Review Article

Role of *Streblus asper* in Systemic and Oral Health: An Overview

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Abstract

Streblus asper Lour is an important medicinal plant belonging to family Moraceae. All parts of the plant are used for medicinal purposes in folk medicines for the treatment of different diseases such as dysentery, relief of toothache, antigingivitis, filariasis, epilepsy, epistaxis, piles and stomachache. The objective of this article is to review the botany, chemistry, traditional uses and pharmacology of this medicinal plant. *S. asper* has proven properties like anti-inflammatory, antioxidant, antimicrobial, antibiofilm and anticancer activity. These findings indicate the multiple advantages of *S. asper* and suggest a potential for developing *S. asper* as a natural oral hygiene product. Therefore, it would be worthwhile to further investigate the mechanism of effect and side effects.

Key words: *Streblus asper*; Herb; Oral health; Ethnomedicine; Pharmacology

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Introduction

Medicinal plants have been used as a traditional treatment agent for numerous human diseases in many parts of the world. It is estimated that there are 250,000 to 500,000 species of plants on the Earth[1] and only 1 % of approximately 500,000 plant species world-wide has been phytochemically investigated until date. According to the World Health Organization (WHO), about three-quarters of the world population relies upon traditional remedies (mainly herbs) for the healthcare of its people.[2,3] The conventional medicine is now beginning to accept the use of botanicals once they are scientifically validated. Indeed today many pharmacological classes of drugs include a natural product prototype.[4] Aspirin, morphine, quinine, atropine, colchicine, ephedrine, pilocarpine and vincristine are a few examples of what medicinal plants have given us in the past. Most of these plant-derived drugs were originally discovered through the study of traditional cures and folk knowledge of indigenous people and some of these could not be substituted despite the enormous advancement in synthetic chemistry.

***Figure 1** Leaves and flower of Streblus asper* Lour

Streblus asper Lour is an important medicinal plant belonging to family Moraceae and has been used extensively in ayurveda and folk medicine for centuries, as it has a variety of therapeutic properties including antimicrobial activity,[5-12] anti-malarial property,[13] antioxidant,[14,15] analgesic,[16,17] antiallergic,[18,19] anti-inflammatory[20] and anticancer activity.[21-25] This review presents the botany, chemistry, traditional uses and pharmacology of this medicinal plant.

1. Botany & Chemical Constituents

Streblus asper Lour, Moraceae, is a small tree known by several common names, including Siamese rough bush, Koi, Bar-inka, Berrikka, Rudi, Sheora, Serut, and tooth brush tree.[26] The leaves are 2 to 4 inches long, rigid, oval-shaped, irregularly toothed, and borne on small petioles (Fig. 1). Staminate flower heads are spherical with minute flowers. Pistillate flowers have longer peduncles. It is known as a medicinal plant which inhabits various Asian countries, such as India, Southern China, Sri Lanka, Malaysia, the Philippines and Thailand. Chemical constituents of different parts of *S. asper* are shown in Table 1.

2. Traditional uses

The various parts of *S. asper* are used in folk medicines for the treatment of different diseases. The bark extract has been used in fever, dysentery, relief of toothache[27] and antigingivitis.[16] The leaf extract has been shown to possess insecticidal activity towards mosquito larvae.[28] The branch of the plant has been used as a toothbrush for strengthening teeth and gums.[29] The root has been applied to unhealthy ulcers, sinuses and locally as antidote to snake bite;[30] and used in the treatment of epilepsy and obesity.[26] The milky juice has been used as antiseptic and astringent applied to chapped hands and sore heels,[30,31] used as sedative in neuralgia treatment, and used in pneumonia and swells of cheek.[27] Fruits and leaves has been used in eye complaints.[27] Seeds has been useful in epistaxis, piles and diarrhea. Stem bark has been used in stomachache and urinary complaints,[27] useful in piles, edema and wounds, decoction effective against lymphadema, chylurea and other effects of filariasis.[32-33]

Table 1 *Chemical constituents of different parts of Streblus asper*

Plant part	Component	References
Aerial parts	Stigmasterol, n-Triacontane, tetraiacontan-3-one, β-sitosterol, betulin, oleanolic acid	43
Stem bark	Strebloside, α-amyrin acetate, lupeol acetate, β-sitosterol, lupeol, α-amyrin, diol, mansonin, sioraside, (7'S, 8'S)-trans-streblusol A, (7'R, 8'S)-erythro-streblusol B, (7'S, 8'S)-threo-streblusol B, 8'R-streblusol C, streblusquinone, (8R, 8'R)-streblusol D, and streblusol E	24, 34, 44, 45
Heartwood	Lignans, flavonoids	36, 46 - 49
Leaves	Cardenolide, triterpenoids, β-sitosterol, α-amyrin, lupeol, phytol, α-farnesene, trans-farnesyl acetate, caryophyllene, trans-trans-α-farnesene, α-copaene, β-elemene, geranyl acetone, germacrene, caryophyllene oxide, δ-cadinene, 8-heptadecene	22, 31, 50
Root bark	Kamloside, asperoside, strebloside, indroside, strophalloside, cannodimemoside, strophanolloside, glucogitodimethoside, glucokamloside, 16-O-acetylglucogitomethoside, sarmethoside, glucostrebloside, cardenolide, β-sitosterol, lupeol, α-amyrin	31, 51 - 54
Root	Lignans, β-sitosterol-3-O-β-D-arabinofuranosyl-O-α-L-rhamnopyranosyl -O-β-D-glucopyranoside, lupanol-3-O-β-D-glucopyranosyl-[1-5]-O-β-D-xylofuranoside, vijaloside, i.e. periplogenin-3-O-β-D-glucopyranosyl-[1-5]-O-β-D-xylopyranoside	35, 55 - 57

3. Pharmacological properties

Several remarkable pharmacological applications of *S. asper* have been reported. Some of the important findings are reviewed briefly below.

3.1 Antibacterial activity

Several studies reported the antibacterial action of *S. asper* leaf extract (SAE) against *Streptococcus mutans* both *in vitro* and *in vivo*.[5, 6, 10, 11] From our previous *in vitro* study, we found that SAE possesses antibacterial activity against endodontic and periodontal pathogens, e.g., *Porphyromonas gingivalis, Prevotella intermedia, Actinomyces naeslundii,* and *Aggregatibacter actinomycetemcomitans*.[8,9] The minimum inhibitory concentration of SAE on *P. gingivalis* W50, *A. actinomycetemcomitans* ATCC 43718, *P. intermedia*, and *A. naeslundii* (T14V) were 3.9, 7.8, 31.3 and 125 mg/ml respectively. While the minimum bactericidal concentration of SAE on *P. gingivalis* W50, *A. actinomycetemcomitans* ATCC 43718, were 31.3 and 15.6 mg/ml respectively, the extract has no bactericidal activity against *P. intermedia* and *A. naeslundii* (T14V).[9] In addition, SAE at concentrations 2 – 16 mg/ml possessed bactericidal activity towards *Streptococcus mutans* ATCC 25175.[5] However, SAE at concentration 2 - 100 mg/ml did not show antibacterial activity against *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 252922, *Pseudomonas aeruginosa* ATCC 27853 and clinical isolates of *Staphylococcus coagulase* positive, *Staphylococcus coaglase* negative, *Serratia marcescens, Klebsiella pneumonia, Enterobacter* and *Burkholderia pseudomallei.*[6]

For *in vivo* study in 30 human subjects, the results revealed that 1 min rinse with 20 ml of SAE at a concentration 80 mg/ml can significantly reduce salivary *S. mutans* counts compared with distilled water and showed no effects in modifying the salivary pH and buffer capacity.[5] Moreover, subgingival irrigation with 5 ml of SAE solution (80 mg/ml) as an adjunct to scaling and root planning in 42 chronic periodontitis patients was effective at reducing the number of *A. actinomycetemcomitans* and/or *P. gingivalis*.[7]

3.2 Antiviral activity

Different parts of *S. asper* and different solvent fractions of them were investigated for anti-Hepatitis B Virus (HBV) activities *in vitro* using the HBV transfected Hep G2.2.15 cell line.[34-37] The results showed that the methanol (MeOH) extracts of the heartwood, barks, and roots exhibited good anti-HBV activities. Further investigations displayed that ethyl acetate and n-butanol soluble parts of their MeOH extracts showed significant anti-HBV activities.[37] Several lignans were isolated from the ethyl acetate-soluble part of MeOH extract of the root of *S. asper* and tested for their cytotoxicities and the abilities to inhibit the secretion of HBV s antigen (HBsAg) and HBV e antigen (HBeAg), and the replication of HBV DNA in HBV-infected 2.2.15 cells.[35] The results demonstrated that the most active lignans, (7'*R*, 8'*S*, 7''*R*, 8''*S*)-*erythro*-strebluslignanol G, magnolol, isomagnolol and isolariciresinol, exhibited significant anti-HBsAg activities with IC_{50} values of 1.58, 2.03, 10.34 and 3.67 μM, respectively, and of 3.24, 3.76, 8.83 and 14.67 μM, respectively, for HBeAg with no cytotoxicity. In addition, (7'*R*, 8'*S*, 7''*R*, 8''*S*)-*erythro*-strebluslignanol G and magnolol showed inhibitory activities on the replication of HBV DNA with the IC_{50} values of 9.02 and 8.67 μM, respectively.[35] Moreover, 6-hydroxyl-7-methoxyl-coumarin and ursolic acid which were compounds that isolated from the n-butanol and chloroform fractions of the heartwood of *S. asper* showed anti-HBsAg activities with IC_{50} values of 29.60 μM and 89.91 μM, respectively, and of 46.41 μM and 97.61 μM, respectively, for HBeAg with no cytotoxicity.[36]

3.3 Antibiofilm activity

Recently, the effects of SAE on biofilm formation and biofilm-grown bacteria were investigated.[38] The results demonstrated that SAE possessed *in vitro* activity in inhibiting biofilm formation and was able to reduce the number of *A. actinomycetemcomitans* and *P. gingivalis* in an *in vitro* subgingival biofilm model. Although adherent populations were not completely eradicated by treatment with SAE, a > 70 % reduction in biofilm formation was detected at SAE concentration 90 mg/ml. Moreover, the results from our previous study revealed that the sublethal concentrations of SAE can block the adherence of *Candida* to human buccal epithelial cells and acrylic surface *in vitro*.[39-40] These findings indicate that the sublethal concentration of SAE may modulate candidal colonization of the oral mucosa and reduce the ability of the yeasts to adhere to denture acrylic, thereby suppressing the invasive potential of the pathogen and possibly preventative of denture stomatitis.

3.4 Anti-inflammatory and anti-allergic activity

The *in vivo* anti-inflammatory effect of SAE on carrageenan-induced paw edema in rats was investigated by intraperitoneal administration.[20] The results revealed that at the maximum concentration of SAE (500 mg/kg body weight), the % inhibition of paw edema was comparable to the standard non-steroidal anti-inflammatory drug diclofenac. Moreover, from our previous study in 35 human subjects, a significant decrease in mean difference from baseline of gingival index (GI) scores after 4 days of rinsing with SAE (80 mg/ml) compared with those after rinsing with distilled water was found.[10] In addition, subgingival irrigation with 5 ml of SAE solution (80 mg/ml) as an adjunct to scaling and root planning in 42 chronic periodontitis patients significantly reduced the GI compared to irrigation with saline solution.[7] These studies in human subjects indicate that SAE is effective at reducing gingival inflammation.

For *in vitro* study, the mechanisms of anti-inflammatory action of SAE were investigated using RAW 264.7 macrophage cells that were stimulated with lipopolysaccharide (LPS), then reverse transcription polymerase chain reaction (RT-PCR) technique was performed to determine cyclooxygenase (COX)-1, COX-2, and inducible nitric oxide synthase (iNOS) mRNA expressions. The results demonstrated the significant suppression on LPS-induced expression of COX-2 and iNOS mRNA by SAE in a dose–response manner.[20]

Anti-allergic activity of *S. asper* was also reported.[18-19] From a previous study, the ethanolic extract of *S. asper* was determined for its anti-allergic effect on the release of β-hexosaminidase in RBL-2H3 cells (rat-basophilic leukemia cell line), a tumor analog of mast cell.[19] It was revealed that *S. asper* extract exhibited anti-allergic activity with an IC_{50} value of 82.2 μg/ml.

3.5 Antioxidant

The potential of aqueous and ethanol extracts of oven and freeze-dried *S. asper* leaves as a strong antioxidant was investigated using the 1,1-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging method.[14] The results indicates that aqueous extracts of freeze-dried *S. asper* leaves is a good potential source of natural antioxidants for preventing free radical-mediated oxidative damage, and higher levels of phenolic content are retained in freeze-dried than in oven-dried samples. Md. Afjalus *et al*. also reported the antioxidant property of ethanolic extract of leaf and bark of *S. asper* which was assessed by DPPH scavenging assay.[15] They found that IC_{50} value of the *S. asper* is 1 μg/ml for leaf and 10 μg/ml for bark which were comparable to the standard ascorbic acid.

3.6 Anticancer activity

Several studies reported the anticancer activity of *S. asper*.[21-25] For example, the methanol extract of *S. asper* stem bark (MESA) was investigated for antitumor effect against Ehrlich ascites carcinoma (EAC) in Swiss albino mice.[21] The results demonstrated that MESA exhibited dose dependent and significant decrease in tumor proliferation ($p < 0.01$). Moreover, MESA extended the survival time of the tumor-bearing mice. The volatile oil from fresh leaves of *S. asper* also showed significant anticancer activity ($ED_{50} < 30$ μg/ml) from cytotoxicity primary screening tests with P388 (mouse lymphocytic leukaemia) cells.[22] In addition, the effects of ethanolic extract of *S. asper* stem bark on crown gall tumor formation at different concentrations were evaluated. Highly significant tumor inhibition e.g. 31.86 and 40.44 % was observed at 100 ppm and 1,000 ppm of the extract, respectively.[25]

Conclusion

Herbs have been used for centuries to prevent and control disease and the use of herbs in traditional medicine systems of many cultures has been extensively documented.[41, 42] Interest in traditional medicine can be explained by the fact that it is a fundamental part of the culture of the people who use it and also due to the economic challenge. People who use traditional remedies know from personal experience that some medicinal plants can be highly effective if used at therapeutic doses, but they may not understand the scientific rationale behind their medicines. Indeed, the discovery of therapeutic compounds from herbs remedies remains a medically and potentially challenging task. According to the variety of chemical constituents as shown in Table 1, *S. asper* has been reported to have diversified biological actions.[5-25] The mixtures of different chemical compounds may act individually, additively or in synergy to improve health.

This paper has given an overview of the role of *S. asper* in systemic and oral health. As mentioned above, *S. asper* may be good alternatives for prevention and/or treatment of several diseases but it is clear that we need more research about the mechanism of effect and side effects.

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