



Ethanobotanical, Phytochemical and Pharmacological Review on *Strychnos nuxvomica*

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ABSTRACT

Strychnos nux-vomica (Kuchla) belongs to the family Loganiaceae used in folklore and traditional medicines. The objective of present review on kuchla outcomes the agronomy, phytochemical constituents, structures and used for treatment of antioxidant, hepatoprotective, antsnake venom, anticonvulsant, antimicrobial, antipyretic, analgesic, neuropharmacological, gastritis, antialcoholic, larvicidal activities. This studies provides valuable information of kuchla for future research and helpful for the other studies to be carried out.

Keywords: *Strychnous nux-vomica*, Ethanobotanical, Phytochemical, Pharmacological.

INTRODUCTION

Strychnos nux-vomica also known as poisonous nut, Dog button, Kuchla, Kanjiramfits to the family of Loganiaceae. It is an evergreen and medium size tree that is native to South Africa and India. The seeds and barks acquire various components that are used in folklore and traditional medicines in different countries. Now-a-days *nuxvomica* is used in 60 formulations of Indian systems of medicine (Ayurveda, Homeopathy, Siddha, Unani and Yoga) out of the 30 of them are used in the disorders of vatadosha [1]. Principally this doesn't possess a role in modern medicine but it has been reported that it is widely used in elevation doses before 2nd worldwar. The effect of *nuxvomica* is due to the presence of Strychnine and Brucine which are indole alkaloids. Strychnine stimulates the motor or sensory ganglia of spinal cord that consequences in fiery convulsions whereas Brucine causes paralysis of peripheral motor nerve and is not as much of harmful than the Strychnine. At low doses it acts as stimulant, laxative and for the treatment of other stomach ailments [2]. Various phytochemical constituents have been isolated and there is progression of investigation on this plant in research of dynamics and kinetics but there is no detailed review about the pharmacological aspects and medicinal uses. Therefore the present review is about the cultivation and its Geographical distribution, Folklore usage, Ethnobotanical characters, Pharmacognostical characters, Phytochemical and Pharmacological aspect.

Topographical distribution

This plant is commercially cultivated in European and United States, Fujian, Taiwan and throughout Tropical Asia. Fundamentally it is indigenous to east India and found profusely in south India largely collected from forests of Tamil nadu, Kerala and Malabar coast. The annual production of *Strychnos nuxvomica* seed in India was estimated at 2000 tones at the beginning of 1970s. In the period of 1965 to 1971 the average production of *Strychnos nuxvomica* seeds in India was 18,000 kg/year. Most of this are exported to European and United States. Currently in 2000 as the technology has been improvised there is increase in exporting of Nuxvomica in India by export houses situated in Mumbai, Hyderabad, Kolkata [3].

Agronomy properties

The climate and soil should be favorable for the plant to grow well in dry humid tropical areas of the country. It grows over laterite, sandy and alluvial soils [4].

Ethnobotanical characters

- Domain: Eukaryote
- Kingdom: Plantae
- Division: Magnoliophyte
- Class: Magnoliopsida
- Order: Getianales
- Family: Loganiaceae
- Genus: *Strychnos*
- Species: *nuxvomica* [5]

Folklore usage

Nuxvomica has been used as the gastrointestinal stimulants, appetizer. Powdered seeds have been used for aptonic dyspepsia, paralysis asthma, piles, anemia and chlorosis [6].

Pharmacognostical characters

The plant is about 25 meters height and evergreen. Fruits are about equal to or more than 140 g that possesses smooth and hard shell during the early stage and when ripened it has a mild shade orange colour. Flowers are pale green in colour with small size and funnel shaped. The leaves are 10 cm long and 7.6 cm wide which are ovate, shiny and smooth on both sides. The young shoots are deep green in colour. The branches are shiny and deep green in colour [7] (Figures 1-3).



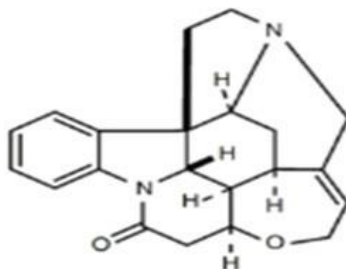
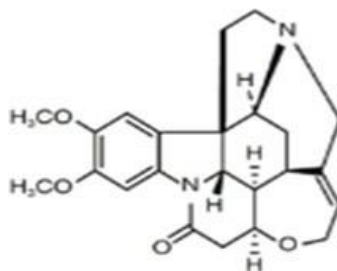
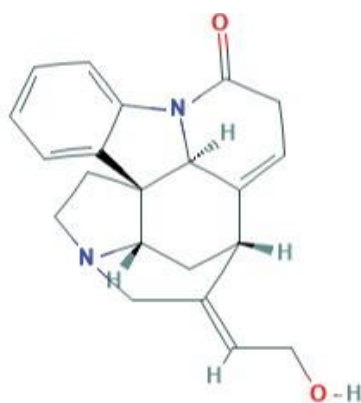
Figure 1. Nuxvomica fruit



Figure 2. Leaves

**Figure 3.** Entire tree*Phytochemical constituents*

These are the compounds that are naturally present in the plants which impart the colour, flavour, smell and taste. They help for the defensive mechanism of plants and helps to treat the diseases for humans and animals. Various numbers of phytochemical constituents have been isolated since decades a few of them are listed below from various plant parts of Nuxvomica (Figures 4-21). Structure of some of the phytochemical constituents isolated from nuxvomica:

**Figure 4.** Strychninine**Figure 5.** Brucine**Figure 6.** Isostrychninine

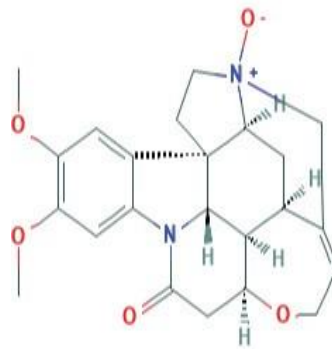


Figure 7. Brucine-N-oxide

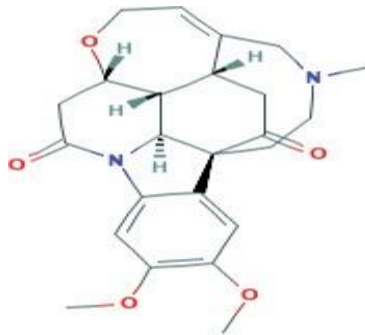


Figure 8. Novacine

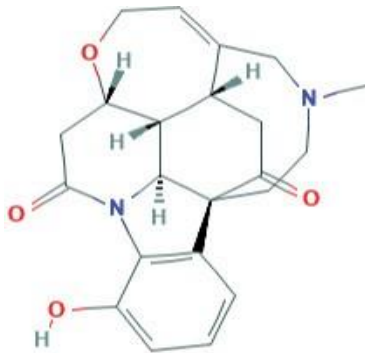


Figure 9. Vomicine

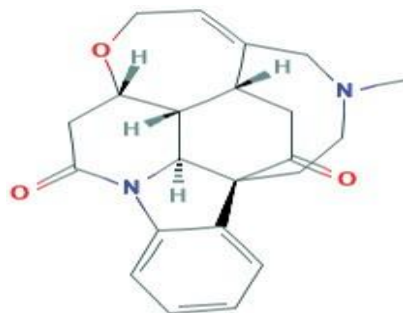


Figure 10. Icajine

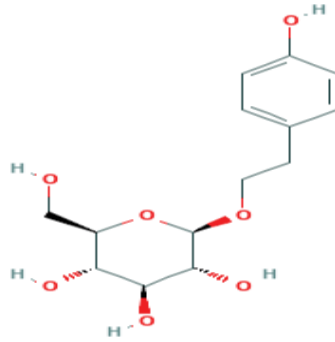


Figure 11. Salidroside

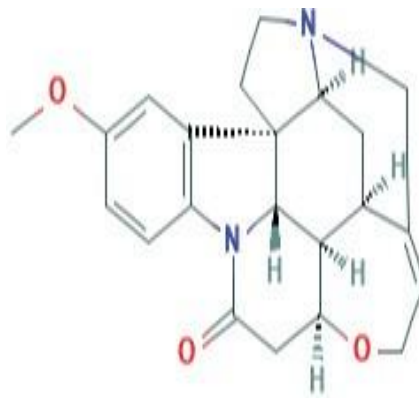


Figure 12. Beta-colubrine

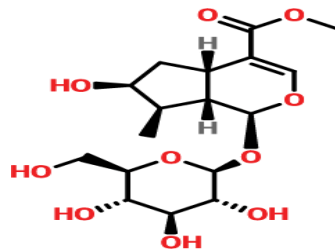


Figure 13. Cuchiloside

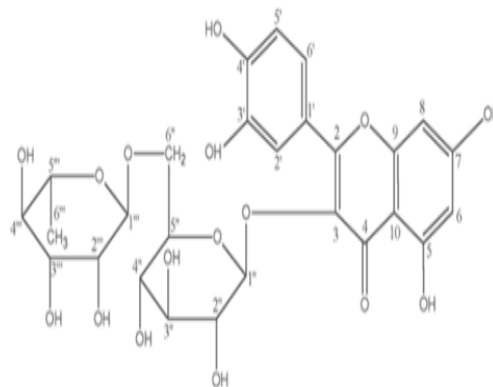


Figure 14. Rutin

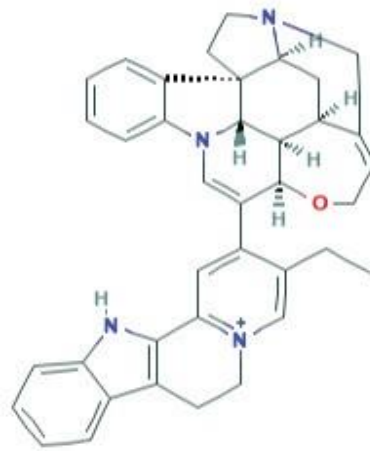


Figure 15. Strychnoflavine

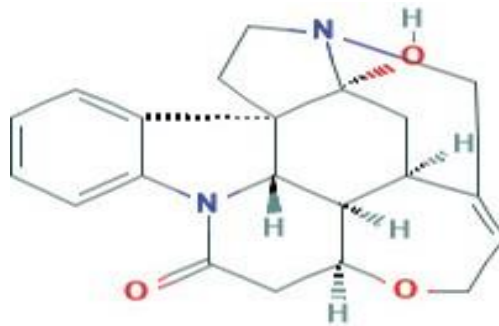


Figure 16. Pseudo strychnine

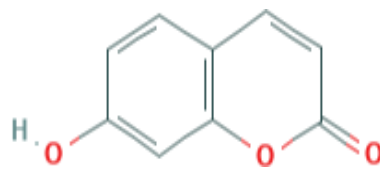


Figure 17. 7-hydroxy coumarin

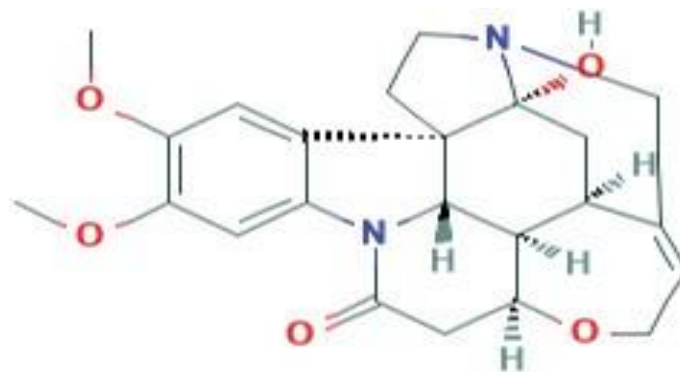


Figure 18. Pseudobrucine

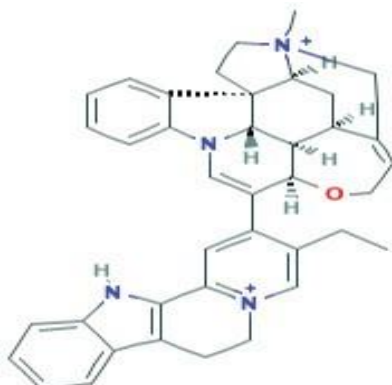


Figure 19. Demethoxyguiaflavine

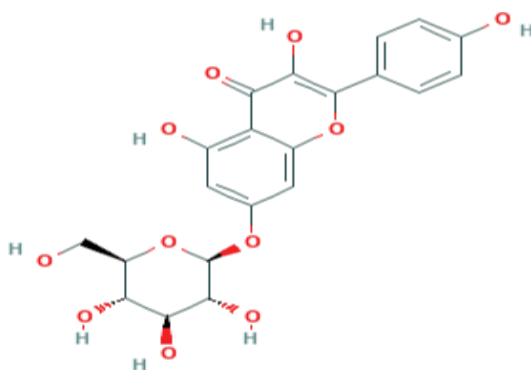


Figure 20. Kaempferol-7-glycoside

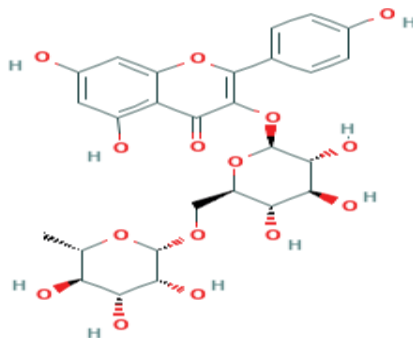


Figure 21. Kaempferol-3- rhamnoside

Seeds

The alkaloids identified by the chemical and spectroscopic analysis are the strychnine, isostrychnine, pseudostrychnine, strychnine N-oxide, isostrychnine N-oxide, Brucine, Brucine N-oxide, Isobrucine, Isobrucine N-oxide, Beta-colubrine, Novacine, Vomicine, Icajine [8].

Fruits

The phytochemicals present in the pericarp and pulp of the fruit are majorly strychnine and brucine along with the 4-hydroxystrychnine and a new base N-methyl-sec-pseudo-beta colubrine and a non-Indolicbase cantleyine. Phenolic glycosides named as salidoside and cuchiloside were present [9].

Leaves

Phytochemical investigation on leaves had an outcome of the isolation of compounds namely Kaempferol-7-glucoside, Umbelliferone, Quercetin-3-rhamnoside, kaempferol-3-rutinoside and Rutin [10].

Flowers

Indole alkaloids were isolated by mass spectra like strychnine, brucine which are isolated first and by mass spectral evidence they have come to know the presence of colubrine in the mixture of strychnine. Others like vomicine, icajine and novacine are present [11].

Barks

The bark contains numerous components like flavonoids, carbohydrates, tannins, triterpenoids and glycosides which was determined by the preliminary phytochemical analysis. The roots consists of the alpha colubrine, loganin, vomicine, pseudobrucine, 16-hydroxycolubrine and compounds like beta-colubrine, brucine, caffeic acid ester, strychnine, strychnocrycine pseudo strychnine, pseudobrucine, vomicine, icajine and novacine. Contemporary work on the root bark of *Nuxvomica* from Srilanka origin divulges the presence of these compounds nor-morcusine B, O-methylmacusine B, nor-melinonine B, isostrychine, protostrychine, 10-hydroxystrychine, 12-hydroxystrychnine, 12-hydroxy-11 methoxystrychnine, 4-hydroxy-3-methoxystrychnine, 4-hydroxystrychnine along with strychnine and brucine. The stem bark consists of brucine, strychnine, mavacuriine pseudo strychnine and caffeic acid ester. Research on stem bark by ¹³C NMR and Mass spectroscopy analysis reveals the presence of four dimeric bisindole alkaloids which are new demethoxyguiaflavine, strychnoflavine, strychnoflavine N-methyl-longicaudatine and strychnocrycine [12].

Pharmacological activities

Anti cancer activity

Strychnos nux-vomica extract exhibits the anti-proliferative property in dose dependent manner. There is accumulation of cells at the sub phase G(0)/G1 phase by using flow cytometry of cells stained by the propidium iodide. There is disruption of mitochondrial membrane potential and subsequent leakage of mitochondrial cytochrome C was observed when *Nuxvomica* extract treated with myeloma cells. This is mainly due to the strychnine and brucine [13].

Screened the antitumor effect of four alkaloids strychnine, brucine N-oxide, isostrychine, brucine, from the seed of *nuxvomica*. They have found that the first three compounds exhibit inhibitory effects on human hepatoma cell line (HepG2) cell proliferation, brucine has not shown much effect. In addition to that brucine showed apoptosis effect on hepG2 it acts by the preventing cells entering S or G2/M phase. Finally they indicate that strychnine, brucine N-oxide, isostrychine are effective against the HepG2 cells proliferation where as brucine results in the apoptosis. *In-vitro* screening investigation of the leaves extract of *nuxvomica* exhibits its activity on the potent anti-proliferative activity against human epidermoid larynx, breast, colon carcinoma cells with IC50 value of 17.8,363 and 41.2 mcg/ml [12].

Analgesic action

Scrutinized the effect of total alkaloid fraction on analgesic property make known that more brucine containing modified total alkaloid fraction shows high effect of analgesic property in all chemical, physical and thermal persuaded nociception models, that's specified the presence of both centrally and peripherally mediated activities. Brucine in modified total alkaloid fraction was absorbed completely through transdermal administration have the advanced pharmacological activity [14]. Investigated the activity by 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 [15].

Anti-diabetic activity

The anti-diabetic activity of methanolic seed extract of *nuxvomica* was executed on the normal and diabetic induced alloxan rats. They are treated with the extract at doses of 100 mg/kg and 200 mg/kg showed a reduction in the blood glucose level at 2nd and 3rd week when compared to initial levels of glucose. And by the study they came to know there is decrease time dependent hypoglycemic effect by the slight decrease in total protein and increase in total cholesterol, serum creatinine [16].

Gastroprotective

Studied the effect of *Strychnos nux vomica* extract on helicobacter pylori on the gene expression of heparin-binding epidermal growth factor using the gastric epithelial cell line KATO-3 even in dilutions beyond Avogadro's number. *Strychnos nuxvomica* was highly diluted (10⁶C) prepared in ethanol was found to reduce the pylori and relieves from the gastritis [17].

Neuropharmacological activity

The ethanolic extract of the *nuxvomica* were studied for the Spontaneous Motor Activity (SMA), phenobarbitone-induced hypnosis, pentylenetetrazole-induced convulsions, diazepam-assisted protection, and morphine induced catalepsy. Studies showed that sub-convulsive dose of processed seed extract inhibited the pentylenetetrazole-induced convulsions and potentiated barbiturate induced hypnosis in animals and shown that there is a marked decrease in the CNS depressant action. They have also found that the extract antagonize the morphine induced catalepsy. By this they found the *Nuxvomica* extract use in muscular rigidity [18]. Studied on brucine effect on the CNS diseases and the study reveals that extract has the property of allosteric enhancers of acetylcholine

binding to the muscarinic one receptor by 2-fold. They have found that *nux vomica* can be used for the preparation of medicines for the treatment of Parkinson's and Alzheimer's disease [19]. Performed their enquiry on the loganin an Indole alkaloid found the fruit of *nuxvomica* on the scopolamine induced learning and memory impairments by two tests Y-maze test and Morris water maze test in mice the results are loganin increased the scopolamine-induced memory impairments by the Y-maze test. By the Morris water Maze test there is reverse of scopolamine-induced impairments initially and after the day of trail session the latency of target time quadrant has been increased by loganin. Later on the loganin significantly inhibited the acetylcholinesterase activity in the frontal cortex and hippocampus. So this loganin is used in the treatment of Alzheimer's disease [20].

Larvicidal activity

Studies were carried on the *nuxvomica* to investigate about the larvicidal activity against the *Culex-quinque-fasciatus*. The analysis exposes that the ethyl acetate leaf extract was more effective by producing 100 percent mortality in 500 ppm at 48 hours [21].

Anti dote for snake venom

Studies passed out on the whole seed extract conceals that *Nuxvomica* neutralized the *Daboiarussellii* venom induced lethal ,haemorrhage,defibrinogenating, PLA2 enzyme activity and *Najakaouthia* venom induced lethal, cardiotoxic, neurotoxic, PLA2 enzyme activity [22].

Anti pyretic

The leaf extract of *nuxvomica* has an dose dependent activity. The high doses of *nuxvomica* extract (400 mg) shows the comparable efficacy when compared to the standard drug paracetamol. This research was carried on the pyrexia induced rats [23].

Anti alcoholic

The study carried out exposes that brucine extracted from the seeds of *Strychnos nuxvomica* suppress voluntary ethanol intake and reduced ethanol preference as measured using ethanol 2 bottle choice drinking paradigm in alcohol-preferring Fawn-hooded rats. They also found that systemic administration but did not decrease sucrose or self administration [24]. Dilutions at 30°C, 200°C and 1000°C of *nuxvomica* showed the significant antialcoholic property in mice. By giving them all the three potencies of *nuxvomica* restored ethanol-induced loss of righting reflex in mice more quickly than the controls. Another study revealed that ethanol induced sleep was reduced by the *Nuxvomica* dilutions at 200°C and 30°C *in vivo* on the toads and mice.

Anti-oxidant

The research on the *nuxvomica* extract given the evidence that it contains non-enzymatic and enzymatic antioxidants. The non-enzymatic antioxidants are specifically superoxide dismutase, ascorbate peroxidase, catalase, peroxidase and polyphenyl oxidase and the enzymatic antioxidants are ascorbic acid, alpha-tocopherol and reduced glutathione [25]. Further studies carried out by others make public that the antioxidant property was due to these enzymatic and non enzymatic antioxidants. They have come to know that the methanolic extract of the *nuxvomica* flower has the DPPH free radicals scavenging activity [26].

Hepatoprotective

The Indole alkaloid extracted from the fruit named as loganin has shown effective hepatoprotective activity *in vitro* and *in vivo* models of liver injury induced by the galactosamine. They established by ameliorating the galactosamine-mediated reduction of hepatocytes viability as well as bile volume and contents [27].

Anti microbial

The ethanolic seed extract of *Strychnos nuxvomica* was prepared and agar disc diffusion method test was carried out against the *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Bacillus subtilis*, *Proteus*, *Salmonella typhi*, *E.coli* strains at a 1000°C which results in the inhibition of only *E.coli*, *Staphylococcus aureus* and *Klebsiella strains* in a dose dependent manner [28].

Anti diarrhoeal

A research was carried out on the *Strychnos nuxvomica* for anti-diarrhoeal activity. The methanolic root bark extract was prepared and test was carried out against castor-oil induced diarrhoea which have the outcome of significant reduction time of diarrhoea and total weight of the faeces [29].

Anti convulsant

The ethanolic seed extract of *Strychnos nuxvomica* which has the Indole alkaloids mainly strychnine and brucine were taken and research was carried out and has an outcome of there action on neurotransmitters of human alpha 1, alpha 1 beta glycine recepto, alpha 7 nicotinic receptor, 5-HT3A Serotonin receptor, shown that strychnine and brucine has different stearic and electronic properties that show anticonvulsant activity [30]. paradigm in alcohol-preferring.

CONCLUSION

This review will be a helpful tool for those who are interested to carry out the research work on *Strychnous nux-vomica* Linn

which has been used in folklore and traditional medicines for several decades and this would be useful of studying different aspects towards *nuxvomica* regarding its geographical, Ethanobotanical, phytochemical constituents and pharmacological activities.

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