



## Review Article

### THE THERAPEUTIC AND TOXICOLOGICAL EFFECT OF *KUPILU* (*STRYCHNOS NUX-VOMICA* L.)- A REVIEW

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#### ABSTRACT

*Kupilu* (*Strychnos nux-vomica* L., family-Loganiaceae) is a poisonous herbal plant, also known as *Kuchla* in *Ayurvedic samhitas* and has been commonly used in Ayurvedic pharmacopoeia. It is also described in *Surasadi gana* of *Sushruta* and *Amradi phala varga* of *Bhavprakash*. It is a deciduous tree which is widely distributed in India and found throughout tropical areas of India, Sri Lanka, Vietnam, Thailand, Cambodia and Malaysia. In this review, an endeavor has been made to explore the therapeutic utilities of *Strychnos nux vomica* and its poisoning effect as mentioned in *Ayurveda*. It is observed that seeds of *Strychnos nux-vomica* are used as an ingredient of compound formulations of *Ayurvedic* medicine, indicated for nervous debility, paralysis and weakness of limbs, sexual weakness, dyspepsia, dysentery and chronic rheumatism. Additionally, it is employed in the treatment of anemia, asthma, bronchitis, colic, intermittent fever, hysteria, etc in a specific therapeutic dose. In higher doses, it produces tetanic convulsions ultimately resulting in death. *Kupilu* has been described as a toxic plant in *Ayurveda* so certain *Shodhan* process of the seeds are considered mandatory before its administration.

#### INTRODUCTION

*Kupilu* (*Strychnos nux-vomica* L.), a well-known plant in *Ayurveda* since long time, is being used extensively, now a days. We have a number of classical formulations with great therapeutic significance. Though the plant is described under the “*Upavisa Vargas*” of *Rastarangani*<sup>[1]</sup>, and *Rasratna Samuchya*<sup>[2]</sup> etc. it has been used successfully in the management of several diseases after proper *Shodhana* process. *Kupilu* was not mentioned in the “*Brihat Trayee*” texts of *Ayurveda* but later it was mentioned in different *Nighantus* with a number of synonyms. Its uses in *Ayurveda* were recorded from the period of “*Vrinda Madhava*” (9th A.D.). The drug *Visamusti* was mentioned in the English translation of *Vrinda's Siddha Yoga* edited by P. V. Tiwari, while describing ‘*Vatavyadhichikitsa*’.

Later different authors mentioned it with a number of synonyms like *Visatinduka*, *Kupilu*, *Visamusti*<sup>[2]</sup>, *Karaskara*<sup>[3]</sup>, *Kakatinduka*<sup>[4]</sup>, *Kulaka*, *Jalada*, *Garadruma*<sup>[5][6]</sup> etc, indicate the toxic nature of this tree. On the other hand, European countries started using this plant from sixteenth century onwards; however it was not abundantly utilized in drugs but was chiefly utilized to poison dogs, cats, crows, etc.<sup>[7]</sup> The ancient texts of *Ayurveda* quoted that the *Visha* (poison) act as an *Amrita* (nectar) if utilized legitimately.<sup>[8]</sup>

Ayurvedic physicians successfully employed this drug in a series of illnesses after proper *Shodhana* through a few particular media like *Godugdha*, *Kanji* and *Goghrita*.<sup>[1]</sup>

*Shodhana* procedures not only represent a process of purification, but also in addition to a process of detoxification and the ultimate objective of *Shodhana* is to enhance the biological efficacy of the drug.<sup>[9]</sup> The seeds are mainly used as an aphrodisiac, appetizer, anti-periodic, digestive, purgative, and a stimulant. They are also used in anaemia, asthma, bronchitis, intermittent and malarial fever and in weakness of extremities.<sup>[10]</sup>

Some scattered references are there regarding different therapeutic utilities as described in Indian medicine. Hence, an attempt has been made to compile them and present in a systemic manner.

#### PHARMACOLOGICAL PROPERTIES OF KUPILU

*Kupilu* has been attributed different pharmacological properties. Its seeds possess *Tikta*, *Katu* and *Kashaya Rasa*; *Laghu*, *Ruksha*, *Teekshna Guna*; *Ushna Virya* and *Katu Vipaka*.<sup>[11]</sup> According to some authors, its unripe fruits are *Sheeta Virya* and the ripe fruits having *Guru* and *Vishada Guna* with *Madhura Vipaka*.<sup>[12]</sup>

## CHEMICAL COMPOSITION

The dried seeds of *Nux vomica* contain 2.6%-3% total alkaloids, out of which 1.25%-1.5% is strychnine, 1.7% is brucine, and the rest are vomicine and igasurine.<sup>[11]</sup> Some other minor alkaloids are  $\alpha$ -colubrine,  $\beta$ -colubrine, 3-methoxycajine, protostrychnine, novacine, *n*-oxystrychnine, pseudostrychnine, isostrychnine, chlorogenic acid, and glycoside.<sup>[13]</sup>

**STRYCHNINE:** C<sub>21</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub> this violently poisonous alkaloid is crystalline, slightly soluble in cold water (1 part in 6700 U. S. P.), the solution being alkaline and bitter. It dissolves in 7 parts of chloroform and 150 parts of 90% alcohol. Strychnine is a terrible tetanic poison, affecting the cerebrospinal system, but it kills without producing marked anatomical change, the muscles and nerves being scarcely altered, although the brain and spinal cord may be congested, stomach and limbs intensely congested, right side of heart gorged (sometimes empty), and the lungs congested. The fatal dose of Strychnine is as low as 4 grain. 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.<sup>[14]</sup>

**BRUCINE:** This related alkaloid is also a product of chemical action on *Nux Vomica*. It is known to chemists as dimethoxyl strychnine C<sub>23</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>. Brucine is very bitter, freely soluble in cold alcohol, soluble (U. S. P.) in 850 parts of cold water.<sup>[14]</sup> It differs in reaction from Strychnine in that strong sulphuric or nitric acid strikes with it a blood-red colour, whereas with Strychnine no coloration appears. If to a hydrochloric acid solution of Brucine and Strychnine, potassium ferrocyanide solution be added, the Brucine precipitates, while the Strychnine remains dissolved. The mixed alkaloids can be quite closely separated by alcohol 0.97 sp. g., which freely dissolves Brucine, but scarcely dissolves Strychnine. Brucine is a poison which has the physiological qualities of Strychnine, but in a markedly less degree. Authorities differ, some considering it one-sixteenth, others from one-fortieth to one-fiftieth less energetic than Strychnine as a convulsant. It is absorbed much slower, and although more energetic as concerns the sensory nerves, is decidedly less dangerous than Strychnine. The antidotes and treatment for poisoning by Brucine are the same as for Strychnine.<sup>[15]</sup>

## THERAPEUTIC USES OF KUPILU

On going through many *Ayurvedic* as well as modern text books, it has been revealed that different parts of this plant have a broad spectrum of activities in a number of diseases.

Classical *Ayurvedic* literatures mentioned the pharmacological actions of *Kupilu* such as *Shothahara*, *Putihara*, *Vedanasthapana*, *Uttejaka*, *Nadibalya*, *Deepana*, *Pachana*, *Grahi*, *Shoolaprashamana*, *Hridayottejaka*, *Kaphaghna*, *Kasahara*, *Vajikarana*, *Balya*, *Kushthaghna*, *Kandughna*, *Swedapanayana* etc.<sup>[11]</sup>

And it also acts as *Vishama jwaranaghna*, *Raktabharwardhaka* etc. *Kupilu* is specially recommended during senility as *Rasayana* since it is considered to be a potent drug in countering old age problems. And it is also useful in the treatment of *Sigrapatanam* and *Dhwajabhanga*.<sup>[11]</sup>

Various text books of medicinal plants also mentioned the therapeutic uses of different parts of *Kupilu* as below:

**FRUIT:** The unripe fruit vitiates *Vata*, causes constipation while the ripe fruit alleviates all three *Doshas* and is used in urinary disorders and in diseases due to impure blood.<sup>[12]</sup>

**SEEDS:** Atonic; anti-diarrhoeal; anti-dysenteric, antispasmodic, emetic, febrifuge, stimulant and tonic; 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.<sup>[16]</sup> *Nux-vomica* seeds produce a sort of intoxication, for which they are habitually taken by some natives as an aphrodisiac by cutting down into small pieces and chewed with a packet of betel leaf.<sup>[17]</sup> The seeds also yield oil, and a dye; the dye gives a brown colour to cotton fabrics. Oil, obtained by heating the fresh seeds, is used externally in rheumatism.<sup>[18]</sup>

**LEAVES:** The leaves when applied as poultice, promote healthy action in sloughing wounds or ulcers, more especially in those cases when maggots have formed. It arrests further formation of them, and those in the deeper parts perish immediately when the poultice is applied.<sup>[19]</sup>

**BARK:** The juice of the stem bark is given in cholera and acute dysentery.

**WOOD:** The juice of the fresh wood is reported to be a popular remedy for dysentery, fever, cholera and dyspepsia.<sup>[20]</sup>

**ROOT:** The root bark is bitter and is useful in cholera and intermittent fevers. In Sri Lanka, the roots are applied externally for the management of snakebite. In Cambodia, the seed is used as an emetic. Internally, an infusion of the bark is given in epilepsy; externally, the bark is used in the treatment of ulcers, atonic and leprotics.<sup>[19]</sup>

## CERTAIN COMMON THERAPEUTIC USES IN AYURVEDA

*Shudha Kupilu* seeds are generally used in a dose of 60-250 mg in different disease conditions<sup>[11]</sup> and a few of its specific indications are given below.

**Indigestion:** *Kupilu*, *Navasagara* (NH<sub>4</sub>Cl) and *Hingu* (asafoetida) are rubbed with sour (lemon juice) and form the pills of the size of Bengal gram. It alleviates loss of digestive power and other disorders<sup>[21]</sup>.

**Visuchika (Cholera):** *Kupilu*, *Hingu* and *Navasagara* each is fried and mixed together. It is rubbed with water and made into pills which control *Visuchika*<sup>[22]</sup>.

**Fever:** *Sudha Kupilu* seeds with equal quantity of *Maricha* (*Piper nigrum*) powder is mixed with decoction of *Indrayava* (*Holarrhena antidysenterica* seeds) and made into pills. It removes constipation and fever due to vitiation of *Vata*<sup>[23]</sup>.

#### SOME COMPOUND FORMULATIONS OF KUPILU

Classical pharmacopoeias of *Ayurveda* prescribe certain compound formulations of *Kupilu* as an ingredient for the treatment of so many disease conditions. Some of them are *Agnitundi rasa*<sup>[24]</sup>, *Shulaharana yoga*<sup>[25]</sup>, *Kupilubeejadi kwatha*<sup>[26]</sup>, *Krimimudgara rasa*<sup>[27]</sup>, *Kitmarda rasa*<sup>[28]</sup>, *Krimighatini gutika*<sup>[29]</sup>, *Mahavisagarbha tailam*<sup>[30]</sup>, *Visatindukadi tailam*<sup>[31]</sup>, *Visatindukadilepa*<sup>[32]</sup> etc.

#### CONTRAINDICATION

*Kupilu* (*Nux vomica*) is contraindicated in pregnancy, breast-feeding, in contact dermatitis. No drug interaction with *Kupilu* has yet been reported<sup>[33]</sup>.

#### LETHAL DOSAGE

The smallest dose, which is known to produce death in humans, is 30 grains, i.e., equal to one seed of *Nux vomica*. The minimal oral dose of strychnine in an adult is 30–120 mg. The lethal dose in children is 15 mg. If strychnine is given parenterally, the lethal dose is again lowered<sup>[33]</sup>.

#### STRYCHNINE TOXICITY (LD50 VALUES)<sup>[34]</sup>

Animal	Body Weight (mg/kg)
Rabbit	0.6
Dog	1
Rat	5
Pigeon	21
Possum	30
Human	1-30

**Note:** LD50 values represent lethal dose for 50% of the population

#### TOXICOLOGICAL EFFECTS

In about an hour after a poisonous dose of Strychnine, the patient begins to feel uneasy from a sensation of impending suffocation. The tetanic convulsions then commence with great violence, nearly all the muscles of the body being affected at once. The limbs are thrown out, the hands are clenched, the head is jerked forwards and then bent backwards, and the whole body is perfectly stiff from the violence of the contractions. The pulse is very rapid, the temperature may rise. Hearing and sight are acute. The convulsion lasts a minute or two, then the muscles relax, and the patient feels exhausted and sweats all over.<sup>[34]</sup> The intermission is short, convulsions soon come on again, and again there is a relapse to the state of muscular relaxation. The convulsions now rapidly increase in severity and owing to the violent contractions of the muscles of the back, the patient is in the position of opisthotonus, resting on his head and his heels. The abdominal muscles are as hard as a board, the chest is

fixed, the face becomes livid, the eyeballs are staring. The contraction of the muscles of the face causes a *Risus sardonicus*<sup>[35]</sup> but those of the jaw are not affected till quite the end, consciousness is retained to the last. The slightest noise or even a bright light will reflex bring on the convulsions, which may jerk the patient out of bed. Ultimately he dies from exhaustion and asphyxia. The smallest dose of Strychnine known to have killed an adult is half a grain. In *Post mortem* -The usual appearances of death by asphyxia are seen.<sup>[35]</sup>

#### TREATMENT OF TOXICITY

If spasms have not closed the jaws, use the stomach pump at once. Employ emetics cautiously and discriminatively. The stomach is then washed out with a dilute solution of potassium permanganate. A suspension of animal charcoal should be introduced to absorb any free strychnine and afterwards removed. However, if the Strychnine is not removed, death is as certain as from the shock of convulsion, put the patient immediately under the influence of chloroform or ether, and keep him in perfect repose in a dark room. Inject large doses of potassium bromide and chloral hydrate per-rectum. Use no stimulants and make no noise, avoiding whispering even, or feeling the sufferer's pulse.<sup>[35]</sup> Chemical substances, such as tannin, simply retard alkaloid absorption without decreasing the final lethal action of the drug. Physiological antidotes, or antagonistic poisons, such as phenobarbitone sodium, sodium amytal intravenously in doses of 500-750mg, repeated in similar or lesser dosage as often as required, mephenesin intravenously in a doses of 3mg/kg body weight, and intravenous diazepam in a dose of 2.5mg.<sup>[36]</sup> chloroform internally, chloral by the rectum; morphine, physostigmine, and aconitine, hypodermically, sometimes delay death, or in case of small doses of the poison, help to bridge the patient over the critical period. But if enough Strychnine has been swallowed they cannot save life unless the stomach be cleaned of the poison. Artificial respiration, oxygen, and supportive therapy may be necessary.<sup>[35][36]</sup>

#### CONCLUSION

From the birth of humans, the plants are being employed by the people for their therapeutic uses and still we tend to have faith in their disease curing properties. Though *Kupilu* is taken into account as a toxic plant, it has been used for thousands of years in Ayurvedic medication after purification. *Nux vomica* was introduced in Europe during sixteenth century, however it was chiefly used as cattle poison at that time. Later, the European countries discovered its medicinal actions and *Nuxvomica* became a wonderful medication to treat many diseases. It also possesses antioxidant, analgesic and anti-inflammatory, nephro-protective, anti-diarrhoeal, anti-cancerous and wound-healing properties. It is additionally used as an aphrodisiac, nerve tonic, and a smart appetizer. However, only a few works has been done on this plant and there is a large scope of investigation for researchers. Hence, it is required to explore its



potential in the field of medicinal research and pharmaceutical sciences for novel and fruitful applications of this plant.

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