



## A COMPREHENSIVE REVIEW ON EFFECTS OF SODHAN KARMA (DETOXIFICATION PROCEDURE) AND THERAPEUTIC POTENTIAL OF VISHA-TINDUKA (*STRYCHNOS NUX-VOMICA*)

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### ABSTRACT

*Strychnos nux-vomica* is a highly poisonous flora which is abundantly found all over India. The seeds of this tree contain significant concentration of alkaloid Strychnine which is a spinal poison and causes mortality at fatal dose. There are no therapeutic uses of *Strychnos nux-vomica* in modern medicine but traditionally its seeds are used in treatment of various ailments. Ayurveda advocates a specialized procedure called as sodhan karma (detoxification process) of Poisonous drugs before using it as a therapeutic agent. Various Ayurvedic medicines like Agnitundi vati, Vishatinduka vati, Vishagarbha taila contains Detoxified *Strychnos nux-vomica* seeds. Research studies report that, after appropriate detoxification of *Strychnos nux-vomica* seeds as mentioned in ancient ayurveda texts, the contents of the major alkaloids such as Strychnine and Brucine declines significantly and exerts the therapeutic action without toxicity. Though it is considered as highly toxic drug, purified form can be utilized for therapeutic uses when administered in an appropriate dosage. *Strychnos nux-vomica* is found to possess medicinal properties like Analgesic and Anti-inflammatory properties, Anticonvulsant activity, Anti-tumor effects, Anti-amnesic activity, Antidiarrhoeal activity, Immunomodulatory effect, Anti snake-venom activity, Hepatoprotective and Anticholestatic activities as reported in various experimental studies. However, more evidence based research work has to be carried out to replicate these results in clinical trials.

**Keywords:** Kupilu, *Strychnos-nux vomica*, Ayurveda

### INTRODUCTION

*Strychnos nux-vomica* is a poisonous deciduous tree of Loganiaceae family which is abundantly found in India. This tree known as Kupilu or Kuchila in ancient Ayurvedic texts has been described as an Akshepajana drug (convulsant) and is included under upavisha varga (poisonous plants). Though it is highly poisonous but, can be used as a therapeutic agent after appropriate sodhan (purification) procedures as described in ancient texts of Ayurveda<sup>1</sup>. This is an evergreen tree usually 30 meters high and 1-1.8 meters in girth. The leaves are 8-15 cm long, broadly elliptical with prominent central nerves. Flowers are greenish white in color and the berries are round and 2.5-5.0 cm in diameter. The ripe fruit contains seeds which are poisonous, flat, circular discs, 2.5 x 0.6 cm, slightly concave on one side and convex on the other, ash grey in color, have a shiny surface and are covered with silky hairs. Unbroken seeds when ingested are not poisonous, as the hard pericarp is not soluble in digestive juices<sup>2</sup>.

The main active principles of seeds are alkaloid such as strychnine, brucine and loganine. They also contain vamicine, colubrine, logamine, logamine glycoside and fatty substance upto 3% alkaloids. Total alkaloids ranges from 2.6% to 5.3% of which approximately half proportion is of strychnine, but bark yields only brucine<sup>3</sup>. Recently, the reinvestigation of *Strychnos nux-vomica* resulted in the isolation of two colorless monoquaternary bisindole alkaloids from the seeds named as named 4-N-hydroxymethyl strychnidin-17-acetic acid and 10, 11-dimethoxy-4-N-hydroxymethyl strychnidin-17-acetic acid<sup>4</sup>. In another study, isolation of a colored monoquaternary bisindole alkaloid (strychnochrysin) from the roots was done<sup>5</sup>. Strychnine is colorless, bitter, odorless, rhombic, prism shaped crystals. It is very stable

and does not change during putrefaction of the dead body. Strychnine competitively antagonizes the inhibitory neurotransmitter glycine by blocking its post-synaptic uptake by brainstem and spinal cord receptors. Its action is particularly in the anterior horn cells. The fatal dose of strychnine is 15-50 mg and fatal period ranges from 1-2 hours<sup>6</sup>. This present paper aims to evaluate the role of detoxification process (Sodhan Karma) of *Strychnos nux-vomica* as mentioned in ancient texts of Ayurveda backed with recent research evidences and to review the therapeutic potential of *Strychnos nux-vomica*.

PUBMED, MEDLINE databases were searched for studies published from January 1990 to June 2011. The key words used for the search was '*Strychnos nux-vomica*, 'Ayurveda', 'Medicinal plants', etc. *In-vitro* analysis, as well as experimental trials was included in the review. Only research articles in English language were considered. Other languages were approved when there was an English abstract containing data essential for extraction.

### Procedure of Sodhan karma (Detoxification procedure)

Ayurveda advocates use of detoxified or purified *Strychnos nux vomica* seeds for the treatment of rheumatoid arthritis, gout, sciatica, backache, lumbago and all types of muscular pain. It is traditionally used as a nervine tonic, digestive stimulant and aphrodisiac traditionally. Various Ayurvedic medicines like Agnitundi vati, Vishatinduka vati, Vishagarbha taila contains detoxified *Strychnos nux-vomica* seeds. Ayurveda advocate Purification Process (Sodhan karma) for the detoxification of poisonous drugs before they can be utilized as therapeutic agent. The seeds of *Strychnos nux-vomica* are considered highly poisonous and are considered inappropriate to be used in therapeutics.

However, it can be used as a medicine after undergoing appropriate purification procedures known as sodhan karma. The description of detoxification process (Sodhan karma) of *Strychnos nux-vomica* seeds is described in detail in ancient Ayurvedic texts. Dried seeds of *nux-vomica* are soaked in cow's milk for 24 hours and its outer coating is removed by scrapping it with a knife. Then it is cut into small pieces and boiled in cow's milk for three days (for about four hours each day). At the end of each day's boiling, it is warmed with warm water and dried before use in subsequent days. After 03 days, it is dried under shade and fried with cow's ghee to be used as a therapeutic agent<sup>7</sup>. It's a matter of great interest to know the changes that take place in *Strychnos nux-vomica* seeds before and after the above mentioned purification process as mentioned in Ayurveda which transforms a potent toxic agent to a therapeutic agent. Research studies reporting the effect of this purification process (Sodhan Karma) of *Strychnos nux-vomica* are scarce. Some of the important research studies are summarized below:-

Katiyar *et al* (2010) evaluated the effect of detoxification on *Strychnos nux-vomica* seeds by traditional processing with aloe and ginger juices, by frying in cow ghee, and by boiling in cow milk. The seeds processed in milk showed the lowest strychnine content in the cotyledons, exhibited marked inhibition of PTZ induced convulsions and maximal potentiation of hypnosis, and were found to be the safest LD<sub>50</sub><sup>8</sup>. In another study it was observed that the content of strychnine in detoxified seeds to be one tenth of unprocessed *Strychnos nux-vomica* seeds. 01 ng of strychnine was detected from detoxified seeds of *Strychnos nux-vomica*<sup>9</sup>.

Similarly, Cai *et al* (1990) studied changes in alkaloid composition of the seeds of *Strychnos nux-vomica* on traditional drug-processing. In their study, the alkaloid composition of the heat-treated seeds of *S. nux-vomica* was compared to that of the untreated seeds. On heat treatment, the contents of the major alkaloids such as strychnine and brucine declined significantly with increases in the amounts of isostrychnine, isobrucine, strychnine N-oxide and brucine N-oxide<sup>10</sup>. These above mentioned studies clearly indicate that, there are definite changes in alkaloid content of seeds of *Strychnos nux-vomica* seeds after detoxification (Sodhan Karma) procedure as mentioned in classical texts of Ayurveda. This alteration of alkaloid content renders *Strychnos nux-vomica* to be regarded as a therapeutic agent.

Systemic review of available research literature reveals that there are only few studies which report the therapeutic potential of *S. nux-vomica*. These studies are summarized as follows:-

#### **Analgesic and anti-inflammatory properties**

In an experimental study, the analgesic and anti-inflammatory activities of brucine and brucine N-oxide extracted from seeds of *Strychnos nux-vomica* was investigated. Both brucine and brucine N-oxide revealed significant protective effects against thermal and chemical stimuli in hot-plate test and writhing test. Brucine N-oxide showed stronger inhibitory effect than brucine in carrageenan-induced rat paw edema, both of them significantly inhibited the release of prostaglandin E2 in inflammatory tissue, reduced acetic acid-induced vascular

permeability and the content of 6-keto-PGF1a in Freund's complete adjuvant induced arthritis rat's blood plasma. Results suggested that central and peripheral mechanisms are involved in the pain modulation and anti-inflammation effects of brucine and brucine N-oxide<sup>11</sup>.

#### **Anticonvulsant activity**

In a recent research study, Katiyar *et al* (2010) reported that ethanolic extracts of *Strychnos nux-vomica* seeds reduced spontaneous motor activity and inhibited catalepsy. The seeds processed in milk exhibited marked inhibition of PTZ induced convulsions and maximal potentiation of hypnosis, and were the safest LD<sub>50</sub><sup>12</sup>.

#### **Anti-tumor effects**

Deng *et al* (2006) reported that the major alkaloids present in the seed of *Strychnos nux-vomica* are effective against HepG2 cells proliferation. MTT assay was used to examine the growth inhibitory effects of these alkaloids on human hepatoma cell line (HepG2). Brucine, strychnine and isostrychnine revealed significant inhibitory effects against HepG2 cell proliferation, whereas brucine N-oxide didn't have such an effect. In addition, brucine caused HepG2 cell shrinkage, membrane blebbing, apoptotic body formation, all of which are typical characteristics of apoptotic programmed cell death. Immunoblot results revealed that brucine significantly decreased the protein expression level of cyclooxygenase-2, whereas increased the expression of caspase-3 as well as the caspase-3-like protease activity in HepG2 cells, suggesting the involvement of cyclooxygenase-2 and caspase-3 in the pro-apoptotic effects exerted by brucine<sup>13</sup>.

#### **Anti-amnesic activity**

In an experimental study, the effect of loganin (an iridoid glycoside found in the *Strychnos nux vomica*) on learning and memory impairments induced by scopolamine (0.5mg/kg, i.p.), using the Y-maze, passive avoidance, and the Morris water maze tests was investigated in mice. It was observed that, loganin (40 mg/kg, p.o.) significantly improved the scopolamine-induced memory impairment in the Y-maze test. In addition, loganin (20 and 40 mg/kg, p.o.) significantly reversed scopolamine-induced impairments measured by the passive avoidance and the Morris water maze tests. A day after the last trial session of the Morris water maze test (probe trial session), loganin (20 and 40 mg/kg) dose-dependently increased the latency time in the target quadrant. Furthermore, loganin significantly inhibited acetylcholinesterase activity in the hippocampus and frontal cortex. These findings clearly suggest that, loganin possess anti-amnesic activity that may hold significant therapeutic value in alleviating certain memory impairments observed in Alzheimer's disease<sup>14</sup>.

#### **Antidiarrhoeal activity**

A study was undertaken to evaluate the effect of aqueous and methanolic plant extracts of *Strychnos nux-vomica* root bark for their anti-diarrheal potential against castor-oil induced diarrhea in mice. It was observed that, the methanolic plant extracts were more effective than aqueous plant extracts against castor-oil induced diarrhea. The methanolic plant extracts significantly reduced induction time of diarrhea and total weight of the faeces<sup>15</sup>.

### Immunomodulatory effect

Duddukuri *et al* (2008) evaluated possible immunomodulatory effect of *Strychnos nux-vomica* on induction of ovalbumin specific IgE antibody response in a murine model, as evaluated by passive cutaneous anaphylaxis (PCA). The ovalbumin specific IgE antibody response was significantly suppressed in BALB/c mice (H-2d), following intraperitoneal administration of aqueous stem extract of the plant along with ovalbumin. Furthermore, the different doses of *Strychnos nux-vomica* extract were found to significantly suppress the induction of ovalbumin specific IgE antibody response. The anti-ovalbumin IgE antibody response was suppressed in different haplotypes of mice viz., C57BL/6 (H-2b) and SWR/J (H-29). However, preliminary findings revealed no significant change in the total IgG antibody response against ovalbumin, as evaluated by ELISA. These findings suggest the suppressive activity of *S. nux-vomica* on allergen-specific IgE antibody response and suggest its possible application in allergic conditions<sup>16</sup>.

### Antisnake venom activity

In a research study, Chatterjee *et al* (2004) reported that the whole seed extract of *S. nux vomica* (in low doses) effectively neutralized *Daboia russelii* venom induced lethal, haemorrhage, defibrinogenating, PLA2 enzyme activity and *Naja kaouthia* venom induced lethal, cardiotoxic, neurotoxic, PLA2 enzyme activity. The seed extract potentiated polyvalent snake venom antiserum action in experimental animals<sup>17</sup>.

### Hepatoprotective and anticholestatic activities

In an experimental study, loganin an iridoid glycoside extracted from the fruit of the plant, *Strychnos nux-vomica*, showed significant hepatoprotective and anticholestatic activities in rat model. Detailed study was carried out in isolated hepatocytes (*ex vivo*) and on bile flow (*in vivo*) against galactosamine induced hepatic damage in rats to determine its pharmacological potential. Loganin was given to rats at preselected doses (3, 6 and 12 mg/kg p.o. ×7). Silymarin a standard compound was given at the same doses for comparison. On 7<sup>th</sup> day galactosamine (400 mg/kg) was injected intraperitoneally. Study on isolated hepatocytes and bile flow was carried out 24 hours after treatment with galactosamine. Galactosamine reduced the viability of hepatocytes as well as bile volume and bile contents. Loganin showed a dose dependent activity (14%–67%) as observed by an increase in the viability of hepatocytes and the reversal of reduced parameters of bile<sup>18</sup>.

### CONCLUSION

*Strychnos nux vomica* is used for various medicinal properties in Indian traditional system of medicine. Recent experimental research evidences suggest that it exhibits various activities like analgesic and anti-inflammatory properties, anticonvulsant activity, anti-tumor effects, anti-amnesic activity, antidiarrhoeal activity, immunomodulatory effect, anti snake-venom activity hepatoprotective and anticholestatic activities.

These evidences validate the ancient claim of Ayurveda regarding the therapeutic potential of *Strychnos nux vomica*. The concept of detoxification (Sodhan karma) as mentioned in Ayurvedic texts holds good on scientific ground as these procedures decreases the total toxic alkaloid content of the *Strychnos nux-vomica* seeds and thus makes it therapeutically safe. However more efforts are needed for subsequent validation and replication of these results in clinical trials.

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