Strychnos potatorum: Phytochemical and pharmacological review

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ABSTRACT

In traditional system of medicine, the seeds of *Strychnos potatorum* Linn. (family: Loganiaceae) are used in the treatment of gonorrhea, leukorrhea leukeorrhea, gastropathy, bronchitis, chronic diarrhea, dysentery, renal and vesicle calculi, diabetes, conjunctivitis, scleritis, ulcers and other eye disease. An attempt has been made to highlight this medicinal seeds through phytochemical and pharmacological study. The present review deals with the phytochemical and pharmacological screening of therapeutic importance from *Strychnos potatorum* L., an important medicinal plant. This study includes the collective information of different medicinal uses of *Strychnos potatorum*. The generated data has provided the basis for its wide use as the therapeutant both in the traditional and folk medicines.

Key words: Medicinal plant; phytochemical; *Strychnos potatorum*

INTRODUCTION

Medicinal plants are used as a source of drugs for the treatment of various human and livestock health disorders all over the world from ancient times to the present day. They are important natural wealth. They provide primary healthcare services to people from all walks of life. They serve as important therapeutic agents as well as important raw materials for the manufacture of traditional and modern medicines. A total of 250,000 species of flowering plants are referred to as medicinal plants. The World Health Organization (WHO) enlisted some 21,000 medicinal plant species. The present global herbal market is worth about US$ 62 billion per annum. The annual growth of herbal market is about 15%and the global herbal market by 2050 is expected to be about US$ 5 trillion. Plants are one of the most important sources of medicines. Today the large number of drugs in use is derived from plants, like morphine from *Papaver somniferum*, Aswagandha from *Withania somnifera*, ephedrine from *Ephedra vulgaris*, atropine from *Atropa belladonna*, Reserpine from *Rouwolfiaserpentina*, etc., The medicinal plants are rich in secondary metabolites (which are potential sources of drugs) and essential oils of therapeutic importance. The important advantages claimed for therapeutic uses of medicinal plants in various ailments are their safety besides being economical, effective and their easy availability.[1,2] The increased global demand for polyherbal formulations is a reflection of positive impact of consolidated efforts aimed at reviving science of phytopharmacy.[3] *Strychnos potatorum* Linn (family: Loganiaceae) is a moderate sized tree found in southern and central parts of India, Sri Lanka, and Burma[4] In traditional system of medicine, the seeds are used in the treatment of gonorrhea, leukeorrhea, gastropathy, bronchitis, chronic diarrhea, dysentery, renal and vesicle calculi, diabetes, conjunctivitis, scleritis, ulcers, and other eye disease. The ripe seeds are used for clearing muddy water. The clarification is due to the combined action of colloids and alkaloids in the seeds[5] Hence in view of immense medicinal importance of the plant this review is therefore an effort to compile all the information reported on its phytochemical and pharmacological activities, this information will be helpful to create interest towards the plant and may be useful in developing new formulations, which are more effective and have more therapeutic values.

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TAXONOMIC CLASSIFICATION

- Kingdom: Plantae
- Class: Angiosperms
- Subclass: Eudicots
- Superorder: Asterids
- Order: Gentianales

- Family: Loganiaceae
- Genus: Strychnos.

PLANT PROFILE

- Common vernacular name[5,6]
- Clearing nut tree: English.

- Ambuprasadanaphala, Ambuprasadani, Chakshushya, Chh edaniya, Guchhaphala, Kata, Kataka, Katakarenu, Kattha, Khataka, Lekhanatmaka, Payaprasadi, Ruchishya, Ruchya, Rushya, Shlakshna, Shodanatmaka, Tiktamaricha, Tiktaphala, Toyaprasadana: Sanskrit
- Neimal, Nelmal, Nirmali: Hindi
- Chilbing, Chilhara, Gajara, Nirwali: Marathi
- Nirmali: Bengal
- Katakam, Tetta, Tettamparap, Titramparala: Malayalam
- Niemali: Punjabi
- Akkolam, Ilalam, Kadali, Sillam, Tatta, Tettankottai, Teru: Tamil
- Nirmali: Urdu

MORPHOLOGICAL CHARACTERS

Strychnos potatorum is a medium-sized, glabrous tree of height 1213 m. Stem is fluted and covered with black, thick, square to rectangular scales. Bark is 1.32 cm thick, black or brownish-black, corky, with very deep and narrow vertical, thin ridges, which easily break off. Branches are swollen at nodes. Leaves are about 57.5 cm long, nearly sessile, subcoriaceous, ovate or elliptic, acute, glabrous and shining, spuriously three or five nerved, with lateral nerves springing from the lower part of the mid rib, nearly reaching the tip. The base rounded or acute, petioles 2.5 mm long flowers large for the genus, in short almost glabrous nearly sessile axillary cymes; peduncles 0.5 mm long; and pedicels very short. Caly ×2 mm long, fivelobed; lobes 2.5 mm long, oblong, acute with a tuft of hair inside towards the base of each lobe. Ovary ovoid, glabrous, tapering into a long glabrous style; and stigma obscurely twolobed. Fruit is a berry, black when ripe, globose, 12 cm in diameter, whitish, shining, with short addressed yellow silky hairs. Seeds are globose in shape. Population of nirmali is depleting fast due to self nongenerative mechanism in fruits. They are often decayed and are prone to fungal attack as soon as they fall. Flowering occurs in September-October, while fruiting occurs in December [Figures 1 and 2].[5-9]

PHYTOCHEMICAL INVESTIGATION

Phytochemical studies revealed the presence of diaboline (major alkaloid) and its acetate[10] brucine, loganin, mannose, sucrose, arachidonic, lignoceric, linoleic, oleic, palmitic, and stearic acids.[11] On saponification of the oil: β-sitosterol, stigmasterol (also in leaves and bark along with campesterol); oleanolic acid and its 3β acetate, saponins containing acid oleanic, galactose and mannose (seeds) and triterpenes and sterols mannogalactans[12]

The curative properties of medicinal plants are perhaps due to the presence of various secondary metabolites such as alkaloids, flavonoids, glycosides, phenols, saponins, sterols etc., The successive extracts of root, stem bark, and seeds of *Strychnos potatorum* have revealed the presence of alkaloids, flavonoids, glycosides, lignins, phenols, saponins, sterols, and tannins. The lignan glycosides vanprukoside, strychnoside, and glucopyranoside isolated from *Strychnos vanprukii* have shown significant antioxidant property. Among the five groups of phytochemicals determined from the root, stem bark, and seeds of *Strychnos potatorum* tannins were found to be the most abundant one followed by saponins and alkaloids. While phenols and flavonoids were low in concentration 20 quenching and fluorescing alkaloids were reported from the various parts of the plant. However, more number of alkaloids were found in the root and stem bark.[13] The interconversion of these compounds into other derivatives owing to the prolonged period of storage and method of processing in case of the market seed. The most abundant alkaloid diaboline is found in all samples of *Strychnos potatorum* and identified by matching with authentic sample.

Figure 1: Lorius - The biodiversity conservation society

Figure 2: Prelude medicinal plants database

Alkaloids are the lead molecules of therapeutic importance from Strychnos species[14] These are heterocyclic indole compounds which have proved to be having pharmacological properties such as hypotensive activity, anticonvulsant activity, antiprotozoal, antimicrobial and antimalarial activities.

Three flavonoid were reported in the root. Collected and market seed samples show different color and Rf values. Whilein the stem bark four alkaloid were observed. Flavonoids are the phenolic substances and are the largest group of phenols. These generally occur as a C6-C3 unit linked to an aromatic ring. Three glycosides with similar color and Rf values were observed both in the root and stem bark whereas, four glycosides were observed in both seed samples.

The highest numbers of phenols were reported in the market seed. However, five phenolic with similar color and Rf values (6.67, 16.67, 44.0, 58.67, and 90.0) were found both in root and stem bark. Further, it is observed that five alkaloids were found to be common for root, stem bark, and collected seed. Plants have the limitless ability to synthesize phenols or their derivatives. The presence of phenols in all types of tissues is a characteristic feature of plants. The data of saponins of *Strychnos potatorum* by thin layer chromatography has revealed the presence of five yellow to intense yellow colored saponins in all parts of the plant. Saponins are glycosides of both triterpenes and sterols generally possessing five sugar units and gluconic unit as a component. The occurrence of saponins has been reported in over 70 families of higher plants.[14] The data of sterols of *Strychnos potatorum* by thin layer chromatography has revealed the presence of four sterols in the stem bark and seeds. While three sterols; which may be isomotiol, sitosterol, stigmasterol, or compesterol were found in the root. The high performance liquid chromatogram (HPLC) has shown 61 peaks. However, 18 peaks were prominent with significant percent area and height (>0.5%). The most abundant peak, which is probably diaboline, the prominent alkaloid of this plant as reported earlier. The total alkaloid fraction isolated from the seeds of *Strychnos potatorum* when administered in mice and rats at the doses of 70-100 mg/kg, intraperitoneally (i.p.) produced restlessness, irritability and tremorsfollowed by convulsions of tonic type all over the body and hypotensive action.[15,16] The methanolic extract of the dried seeds was found to have diuretic and antidiarrheal activities. The seed powder (SPP) was found to possess antidiabetic activity. Mannogalactans isolated from the seeds of *Strychnos potatorum* showed antihypercholesterolemic activity in experimental rats.[17]

Traditional uses

According to Ayurvedaseeds are acridalexipharmiclithotriptic and cures strangury, urinary discharges, head diseases etc., Roots cureleukeoderma whereas fruits are useful in eye diseases, thirst, poisoning, and hallucinations. The fruits are emetic, diaphoretic, alexiteric, etc., According to Unani system of medicine, seeds are bitter, astringent to bowels, aphrodisiac, tonic, diuretic and good for liver, kidney complaints, gonorrhea, colic, etc.

- Powdered stem bark mixed with lime juice given in cholera
- Leaves: As poultice over maggot infected ulcers
- Seed: Tonic stomachic demulcentemetic and used in acute diarrhea, diabetes, gonorrhoea, and eye diseases like conjunctivitis, lachrymation, or copious watery of eyes. The paste of seed is reported to be consumed internally along with little tender coconut milk in urinary disorder and retention of urine.[17]

Toxicological studies

The acute and chronic toxicity studies of aqueous extract (SPE) and of *Strychnos potatorum* Linn. were carried out on Wistar albino mice and rats. Both extracts did not produce any signs of toxicity and mortality up to the dose level of 2000mg/kg body weight orally in mice. The drug is categorized as unclassified. In chronic toxicity studies, both SPE and SPP at the dose of 100-200 mg/kg did not produce any significant changes in body weight from day 0 to 90 when compared with control group. Various parameters are taken into consideration like Red blood corpuscles white blood corpuscles hemoglobin erythrocyte sedimentation ratebiochemical parameters like blood glucose, urea, and serum creatinineenzyme parameters like alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and acid phosphatasewere studied.[18]

PHARMACOLOGICAL INVESTIGATION

Although many pharmacological studies have been performed on the basis of chemical constituents present, a lot more are still to be exploited, explored, and utilized. Important pharmacological findings are summarized below:

Anti-diabetic activity

Strychnos potatorum has antidiabetic activity. In Wistar albino rat, the diabetic state was induced by intraperitonial injection of alloxan at a dose of 100 mg/kg of body weight. Animals were grouped into normal rat (control), diabetic rat (alloxan), diabetic but extract treated rat, only extract treated rat, and diabetic but standard antidiabetic drug tolbutamide treated rat groups. Animals were screened for the parameters such as body weight, blood glucose level, total proteins, and cholesterol and enzyme levels such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) for deducing the antidiabetic activity of the test plant. The alloxan treated rat shows reduced body (26%) and liver (40%) weight. The blood glucose level falls by 53% with extract treatment, demonstrating the antidiabetic potential of the plant. The serum enzymes AST and ALT were increased from 24 and 18 IU/1 to 60 and 65 IU/1 respectively whereasALP was decreased to 5 IU/1 from 14 IU/1. The total serum protein level also increased up to 5 mg/ml in the extract treated animal. The insulin level also increased up to 61 μg/ml within 30 days of extract treatment compared to control with 51 μg/ml. The plant extract efficiently decreased the initial cholesterol 219 μg/ml level into 170 μg/ml.

In liver, the AST, ALT and ALP enzymes were decreased to 160, 60, and 140 IU/1 from 178, 79, and 156 IU/mlrespectively.[19]

Anti-inflammatory effect

The anti-inflammatory effect of SPP and SPE of *Strychnos potatorum* Linn. Seeds was studied in carrageenin-induced hind paw edema and cotton pellet granuloma models. Both SPP and SPE were found to normalize the increased alkaline, acid phosphatases, and lipid peroxide levels indicating their membrane stabilization and free radical scavenging properties, respectively. Both SPP and SPE exhibited dose dependent anti-inflammatory activity in acute and subacute inflammatory models, and its effect was also comparable with the standard drug diclofenac sodium.[20,21]

Antiulcerogenic potential

The antiulcerogenic potential of *Strychnos potatorum* Linn seeds on aspirin plus pyloric ligation (aspirin PL)-induced gastric ulcer model was studied. The SPP and SPE exhibitantiulcerogenic activity by both antisecretory and mucoprotective actions. The mucoprotective action of SPP and SPE may be due to the presence of polysaccharides in seeds. The antiulcerogenic potential of SPP and SPE was compared with the standard antiulcer drug, ranitidine. The antiulcerogenic potential was confirmed by the histopathological studies of stomach mucosa.[22]

Hepatoprotective and antioxidant activity

The SPP and SPE of *Strychnos potatorum* seeds possess hepatoprotective and antioxidant activities against CCl_4-induced acute hepatic injury. Hepatoprotective action is by reducing the serum marker enzymes like serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT). They also reduced the elevated levels of ALP and serum bilirubin. Reduced enzymic and nonenzymic antioxidant levels and elevated lipid peroxide levels were restored to normal by administration of SPP and SPE. Histopathological studies confirmed the hepatoprotective activity of SPP and SPE when compared with the CCl_4 treated control groups. The standard used for this study was silymarin.[23]

Antiarthritic activity

The effect of the SPE and the whole SPP of *Strychnos potatorum* Linn seeds on the Freund's complete adjuvant (FCA) induced arthritic rat paw edema, body weight changes and alterations in hematological and biochemical parameters in both developing and developed phases of arthritis was investigated in the laboratory on rats. Histopathology of proximal interphalangeal joints and radiology of hind legs were studied. Both SPP and SPE at the specified dose level showed reduction in rat paw edema volume and it could significantly normalize the hematological and biochemical abnormalities in adjuvant induced arthritic rats in both developing and developed phases of FCA induced arthritis. Further the histopathological and radiological studies confirmed the antiarthritic activity of SPP and SPE.[24]

Antinociceptive and antipyretic effect

The antinociceptive and antipyretic effect of SPP and SPE of *Strychnos potatorum* was evaluated in albino mice and rats respectively. The antinociceptive activity was studied in both chemical induced writing and thermal models of inducing nociception. SPP and SPE of *Strychnos potatorum* were found to exhibit antinociceptive activity in both chemical and thermal models indicating their central as well as peripheral mechanism in inhibiting the nociception respectively. Antipyretic activity is dose dependent.[25]

Antidiarrheal activity

The antidiarrheal activity of the methanol extract of the dried seeds of *Strychnos potatorum* (MESP) has been evaluated in rats using different models diarrhea (castor oil-induced), effects on gastrointestinal motility and on prostaglandin (PG) E2-induced gastric enteropooling. It significantly inhibited the frequency of defecation and reduced the wetness of fecal droppings in castor oil-induced diarrhea, decreased the propulsion of charcoal meal through the gastrointestinal tract, and also reduced the PGE2-induced enteropooling.[26]

Diuretic activity

(SPSE) was evaluated for its diuretic activity in Wistar albino rats. The parameters which were taken into account during the experimental on each rat were: Total urine volume (corrected for water intake during the test period), body weight before and after the experiment, and the concentration of sodium, potassium, and chloride ions in urine. The total urine volumes of the SPSE (600 mg/kg)-treated rats were evaluated nearly two and halffold then compared with the control (saline treated) group. Excretion of cations (sodium and potassium ions) and anions (chloride ions) also increased significantly with respect to the control group. The diuretic effect was comparable with that of the standard drug furosemide. The increase of cations in the urine on treatment with *Strychnos potatorum* seed extract (SPSE) was dose-dependent. This effect supports the use of the *Strychnos potatorum* seeds as a diuretic in folk remedies.[27]

Contraceptive efficacy

The 70% methanolic extract of *Strychnos potatorum* seeds shows contraceptive efficacy. The aqueous solution of extract was administered orally to male rats of proven fertility for 60 days. Sperm motility, sperm density, serum testosterone level, biochemical analysis and testicular cell population dynamics were carried out to assess the contraceptive effect of *Strychnos potatorum*. *Strychnos potatorum* seed possesses suppressive effects on male fertility and could be useful in development of male contraceptive agent.[28]

Surface active agents from the seed oil of Strychnos potatorum

The sodium soaps and sulfonated sodium surfactants prepared from the seed oil of *Strychnos potatorum* are found to be better critical micelle concentration (CMC), surface active matter and dispersive powers in comparison to the sodium and sulfonated sodium surfactants prepared from castor oil. *Strychnos potatorum*

detergents also exhibited a good inhibition activity on the growth of *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* that adds to their safe use.[29]

Clarification of turbid water

In developing countries, ground water, which is contaminated with domestic and industrial waste, is commonly used for drinking. Color, turbidity and microbial content affect quality of potable water. The seed of nirmali tree *Strychnos potatorum* Linn. shows coagulation properties in clarifying turbid water. This property was attributed to the presence of anionic polyelectrolytes having -COOH and free -OH surface groups that are present in the seed protein.[30]

Metal binding properties

The metal binding property of these seeds is of recent interest where some bench scale experiments were conducted in order to establish the binding of metal ions from dilute HCl solutions. The seeds collected from the trees of *Strychnos potatorum* Linn. were ground to 0.5 mm size for experimentation purpose. The binding of different transition metals from aqueous solutions by these seeds was studied for Au (I), Ag (I), Cu (I), Cu (II), Co (II), Ni (II), Pb (II), Zn (II), Fe (II) and Fe (III) by shaking 1.0 g of the powdered seed in a 5% v/v HCl solution containing 50.0 and 1.0 ppm of the respective metal ion in a 50 ml solution for 5 min. The filtrate obtained after each experiment was analyzed for the respective metal ions and the results obtained are Au (I) = 40.80 ppm; Ag (I) = 41.10 ppm; Cu (I) = 38.00 ppm; Zn (II) = 41.70 ppm; Fe (II) = 42.10 ppm, and Fe (III) = 38.20 ppm. On an average the seed binds 0.5 mg of the respective metals per 1.0 g of the seed. These seeds were fractionated into three different fractions, namely, fractions A B, and C using solvent extraction, distillation, and centrifuging techniques in order to investigate what fraction of the seed is responsible in metal ion binding, and the weight percentages of each fraction were found to be 655, and 30%, respectively. Fraction A mostly comprises of carbohydrates and some protein, whereas, fraction C is pure protein. Fractions A and C are found to be equally responsible for the binding of metals.[31]

Antimicrobial properties

The alcoholic extracts of *Strychnos potatorum* showed antibacterial activity against pathogenic gram positive, gram negative, and acid-fast bacteria and fungi, *Staphylococcus aureus*, and *Escherichia coli*. These fractions have shown considerable antimicrobial activity against both bacteria and fungi at the tested concentrations (100 and 200 μg/ml). Further, the growth of *Proteus vulgaris*, *Staphylococcus aureus*, *Salmonella typhimurium, Vibrio cholerae, Mycobacterium tuberculosis, Aspergillus niger,* and *Candida albicans* were significantly inhibited.[32]

CONCLUSION

Strychnos potatorum, the versatile medicinal plant is the unique source of various types of compounds having diverse chemical structure. Very little work has been done on the biological activity and plausible medicinal applications of these compounds and hence extensive investigation is needed to exploit their therapeutic utility to combat diseases. Although crude extracts from various parts of nirmali have medicinal applications from time immemorial, modern drugs can be developed after extensive investigation of its bioactivity, mechanism of action, pharmacotherapeutics, toxicity, and after proper standardization and clinical trials. As the global scenario is now changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from nirmali should be emphasized for the control of various diseases. Quite a significant amount of research has already been carried out during the past few decades in exploring the chemistry of different parts of nirmali. An extensive research and development work should be undertaken on nirmali and its products for their better economic and therapeutic utilization.

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