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A REVIEW: PHARMACOLOGICAL ACTIVITIES OF "*SALACIA RETICULETA* WIGHT

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ABSTRACT

The genus, *Salacia* belongs to the family, Celastraceae and is distributed across the world. Specially in In India and Srilanka this plant is widely used. Extracts of ***S****alacia* roots, stems, and leaves have been used in Asia for hundreds of years for this folkloric treatment of diabetes and other health problems. Mugs made from *Salacia* wood are used by people with diabetes to drink water. The roots are either chewed directly or taken in dried powdered form or as decoction. Apart from antidiabetic activity, several species of the genus *Salacia* are known to possess anti-inflammatory, anti-lipidaemic, anti-peroxidative, anti-microbial, anti-leukemic, astringent and anti-malarial activities. *Salacia* is being used in several herbal formulations for treating diabetes and obesity. Mugs made from *Salacia* wood are used by people with diabetes to drink water. Literature review was done through published works to gather information on nutritional and ethnic values, phytochemical and pharmacological properties of *Salacia*. Information about the plant and phytochemical constituents, pharmacological activities were collected from the published reports. The plant was found to be significant antihyperglycemic, antidiabetic, and hypoglycemic activity. The phytoconstituents which are present in the plant are mainly coumarins and flavonoids which are responsible for the actions. It is also used to treat skin diseases such as leprosy, ulcers, hyperhydrosis, hepatopathy and dyspepsia. The present study is focussed on reviewing the progress made on the active principles of *Salacia Reticulata.*

KEYWORDS: *Salacia*, antidiabetic activity, glucosidase inhibitors, postprandial hyperglycemia, postprandial hyperlipidaemia.

INTRODUCTION

Medicinal plants are an important element of the indigenous medical systems in India, where about 35 % of the population, even at present, de-pends on traditional systems of medical care.[1] (*Salacia reticulata*), a species widely known for its antidiabetic properties has been investigated in Japan and the United States and patented.[2] Di-abetes has now become an epidemic affecting mil-lions of people worldwide. However, neither insu-lin nor other modern pharmaceuticals has been shown to modify the course of diabetic complica-tions mainly due to the multifactorial basis that in-volves both genetic and environmental risk factors. Therefore, new therapeutics aimed at multiple tar-gets have been extensively investigated. In this con-text, the discoveries on *S. reticulata* have lead to increase the consumption of the species across the world and it has now become a subject of broad studies for diabetes management. In order to meet the ever increasing demand, commercial exploita-tion of the species simultaneously with the scien-tific investigations is of paramount important. The present paper reviewed, the pharmacological activities of Kothala himbatu (*S.reticulata).* Ayurvedic medicine is an ancient system of healthcare thatis native to the Indian subcontinent. It is presently in daily use by millions of people in India, Nepal and Sri Lanka.[1] *Salacia reticulata* is a climbing plant in the Hippocrateaceae family that has been used traditionally in Indian *Ayurvedic* medicine and is said to be effective for the prevention and treatment of diabetes, rheumatism, gonorrhea and skin diseases.[2] *Salacia reticulate wright*. is commonly known as Saptarangi, Chundan in Tamil, Ponkoranti in Malayalam, Vairi in Sanskrit and Anukuducettu in Telugu. *S. reticulata* Wight is known as Himbutu in Sinhalese, Kothala himbutu in Hindi, Saptachakra in Sanskrit and Ekanayakam in Kannada. *S. chinensis*is.

Distribution

S. reticulata is known to be distributed in Sri Lanka and the Southern region of India (Matsuda *et al*. 2002). Though rare, this species could also be found in evergreen forests of Western Ghats.[2] In Sri Lanka, *S.*

reticulata is known to be found mainly in dry zone, which includes districts such as Ham-banthota, Anuradapuraya, Pollonnaruwa, Monara-gala, Kurunegala and Puttalm. However, documen-tary evidence is lacking on the precise locations in which the species is abundantly distributed. The leaves are usually opposite, petioled and coriaceous. Flowers are small, axillary, extra-axillary, facicled or cymose, and seldom solitary. Fruit is baccate, edible, 1- 3 celled with 1-4 seeded each and pulp is mucilaginous. Seeds are large, angular, with thick testa, cotyledons are thick and usually conferruminate.[3]

Botanical Description

S. reticulata WIGHT (Sinhala: *Kothala himbatu*) is a large woody climbing shrub belongs to family Hippocrateaceae.[4] The green-ish grey color bark of the plant is smooth, with white inside. The average dimension of a leaf is 3 – 6 inches long and 1 – 2 inches broad.[5] They are opposite and elliptic-oblong, base acute, apex abruptly acuminate, margin toothed with minute rounded teeth, leathery, hair-less, shiny, lateral nerves about seven pairs, promi-nent beneath. *S. reticulata* produces greenish white to greenish yellow color flowers as clustered (2-8) in leaf axils.[6] Flowers are bisexual, calyx lobes entire, anthers dehiscing transversely. Fruits are globose, tubercular, pinkish orange when ripe. They contain 1 - 4 seeds.[7] The plant flowers in December under Indian condi-tions,[8] whereas in Sri Lanka, flowering starts in late November and seeds are available from March to June.[9] laboratory in-vestigations have confirmed that high germination percentage can be obtained by sowing them in coir dust media after pre-soaking in cold water for 24 hrs. Therefore, poor regeneration capacity of the species might be attributed to the poor moisture availability of the soil at the time of seed maturity. Low survival ability of seedlings in a dry spell might be another possible reason for poor regenera-tion capacity.

Therapeutic Attributes in Ayurveda

Salacia and its uses in traditional system of medicine Different species of *Salacia* have medicinal principles with a high pharmacological significance. In traditional system of medicine, different species of the genus, *Salacia* are being used as acrid, bitter, termogenic, urinary and as liver tonic. The aerial parts and roots of *Salacia* are extensively used in Ayurvedic system of medicine,traditional Indian medicine and Unani for treating diabetes, gonorrhoea, rheumatism, itching, asthma, ear diseases, leukaemia and inflammations.[10]

Table: 1 Therapeutic activities of *Salacia* species.

Species	Therapeutic Utility	References
S. reticulate	Antidiabetic activity	Karunanayake *et al.* (1984) species Serasinghe *et al.* (1990) Shimoda *et al.* (1998) Kajimoto *et al.* (2000) Tanimura *et al.* (2005) Jayawardena *et al.* (2005)
	Antibacterial activity, Antimicrobial activity	Deepa and Narmatha (2004); Choudhary *et al.* (2005); Samy (2005); Subhasree *et al.* (2009)
	Antiproliferative activity	Antiproliferative activity Medagama *et al.* (2015)
	Antirheumatic activity Hepatoprotective activity	Yoshikawa *et al.* (2002)

Pharmacological Actions

1. α--Glucosidase inhibitors of *Salacia*

Stems and roots of *Salacia* contain potent α-glucosidase inhibitors (salacinol and kotalanol) and also the aldose reductase inhibitor, kotalgenin-16-acetate. Salacinol and kotalanol competitively bind to α-glucosidase present in the brush borders of small intestine and prevent the breakdown of oligosaccharides into monosaccharides and thus, maintain the normal blood levels in the human body.[11] The enzyme aldose reductase catalyse the conversion of glucose to sorbitol (sugar alcohol). Sorbitol do not readily diffuse across the cell membranes and gets accumulated in the lens resulting in cataract formation. Kotalgenin-16-acetate competitively binds to the aldose reductase and thus, prevents cataracts.[12] The various other active principles of *Salacia* are mangiferin, diterpenes, triterpenes, megastigmane glycosides, thiocyclitol, quinonemethides, friedelanes, oleananes, polyols and others.[13]

2. Studies on antidiabetic activity of *Salacia* extracts

Karunanayake *et al.* (1984) have evaluated the aqueous decoction of 40 Sri Lankan medicinal plants that are known to lower blood glucose levels.[14] Amaximum reduction of 30% blood glucose was seen in the Sprague-Dawley rats fed with decoction of *S. reticulata.* Serasinghe *et al.* (1990) have evaluated the aqueous extract of *S. reticulata* on streptozotocin induced diabetes rats to study its effect on plasma glucose levels.[15] The experimental rats were orally fed with 0.5, 1 and 5 g/kg body weight and the plasma glucose levels were reduced by42.8%, 45.4% and 87.5%, respectively. Aqueous extract of *S. reticulata* stems showed decrease in serum glucose levels when the rats were fed with sucrose, maltose and starch. Shimoda *et al.* (2000) also

showed the strong inhibitory activities of α-glucosidase prepared from yeast and rat jejunum. Aqueous extracts from the roots of *S. reticulata* (200 mg) significantly suppressed the postprandial hyperglycemia when healthy human volunteers were loaded with 50 g of sucrose.[16] Yoshikawa *et al.* (1998) used bioassay guided separation to isolate kotalanol from *S. reticulata* root. Significant reduction in serum glucose level was noticed in hydrocortisone induced hypoglycemic rat models when fed with 500 mg/kg body weight of hydroalcoholic extract of *S. reticulat.*[17] Oe and Ozaki (2008) isolated a thiocyclitol, novel 13-membered ring from the aqueous stem extracts of *S. reticulata*. The activity was tested on maltose and sucrose loaded Wistar rats and the extract significantly lowered the postprandial glucose levels. Thiocyclitol was also checked for α-glucosidase inhibitor activity in *in vivo* conditions.[18] Shivaprasad *et al.* (2013) have evaluated the efficacy and safety of leaves and root bark of *S. reticulata* in a randomized, double-blind, placebo controlled method. The study was carried on patients with prediabetes and mild to moderate hyperlipidemia for 6-weeks. Twenty nine patients were fed with placebo or 500 mg twice a day with *S. reticulata*. Nine individuals were fed with placebo, 11 with *S. reticulata* leaves and 9 with *S. reticulata* roots. The results revealed a statistically significant decrease in fasting blood sugar levels and low-density lipoprotein cholesterol with no side effects.[19] Jayawardena *et al.* (2005) investigated the effect of herbal tea extracts of *S. reticulata* in patients with type II diabetes in a randomised single centre, double blind method. The extract showed significant decrease in HbA1C and he concluded that *S. reticulata* herbal tea is safe and effective.[20] Kajimoto *et al.* (2000) recorded a significant reduction in fasting plasma glucose levels, HbA1C and BMI in placebo group fed with aqueous stem extracts of *S. reticulate*.[21]

3. Hepatoprotective activities of *Salacia*

Yoshikawa and co-workers have tested the hepatoprotective activities of *S. reticulata,* using an oxidative stress-induced liver injury model. The extracts of the plant (400 mg/kg weight) considerably suppressed the glutamic oxaloacetic transaminase (GOT), and glutamic pyruvic transaminase (GPT) activities in carbon tetrachloride (CCl4) treated mice. The extracts of *S. reticulata* also inhibited CCl4 induced thiobarbituric acid reactive substance (TBARS) formation. These results indicated that the CCl4 induced increase in lipid peroxidation in the liver is being protected by *Salacia* extracts.[22]

4. Antioxidant activities of *Salacia*

Yoshikawa *et al.* (2002, 2003) studied the antioxidant activities of hot aqueous and methanolic extracts of *S. reticulata*. They used mangiferin, (-)-4'-O-methylepigallocatechin and (-)- epicatechin-(4β-8)-(-)-42 –O methylepigallocatechin for antioxidative activity. They observed scavenging activity of DPPH radicals by the above compounds.[23]

5. Antiobese activities of *Salacia*

Salacia has been known to control obese problems. Its activity on obese patients has been extensively studied. Pancreatic lipase, a well-known enzyme is highly critical for the digestion of dietary fat. Therefore, it is believed to contribute towards weight reduction in humans.[24]

6. Antiproliferative activities of *Salacia*

Sekiguchi *et al*. (2012) studied the antiproliferative activities of *S. reticulata* leaves in interleukin-1-β-activated cells. The extract (850 μg/ml) showed 50% inhibition in synoviocyte like cell lines (inflammatory synovial tissues) and also suppressed matrix metalloproteinase genes.[25]

CONCLUSIONS

The important active principles of *Salacia* species such as salacinol and kotalanol, the potent α-glucosidase inhibitors showed effective reduction of plasma glucose in animal and human studies. All the studies discussed above provide an insight of the antidiabetic action similar to standard glucosidase inhibitors. The above studies showedα-glucosidase inhibition is an important mechanism in reducingpostprandial glucose levels, reduced fasting glucose and improves glucose handling. Since toxicity levels are negligible, the compounds have the potential to be used as effective α-glucosidase inhibitors and for controlling glucose levels. Further, the extracts also proved to have excellent antioxidant capacity besides antiobese activity. It is a highly promising herbal drug that can be used for effectively treating ailments like diabetes and obesity, the two dreaded disorders.

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