT** In traditional medicine, Strychnos nux-vomica L. (family Loganiaceae) is a well-known drug plant. Though it is poisonous, after adopting suitable detoxification process its seeds have been used successfully as a component in numerous compound formulation. Seeds are frequently used to treat chronic debility, paralysis, dyspepsia, dysentery, and hysteria, intermittent fever, malarial fever, colic, rheumatism, limb weakness, sexual weakness, etc. The current review lays an emphasis on collective data on phytochemical, pharmacological application and therapeutic application in classic with the ethnomedicinal applications and clinical studies in order to provide a scientific basis for future natural medication development from this plant for treating a variety of ailments.

**KEYWORDS :** Poisonous, Strychnous, Phytochemicals, Pharmacological, Therapeutics, Ethnomedicinal

### INTRODUCTION:

Strychnos nux-vomica, also referred to as kupeelu in traditional medicine is a poisonous plant that is commonly found. It belongs to Upavishacategory (poison of mild potency) in Ayurvedic pharmacopoeias. It belongs to family loganiaceae and listed under schedule E of Drug & cosmetic act 1940<sup>2</sup>. Nuxvomica is found in tropical India up to 360 m height most frequently in the forest along the western coast<sup>3</sup>. The Ayurvedic treatises mention how, after logical administration, poison turns into medicine. Strong poisons have been categorically stated to have the potential to be the best medicine, if they are used appropriately in terms of therapeutic dose and formulation following adequate detoxification process. Physicians of Ayurveda successfully employed this drug & formulation containing it to treat variety of ailments after proper detoxification.

**Table no 1. Reference of Kupeelu in Ancient literature:**

| Name of classic                                 | Reference             |
|-------------------------------------------------|-----------------------|
| • Bhavprakash Nighantu and Dhanvantari Nighantu | • Amradi class        |
| • Shodhal Nighantu                              | • Karveeradic class   |
| • Nighantu Adarsh                               | • Vishtindukadi class |
| • Raj Nighantu                                  | • Prabhadradi class   |

### Phytochemical constituents:

More than 90 chemical compounds have been isolated from different parts of Nuxvomica but strychnine and brucine are the principal toxic alkaloids. In classical pharmacopeia Nuxvomica seeds is commonly used which 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. A number of minor alkaloids importance are also recorded and are as follows.

**Table no. 2- Phytochemical constituents**

| Part  | Chemical constituent                                                                                                                                                                                                                                                                                                                                                                                  |
|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Seed  | Strychnine, Isostrychnine, Pseudostrychnine, Strychnine N-oxide, Isostrychnine N-oxide, Brucine, Brucine N-oxide, Isobrucine, Isobrucine N-oxide, Beta-colubrine, Novacine, Vomicine, Icajine <sup>4</sup>                                                                                                                                                                                            |
| Fruit | Strychnine, 4-hydroxystrychnine, Pseudobrucine, Strychnine N-oxide, N-methyl-sec-pseudo β-colubrine, Nonindolic base cantleyine, Phenolic glycoside named as salidroside and cuhiloside <sup>5</sup>                                                                                                                                                                                                  |
| Bark  | Root bark shows compounds nor-morcusine B, O-methylmacusine B, Nor-melinonine B, Isostrychnine, Protostrychnine, 10-hydroxystrychnine, 12-hydroxystrychnine, 12-hydroxy-11 methoxystrychnine, 4-hydroxy-3-methoxystrychnine, 4-hydroxystrychnine along with strychnine and brucine. The stem bark consists of brucine, strychnine, mavacurine pseudo strychnine and caffeic acid ester <sup>6</sup> . |

|         |                                                                                                                          |
|---------|--------------------------------------------------------------------------------------------------------------------------|
| Leaves  | Kaempferol-7-O-β-D-glucopyranoside, umbelliferone, quercetin-3-rhamnoside, kaempferol-3-O-rutinoside, Rutin <sup>7</sup> |
| Flowers | Strychnine, Brucine, Vomicine, Icajine, Novacin <sup>8</sup> .                                                           |

### Pharmacological activities:

A number of experimental studies have been conducted on Strychnos Nuxvomica including effects on nervous system, immune system, analgesic and anti-inflammatory activity, antitumor activity, inhibition of the growth of the pathogenic microorganism.

**Table no 3 - Pharmacological activities of Strychnos nuxvomica on the basis of experimental study:**

| Sr No. | Activity        | Research                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|--------|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1      | Antioxidant     | Alcoholic seed extract<br>The ethanol extract of nux vomica dose dependently inhibited the FeSO <sub>4</sub> -induced lipid peroxidation through the chelation of Fe <sup>++</sup> /Fe <sup>+++</sup> ions not by tapping the hydroxyl radicals <sup>9</sup> .                                                                                                                                                                                    |
|        |                 | Leaf extract<br>Scavenging of enzymatic and nonenzymatic free radical <sup>10</sup> .                                                                                                                                                                                                                                                                                                                                                             |
| 2      | Antinociceptive | Nux vomica seeds extract has been used in various analgesic preparations of traditional Chinese medicine. Using tail-pressure, hotplate and acetic acid-induced writhing tests models, the intraperitoneal administration of crude alkaloid fractions (CAF) and processed alkaloidal fractions (PAF) of nux vomica seeds extract exhibited antinociception potential in mice; however PAF showed stronger antinociception than CAF. <sup>11</sup> |
| 3      | Antimicrobial   | The methanolic extract of nux vomica flowers showed significant anti-microbial activity against both pathogenic bacterial and fungal strains viz. P. aeruginosa, S. aureus, B. subtilis, K. pneumoniae and Candida albicans in disc diffusion method <sup>12</sup>                                                                                                                                                                                |
| 4      | Anticancer      | Leaves<br>Preliminary in vitro screening study by Eldahshan and Abdel-Daim revealed that the                                                                                                                                                                                                                                                                                                                                                      |

| Sr No. | Activity                                |                                   | Research                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--------|-----------------------------------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|        |                                         |                                   | 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, respectively13.                                                                                                                                                                                                                  |
|        |                                         | Aq. Seed extract                  | G2/M phase arrest and apoptosis in AGS gastric carcinoma cells14                                                                                                                                                                                                                                                                                                                                                                      |
|        |                                         | 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 membrane15.                                                                                                                                                                                                                                       |
| 5      | Antitumor                               | Major alkaloids from seed extract | Inhibits human hepatoma cell line SMmC-7721(Hepg2) proliferation. Apoptosis (by brucin)via participation of caspase-3and cyclooigense-2.mitochondrial membrane depolarization through Ca2+and Bcl-2 mediated pathway.16,17,18                                                                                                                                                                                                         |
| 6      | Anticonvulsant/Neuropharmacological     | Ethanol seed extract              | 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. Further, the brucine was found to allosteric enhancers of acetylcholine binding to the muscarinic 1 receptor by 2-fold19. |
| 7      | Anti-snake Venom                        | Seed                              | 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 Najakaothia venom induced lethal, cardiotoxicity, neurotoxicity, PLA2 enzyme activity20.                                                                                                                                                |
| 8      | Antialcoholic                           |                                   | Different dilutions (30C, 200C and 1000C) of nux vomica were reported to exhibit antialcoholic 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. Despite, other In vivo studies on toads and mice revealed that the nux vomica dilution 30C and 200C significantly reduced ethanol induced sleep time 21,22,23,24.         |
| 9      | Anti-allergic/Immunomodulatory property | Aq. stem extract                  | Suppressive activity on allergen- specific IgE antibody response25                                                                                                                                                                                                                                                                                                                                                                    |
| 10     | Antipyretic                             |                                   | The methanolic leaves extract showed dose dependent                                                                                                                                                                                                                                                                                                                                                                                   |

| Sr No. | Activity                   |  | Research                                                                                                                                                                                                                                                                                                                                                                                                                         |
|--------|----------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10     | Antipyretic                |  | antipyretic activity however higher dose of extract (400 mg/kg) showed comparable efficacy as compare to the standard drug, paracetamol (150 mg/kg)26.                                                                                                                                                                                                                                                                           |
| 11     | Anti-diarrhoeal            |  | Methanolic root bark extract was tested against castor oil induced diarrhoea which significantly reduced the time of diarrhoea and total weight of faeces27                                                                                                                                                                                                                                                                      |
| 12     | Hepatoprotective           |  | Loganin extracted from fruit has shown effective hepatoprotective activity in vitro and in vivo models of liver injury induced by galactosamine . it was established by ameliorating the galactosamine mediated reduction of hepatocyte viability as well as bile volume and contents28                                                                                                                                          |
| 13     | Analgesic                  |  | Brucine and Brucine-oxide exposes their effect against thermic and chemical stimuli in hot-plate test and writing test. The content of 6-keto-PGF1a in Freud's complete adjuvant induced arthritis rat's blood plasma. These results disclosed that central and peripheral mechanism are involved in pain modulation 29.                                                                                                         |
| 14     | Anti-diabetic              |  | Methanolic seed extract of nuxvomica was studied on the normal and diabetic induced alloxan rats. At the doses of 100mg/kg and 200mg/kg. It showed a reduction in blood glucose level at 2nd and 3rd week when compared with initial levels of glucose.it was also observed that there is decrease time dependant hypoglycaemic effect by slight decrease in total protein and increase in total cholesterol, serum creatinine30 |
| 15     | Gastro protective activity |  | Nuxvomicaextract studied on helicobacter pylori on the gene expression of heparin - binding epidermal growth factor using gastric epithelial cell line keto - 3 even in dilution beyond Avogadro number . It was highly diluted (10°C) prepared in ethanol was found to reduce the pylori and relieves from the gastritis 31.                                                                                                    |

**Table 4:Name of formulation with its indication in Ayurvedic classics containing Nuxvomica seeds:**

| Sr No. | Formulation        | Indication                                               |
|--------|--------------------|----------------------------------------------------------|
| 1      | Agnitundi Vati     | Indigestion32                                            |
| 2      | Laxshmi Vilas Rasa | Cough, fever, Skin diseases, Diabetes33                  |
| 3      | Krimimudga Rasa    | Anthelmintic34                                           |
| 4      | Shholharan Yoga    | Diarrhoea- Antispasmodic35                               |
| 6      | Suptivatari Rasa   | Tingling, Numbness36                                     |
| 7      | Vishtinduk Vati    | Neurological disorder                                    |
| 8      | Vishtinduk tail    | Gout- Analgesic37                                        |
| 9      | Mahavishgarbha oil | Local application in Vatvyadhi (neurological disorder)38 |

|    |                                |                        |
|----|--------------------------------|------------------------|
| 10 | VistindukadiLepa (Paste)       | Syphilis39             |
| 11 | KupilubeejadiKawath(decoction) | LasikaMehadiChikitsa40 |

**Table no. 5 -Therapeutics Uses of different parts of Kupeelu**

| Part Use | Indication                                                                                                                                                                                                                                                                                                |
|----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Fruit    | Urinary disorders41 Paralysis42                                                                                                                                                                                                                                                                           |
| Root     | Cholera and intermittent fever43                                                                                                                                                                                                                                                                          |
| Seeds    | Diarrhoea, Dysentery, Diabetes Emotional Disorders, Hysteria, Epilepsy, Intermittent fever, Gout, Rheumatism, Hydrophobia, Impotence, Insomnia, Paralytic and Neuralgic disorders, Prolapsed Rectum, Antidote to Alcoholism, for general exhaustion in opium poisoning, Urine retention, spermatorrhoea44 |
| Bark     | Cholera and acute dysentery45                                                                                                                                                                                                                                                                             |
| Wood     | Dysentery , Fever, Cholera, Dyspepsia46                                                                                                                                                                                                                                                                   |

**Ethno-medicinal Application:**

In India the fruits are used in both the Ayurvedic and Unani systems of medicine as an aphrodisiac, tonic, and appetiser. It has been also claimed to be a curative medicine for Leucoderma, blood illnesses, itching, ringworm, piles, ulcer, anaemia, jaundice, urinary disorders, joint discomfort, lumbago, and limb weakness<sup>47</sup>. Nux vomica seeds are used as a remedy for a variety of conditions in India, including hysteria, epilepsy, gout, rheumatism, hydrophobia, sleeplessness, spermatorrhoea, chronic dysentery, atonic diarrhoea, cholera, diabetes, emotional disorders, and paralytic and neuralgic affections. They are also used as an antidote to alcoholism and for opium deaddiction. It is said that the juice from the stem and root barks can help with acute dysentery, cholera, and sporadic fevers. Barks infusion is used to treat epilepsy and is externally applied for the treatment of ulcers and leprotics. Externally leaves are applied as poultice and promote healthy action in sloughing wounds or ulcers especially when maggots have formed<sup>48</sup>.

**Clinical studies:****Sinusitis:**

The efficacy of nux vomica dilutions (potencies) in treating acute and/or chronic frontal, fronto-maxillary, sphenoidal, ethmoidal, and maxillary sinusitis was investigated in an open, multi-center observational study. Nux vomica 30C, 200C, and 1000C dilutions were used on 16 different sinusitis cases, and in 14 cases dilutions reported to be effective in alleviating sinusitis symptoms<sup>49</sup>.

**Rhinitis:**

Homoeopathic nux vomica dilution (potency) has been shown to be effective in treating acute rhinitis in children in an open, multicenter clinical trial. 109 kids with acute rhinitis received a dilution of nux vomica 6C. Of these, within 7 days of the trial period, 79.82% of the children were completely cured, 14.68% of the children showed remarkable improvement, and 5.50% of the children showed moderate improvement<sup>50</sup>.

**Insomnia:**

Nux vomica extract at high dilutions are known to be clinically useful for the treatment of insomnia. A clinical study on 10 patients showed that the nux vomica dilutions (3C and 15C) significantly lowered the serum cortisol levels in 38% patients. Nevertheless, there were insufficient patients in the trial to draw a conclusion about the clinical effectiveness of nux vomica dilutions<sup>51</sup>.

**Peripheral neuropathy:**

In 19 patients of boretzeyomib induced peripheral neuropathy in cases of multiple myeloma, nuxvomica capsule 0.4g thrice daily were orally administered for 30 days. It showed that peripheral neuropathy grade was lowered, neurotoxicity score was obviously decreased and total neuropathy score was remarkably decreased<sup>52</sup>.

**DISCUSSION:**

Nux vomica is a well-known spinal poison to modern science although many therapeutic indications of nuxvomica are widely described in Ayurvedic literature. Different parts of the plant especially seeds and bark possesses wide variety of indications. It is rich in different classes of phytochemicals of which mostly of indole alkaloids strychnine and brucine which are responsible for wide range of therapeutic potential. In preclinical studies it shows antioxidant, antinociceptive, antimicrobial, anticancer, antitumor, anticonvulsant, anti-snake venom, anti-alcoholic, antipyretic, anti-allergic, anti-diarrhoeal, hepato-protective, analgesic, anti-inflammatory, anti-diabetic, gastro-

protective effect. In clinical studies it shows efficacy in case of sinusitis, rhinitis & insomnia. Classical pharmacopoeias of Ayurveda prescribed many compound formulation of nuxvomica for the management of different diseased condition. The

**CONCLUSION:**

Various extracts, fractions as well as pure compounds obtained from different parts of nuxvomica shows their possible pharmacological effects in both in vivo and in vitro models. The Ayurvedic literature contains vague, generalised descriptions of S.nux-vomica's medicinal uses still there is lack of clinical trial. Hence for further evaluation and validation of clinical trials is necessary. Thus, there is a great scope for clinical research on this plant's holistic uses.

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