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Review Article

Potential Therapeutic use of *Streblus asper*: A Review

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ABSTRACT: *Streblus asper* (Family: Moraceae) is a small tree which mainly located in India, Thailand, Malaysia and Philippines. Generally, it is usually known as Sihor (Hindi), Sheora (Bengali), Pitaphalaka (Sanskrit) and Piraayan (Tamil). The present review thus attempts to observe the ethno-pharmacological information base for targeting of various activities (Anti- cancer activity, Neuro-pharmacology, Anti-filarial Activity and Anti-diabetic activity). This pharmacological validation on *Streblus asper* is very restricted and *Streblus asper* used in tribal and folklore with massive potential have not been validated for above activity. This review therefore attempts to link the gaps in the existing literature and offers immense scope for researchers engaged in validation of the traditional claims and development of safe and effective and globally accepted of this plant as a potent therapeutic target. Therefore, this review attempts botany, chemistry and biological use of *Streblus asper*.

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INTRODUCTION

Herbal remedies are the ancient medicines known to man folk. Herbs had been used by all ethos throughout history, but India has one of the oldest, abundant and most different cultural present traditions allied with the use of medicinal plants [1]. In the present situation, the demand of herbal agents is increasing day- by-day so the pharmaceutical companies doing the efforts on research of medicinal agents on their potential medicinal value.

Herbal medicines form a key part of cure in traditional medical systems such as Ayurveda, Rasa, Siddha, Unani, and Naturopathy. Recently, there has been a modified in global trend from synthetic to natural drug, which we can perceive 'Back to nature'. Medicinal herbs have been recognized for millennia and are highly valued all over the world as an abundant source of therapeutic agent for treatment of disease and ailment.

India is chief producer of herbal drug and is rightly named as "Botanical garden of the world". India in this concern has a very unique position in the world, where several recognized indigenous systems of medicine *viz.,* Ayurveda, Siddha, Unani, Homeopathic, Yoga and Naturopathy are practiced and applied for the health care of the people [2].

India has an oldest legacy of traditional medicine. Materia medica of India provides wide knowledge on the folklore practices and traditional features of therapeutically significant natural agents. The various numerous systems including Ayurveda, Siddha and Unani are based on Indian traditional medicine. The assessment of these medicines is commonly based on phytochemical, pharmacological and allied approaches including various analytical methods like chromatography, microscopy and others. Traditional systems of Indian medicine have their characteristics no doubt but there is a common barrier running through these systems in their vital theory and practices.

With the emerging consideration in the world to adopt and work the traditional system and to discover their potential based on different healthcare system, the research work and assessment on the traditional medicine is essential. The government and private sectors are trying their best to discover all possibilities for the assessment of these systems to bring out therapeutic approaches existing in original system of medicine as well as to aid in generating data to put medicinal agents on national health care program.

Current Regulations for Standardization of Crude Drugs -

In India a great deal of wide knowledge exists among ordinary people about the traditional application of herbal medicine. It is difficult to measure the market demand of the traditional Indian system. Since most practitioners formulate and dispense their individual recipes. According to the research on the outlook of current medicine practitioners are not relatively familiar with Ayurvedic drug even though some are practiced. They are willing to try an Ayurvedic product if its efficiency is pharmacological validated and would try disease such as cold, stomach problem, skin disease, cough, diarrhoea, reproductive and liver disease [3].

Pharmacy provides Patent proprietary Ayurvedic medicines over the counter. These medicinal agents appear to show a major share of renowned traditional medicine in India. Nevertheless, systems like Ayurveda still require gaining an empirical support of modern medical system to make them trustworthy and suitable for all. An innovative research work to define the benefit of traditional system of drug with respect to their safety and efficacy could result in a better use of these complementary systems of medicine. Internationally numerous pharmacopoeias have mentioned monographs showing parameter and standard of many herbs and several new dosage forms made of these herbs. Several pharmacopoeias like Pharmacopoeia Committee -

- Chinese Herbal Pharmacopoeia
- United States Herbal Pharmacopoeia
- British Herbal Pharmacopoeia (BHP)
- British Herbal Compendium (BHC)

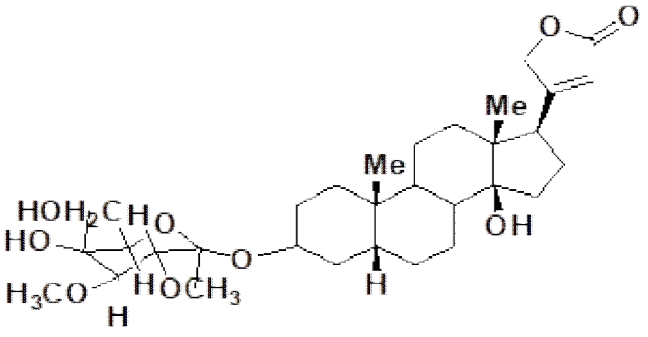
Streblus asper is a gnarled tree or rigid shrub; branchlets tomentose or pubescent. Leaves are 2–4 inch, rigid, rhomboid, elliptic, obovate or ovate, irregularly toothed; petiole 1/12 inch. It is habitat in the drier portion of India, from eastward, Rohilkund, eastward and southwards to Penang, Travancore and the Andaman Islands.

The pharmacognostical study of its stem bark as well as its root bark has been carried out [4, 5]. It finds place in the Ayurvedic Pharmacopoeia of India [6] and has also been explained in some monographs [7], but none have mentioned the whole chemistry and pharmacology of this significant ethnomedicinal plant. Therefore, we objected to assemble an up-to-date and complete review of *S. asper* that covers its folk medicinal, traditional uses, phytochemistry and pharmacology.

Fig. 1: *S. asper*. (A) Whole tree. (B) Flowering twig

Phytochemistry

Streblus asper is an abundant source of cardiac glycosides. Reichstein and co-workers [8-11] have isolated more than 20 cardiac glycosides from the root bark of *S. asper* and were able to structurally characterize 15 such compounds, mainly because of the use of degradative techniques, namely asperoside, kamloside, strebloside, indroside, cannodimemoside, strophalloside, strophanolloside, 16-O-acetylgluco-gitomethoside, glucogitodimethoside, gluco- kamloside, sarmethoside and glucostrebloside.



Asperoside

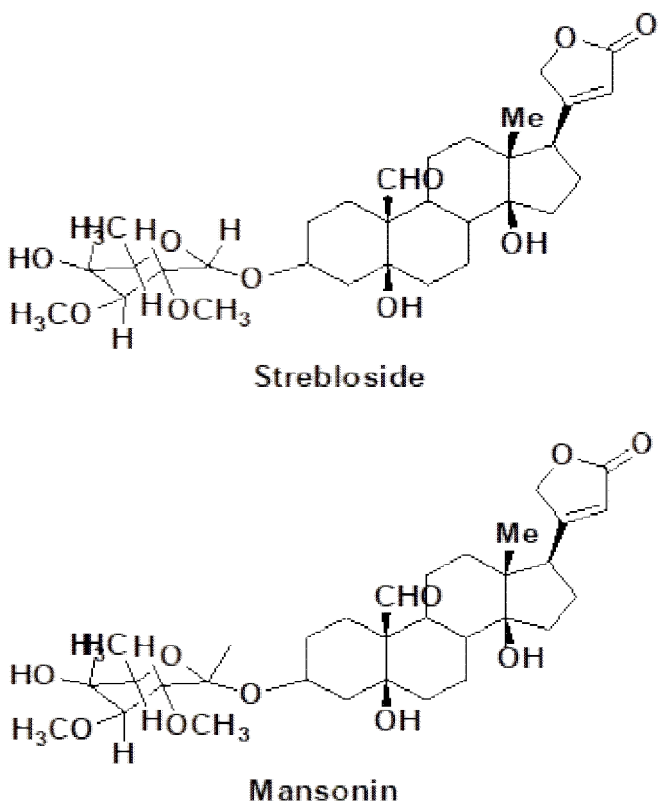


Fig. 2: Structure of biologically active constituents extracted from *S. asper*

Pharmacological Properties

Different portions of this plant have been found to show cardiotonic, antifilarial, anti-cancer, antimicrobial, anti-allergic and antimalarial activities. These have been described in greater feature in the following.

Cardiotonic Activity

The total ethanolic extract of the root bark of *Streblus asper* was found to indicate remarkable activity on isolated frog heart, blood pressure, isolated rabbit intestine and guinea pig uterus. A αβ-unsaturated lactone was separated. It administered by i.v. route gave the LD_{50} of 4.8 mg/kg in white mice. Examinations on isolated frog heart indicated that it induces a stimulating ionoptropic effect in 10^{-5} dilution and a systolic response in 10^{-4} dilution. Pronounced in vitro spasmodic effect of the compound was observed on the smooth muscles of the rabbit intestine and guinea pig uterus in those high dilutions [12]. Pharmacological works carried out have showed that the crude drug has got positive action on cardiac muscle [13].

Antifilarial Activity

The plant extract (aqueous extract) indicated significant macro-filaricidal potential against *Brugia malayi* and *Litomosoides carinii* in rodents. The study shown two cardiac glycosides, strebloside and asperoside found in extract which responsible for antifilarial potential. Asperoside is more effective glycosides than other glycosides, which is more effective as macro-filaricide. It was active at 50 mg/ kg orally against *L. carinii* in cotton rats. Shakhotaka Ghana Vati produced from its stem bark which was useful in filariasis [14].

Antineoplastic activity

Streblus asper has been recognized as anticancer activity [15]. Methanol and dichloromethane extracts of stem bark of *S. asper* were shown to be KB cytotoxicity. Two cytotoxic cardiac glycosides (strebloside and mansonin) were separated which exhibited significant activity in KB cell culture system with ED_{50} values of 0.035 and 0.042 mg/ ml, respectively. An isolate is active in this system if it indicates an ED_{50} of ≤4 mg/ ml [16].

The volatile oil was extracted from fresh leaves of *S. asper* which showed significant antineoplastic activity (ED50 <<30 mg/ ml) from cytotoxicity primary evaluation tests with P388 (mouse lymphocytic leukemia) cells, but it was not showed significant antioxidant activity (IC_{50} values >> 100 mg/ ml) in a DPPH radical scavenging assay [17].

Anti-allergic Activity

Streblus asper indicated significant anti-allergic activity in pharmacological models. It was investigated Anti-PCA (passive cutaneous anaphylaxis) and mast cell stabilizing potential in rodents. Disodium cromoglycate (DSCG) is anti-allergic drug which used as standard drug in this model. *Streblus asper* (50–100 mg/kg, p.o.) in mice indicated 60–74% anti-PCA potential. It also showed dose-dependent (50–200 mg/ kg, p.o.) anti-PCA activity (56–85%) in rats. The mast cell stabilizing activity in rats (10 mg/kg, p.o. 4 days) indicated 62% protection against comp. 48/80 induced degranulation. In egg albumin induced degranulation in sensitized rats, *S. asper* showed 67% protection against egg albumin induced degranulation in sensitized rats. These results were comparable with that of DSCG (50 mg/kg, i.p.) [18].

Antimicrobial Activity

Several works were done to find out bactericidal activity of leave extract of *S. asper* [19–24]. Ethanol extracts derived from the stems and leaves of this plant have been exhibited to inhibit the growth of *Streptococcus mutans* [19].

Anti-Parkinson activity

The leaf extract of *S. asper* possesses anti- Parkinson activity by MPTP-induced disease's model in C57BL/6 mouse and H_2O_2-produced ROS in SK-N-SH cells and. The result confirmed that leaf extract having the antioxidant potential and reverses the functional outcomes. It was included motor and cognitive functions in MPTP-treated C57BL/6 mice [25].

Hepto-protective activity- The CCl4 was used as hepatotoxic substance. CCl4 + extracts (SAALE, SAMLE) administered rats showed the reduced levels of SGOT, SGPT and ALP. These results explain the hepato-protective activity and there is a need of further studies to confirm the hepato-protective activity of *Streblus asper* [26].

Hypoglycemic activity- *Streblus asper* exhibited hypo-glycemic activity in experiment models. Anti- diabetic activity was evaluated by streptozotocin-induced hyper-glycemic and Alloxan-induced hyper-glycemic condition. The petroleum ether extract of *Streblus asper* showed hypo-glycemic activity in Alloxan-induced experimental model. The α-amyrin isolated from petroleum ether extract of *Streblus asper* is a steroid compound which showed significant hypo-glycemic activity in streptozotocin-induced Diabetes Mellitus [27-28].

Anti-Hepatitis B virus (HBV) activity - The anti-HBV effect of extracts from dried leave, roots, barks, heartwood of this plant and different solvents (Water, n- butanol, Ethyl acetate, Chloroform and Petroleum ether) extraction was observed in low-dose (25 g/mL), medium-dose (50 g/mL, 100 g/mL) and high-dose (200 g/mL), respectively. The results recommended that the methanolic extracts of the roots, barks and heartwood showed significant anti-HBV potential. Further research work indicated that n-BuOH and ethyl acetate soluble parts of their methanolic extracts showed more significant anti-HBV activities. Honokiol showed significant anti-HBV effect with IC_{50} values of 3.14 M and 4.74 M for HBV surface antigen (HBsAg) and HBV e antigen (HBeAg) with no cytotoxicity respectively, while lamivudine (3TC, positive control) exhibited weak anti-HBV activity with IC_{50} values of 11.81 M and 25.80 M for HBsAg and HBeAg respectively [29].

Analgesic activity

Parenteral administration of extracts of aerial parts of this plant in the Eddy- Hot Plate model (100 and 200 mg/kg) and acetic acid produced abdominal constriction Test (100 and 200 mg/kg) indicated good analgesic activity. The plant extract exhibited pain analgesic activity in the Eddy- Hot Plate model when extract given parentally (200 mg/kg) to the mice. The stem bark extracts of *S. asper* stem were shown analgesic activity in various analgesic models. Therefore, the study revealed that the plant extract has centrally and peripherally mediated analgesic propertie [30].

Anti-inflammatory activity - The anti-inflammatory activity was carried out in carrageenan-induced paw edema which *S. asper* leaf ethanolic extract (SAE) administered intraperitoneally in doses (125, 250, 500 mg/kg) to the rats. SAE produced a significant dose-dependent blockage of edema ($p < 0.05$). Reverse transcriptive polymerase chain reaction (RT-PCR) is method to determination of expression of gene. It was also performed to find out the activity of SAE on the expression of inflammation- associated genes in RAW 264.7 macrophage cells stimulated with lipopolysaccharide [31].

SUMMARY AND CONCLUSION

Streblus asper is established plant described in the Ayurveda. The therapeutic benefit of stem bark of *S. asper* is recommended strongly due to filariasis infection for which there is no effective treatment in the modern system of medicine. Apart from this, this ayurvedic drug is giving also privileges for its use in ulcer, toothache, dysentery, cancer, ulcer, etc. Investigation was performed using by different *in vivo* and *in vitro* method of pharmacological assessment support most of these claims.

Due to importance of public health, Filariasis is main targeting for ayurvedic medicine. Filariasis is parasitic infection which spread by vector-borne helminthic and black flies. The data obtained epidemiologically study, Filariasis is mainly observed in subtropical and tropical nations of the world. Diethyl carbamazine (DEC) and ivermectin most commonly used drug for filariasis is inadequate because of their insufficient effect on parasites. Asperoside is cardiac glycoside showed as cardio tonic and antifilarial activity which extract out stem bark of this plant. It has unique activity against *Brugia malayi*, *A. viteae* and *L. carinii* in their respective hosts and one of cardiac glycoside was demonstrated antifilarial activity.

The active antifilarial compounds are cardiac glycosides, they are to produce cardiotoxicity and thus it is required to separate the two activities. Attempts in this direction were made by the authors [32] by subjecting strebloside and asperoside to hydrogenation to reduce the αβ - unsaturated lactone ring. The results depicted that at a dose of 50 mg/kg orally, even though there was a decrease in the macrofilaricidal activity showed by dihydroasperoside as well as dihydrostrebloside, but there was an obvious absence of cardiotonic potential as compared to the parent compounds. This works provide credence to the ethnomedicinal shows that *S. asper* being an antifilarial agent.

Traditionally, the stick part of this plant was used as a tooth brush for strengthening gums and teeth [33]. *S. asper* indicated anti-bacterial activity against *Streptococcus*, especially to S. mutans was already depicted which has been exhibited to be strongly associated with dental caries. For controlling of dental caries, *S. asper* was being used as a nature remedy. The α-amyrin isolated from petroleum ether extract of *Streblus asper* is a steroid compound which showed significant hypo-glycemic activity in streptozotocin-induced Diabetes Mellitus. Strebloside and mansonin is active principle recognized as anti-cancer agent, but some volatile oil extracted from fresh leave has been shown definite anticancer activity.

Research studies have identified that *S. asper* possesses anti-allergic, antifilarial, cardiotonic, anti- microbial, anti- Parkinson, hepto-protective, anti-diabetic, anti- inflammatory, anti-viral and analgesic activity.

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