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REVIEW

Economic and Medicinal Aspects of Salacia L. (Celastraceae)

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Introduction

The genus Salacia L., comprising of ca. 200 species in the New and Old World tropics (Dandy, 1969; Mabberley, 2005), was formerly placed under the Hippocrateaceae and is presently included in the staff-tree family Celastraceae, as the former Hippocrateaceae is now considered to be nested within the present Celastraceae s. l. (Simmons *et al.* 2001 a & b; APG III, 2009). About 21 species of Salacia have been reported from India, 15 from Peninsular India and eight from Kerala (Singh *et al.*, 2000; Sasidharan, 2004; Ramamurthy and Venu, 2005; Nayar et al. 2006). The eight species reported from Kerala include *S. beddomei* Gamble, *S. brunoniana* Wight and Arn., *S. chinensis* L., *S. Fruticosa* Heyne ex Lawson, *S. macrosperma* Wight, *S. malabarica* Gamble, *S. oblonga* Wall. ex Wight & Arn. and *S. reticulata* Wight. Of these, the occurrence of *S. brunoniana* and *S. reticulata* in the State is currently doubtful (UdayanandPradeep, 2012). Recently Udayan *et al.* (2012; 2013) have reported two new species of Salacia from the Southern Western Ghats viz. *S. agasthiamalana* and S. *vellaniana*.

The members of the genus are scandent or erect shrubs, lianas or small trees with opposite or subopposite leaves, axillary or extra-axillary fascicled or panicled flowers, pulvinar or conical disks and drupaceous, red globose fruits with mucilaginous pulp having 1-3 large, angular seeds embedded in it. Salacia, commonly known as the Ekanayaka (Sanskrit) or Ponkoranti (Malayalam) is much valued in the Ayurvedic system of medicine as an important medicinal plant. The economic and medicinal aspects of the species of Salacia are discussed here under different heads.

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Antidiabetic Property

The roots of the different species of Salacia viz. *S. beddomei, S. chinensis, S. fruticosa, S. macrosperma, S. reticulata* and *S. oblonga* are used in the treatment of diabetes in traditional medicine (Jayakumar *et al.* 2010). *S. reticulata* has been used as a supplementary food in Japan to prevent diabetes (Yoshikawa *et al.* 2002). The infusion of the root is used to allay thirst associated with diabetes (Chandrasena, 2005).

Salacia species contain sulfonium inner salts like salacinol and its side chain analogs such as kotalanol, salaprinol and ponkoranol together with their de-O-sulfonated analogs. These compounds possess a unique zwitterionic sulfonium sulfate structure and competitively inhibit α-glucosidase activity within the lumen of the intestinal tract(Yoshikawa *et al.* 2002; 2008; Matsuda *et al.*, 2005). Inhibition of such carbohydrate-digesting enzymes prevents the breakdown of oligosaccharides and polysaccharides into monosaccharides causing a delay in glucose absorption into the blood. This results in the lowering of postprandial blood glucose, thereby improving glycemic control. This has also been reported in the case of humans by Williams *et al.* (2007).

Salacia species also contain mangiferin (a xanthone from the roots), which is reported to be a potent α-glucosidase inhibitor and prevents increase in serum glucose levels. Mangiferin has also been reported to decrease the expression of fructose-1,6-bisphosphatase (FBP), a key enzyme involved in gluconeogenesis in the liver (Im et al. 2009). Extracts prepared from leaves also showed considerable hypoglycemic activity (Prajapati, 2003). The stem bark of *S. fruticosa* is considered useful in treating polyurea, diabetes. The hypoglycemic effect of *S. reticulata* in alloxan diabetic rats has been suggested to involve an extra pancreatic effect on glucose production or clearance (Ruvin Kumara *et al.* 2005). Jayawardane *et al.* (2005) reported good glycemic control and less side effects for the aqueous extract of the same plant in human clinical trials on type 2 diabetes. Bipha drug Laboratories, Kottayam, Kerala, South India have come out with an Ayurvedic medicine called "Rajanyamalakadi" containing Curcuma longa, Emblica officinalis and *S. oblonga* for treating type 2 diabetic patients.

According to Li *et al.* (2008), "Diabetes and obesity have a multi-factorial basis involving both genetic and environ-

mental risk factors. Recent pharmacological studies have demonstrated that Salacia roots modulate multiple targets: peroxisome proliferator-activated receptor-alpha-mediated lipogenic gene transcription, angiotensin II/ angiotensin II type 1 receptor, α-glucosidase, aldose reductase and pancreatic lipase. These multi-target actions may mainly contribute to Salacia root-induced improvement of type 2 diabetes and obesity-associated hyperglycemia, dyslipidemia and related cardiovascular complications seen in humans and rodents. Thus Salacia serves as a unique traditional medicine fulfilling a multiple-target strategy in the prevention and treatment of diabetes and obesity".

Activity against Development of Diabetic Complications

The aqueous extract of the roots of S. oblonga containing specific concentrations of mangiferin marker has been suggested to prevent or delay the onset of diabetic complications like cardiovascular diseases, cataract, peripheral neuropathy, retinopathy etc. (Li *et al*. 2004; Huang *et al*. 2006 a & b). Mangiferin inhibits aldose reductase activity, thereby delaying the onset or progression of diabetic complications (Yoshikawa *et al*. 2001, as cited in Arunakumara and Subasinghe, 2010).

Antiobesity Effect

S. reticulata has been used as a supplementary food in Japan to prevent obesity (Yoshikawa *et al*. 2002). The phenolic constituents of *S. reticulata* were found to exhibit pancreatic lipase inhibitory and anti-obese effects (Matsuda *et al*. 2005). Kishino *et al*. (2006) attributed the starch-blocking effect of the plant extract to the inhibition of carbohydrate and lipid absorption from the small intestine. Li *et al*. (2008) opined that multi-target actions of Salacia root extract may contribute to improvement of obesity-associated hyperglycemia, dyslipidemia and related cardiovascular complications seen in humans and rodents.

Hepatoprotective Activity

Hepatoprotective effect of ethanolic extracts from the roots of *S. chinensis* against CCl4 induced hepatic injury in albino rats were reported by Naveen (2010). In a study conducted in Thailand, Nakamura *et al*. (2011) also observed that methanolic extract from the leaves of *S. chinensis* showed a protective effect on D-galactosamine-induced cytotoxicity in primary cultured mouse hepatocytes

Anti-inflammatory Property

Some Salacia species have long been used in India, Sri Lanka, and China as traditional medicines for their anti-inflammatory properties (Carvalho *et al*. 2005). Ismail *et al*. (1997) assessed the anti-inflammatoryactivity of the decoction of powdered root bark of *S. oblonga*, with sugar in male albino rats. They observed that the formulation was effective against both carrageenan-induced paw oedema and cotton pellet granuloma characterising acute and chronic inflammations respectively at a dose of 1000mg/kg. They attributed the activity to the antiproliferative, antioxidative and lysosomal membrane stabilization effected by the decoction.

Antioxidant Effect

The methanolic extract from the stems of *S. chinensis* showed potent anti-hyperglycemic effects and radical scavenging activities (Yoshikawa *et al*. 2003). Vellosa *et al*. (2009) reported free radical scavenging and antioxidant action of root bark ethanol extract of *S. campestris*. Antidiabetic and antioxidant activities of the petroleum ether extract from the root bark of *S. oblonga* have been reported by Krishnakumar *et al*. (1999). Palani *et al*. (2011) reported that the ethanolic extract of *S. oblonga* exhibited antioxidant activities against acetaminophen-induced toxicity in rats.

Anticancer Efficacy

Augusti *et al*. (1995) noted that the methanol eluted fraction of the petroleum ether extract of *S. oblonga* showed 100 percent cytotoxicity on Ehrlich ascites tumour cells. They suggested that the active principle from the root bark of the plantmay inhibit the growth of tumours, and aid in the cytotoxicity of cancer cells. Sneden (1981) isolated isoiguesterin, an antileukemic bisnortriterpene from *S. madagascariensis. S. chinensis* is widely used by Thai folk doctors in cancer preparations to treat cancer (Itharat and Ooraikul, 2007). Triterpenoids from *S. chinensis* exhibited significant anticancer efficacy against Hep-G2, LU, KB, and MCF-7 cell lines (Tran *et al*. 2010).

For Cardiac Problems

The aqueous extract of the roots of *S. oblonga* containing a defined content of mangiferin marker has been shown to inhibit postprandial hyperglycemia and ameliorate cardiac fibrosis in type 2 diabetic obese zucker rats (Li *et al*. 2004). It also functions as a PPAR-α activator to improve hypertriglyceridemia, hypercholesterolemia and hepatic steatosis (Huang *et al*. 2006 a) and suppress cardiac triglyceride (TG) accumulation in Zucker diabetic fatty (ZDF)rats (Huang *et al*. 2006 b). The plant may be used to prevent or delay the onset of diabetic complications like cardiovascular diseases, cataract, peripheral neuropathy, retinopathy etc.

Antimalarial Activity

Salacia kraussii is used against dysentery and malaria in Mozambican traditional medicine (Kim and Park, 2002). The roots of *S. madagascariensis* are used in the treatment of malaria, fever, and menorrhagia in Tanzania. It is rich in bisnortriterpenes with potent antiprotozoan activity. Antileishmanial natural products have been reported from the roots of *S. madagascariensis* (c.f. Magadula and Erasto 2009). Gessler *et al.* (1994) evaluated the antimalarial activity of forty-three plant species against Plasmodium falciparum in vitro. They reported that *S. madagascariensis* to be one among the four most active plants.

Antimicrobial Activity

Poh (2000) reported inhibitory action of the ethanolic extracts of *S. pyriformis* on the growth of Proteus mirabilis and Escherichia coli. Deepa *et al.* (2004) reported significant antibacterial activity of ethyl acetate extracts of *S. beddomei*, effecting cent percent mortality in Spodoptera litura. Venkateshwarlu *et al.*(1990; 1992) recorded significant hypoglycemic and antimicrobial activities of the ethanolic extract of *S. macrosperma*. Deepa and Narmathabai (2004) reported antibacterial activity of petroleum ether, ethyl acetate and chloroform extract of leaves and stems of *S. beddome*i. Rao and Murthy (2010) observed that *S. oblonga* possesses wide spectrum activity against several human pathogenic bacteria.

Anticaries Activity

Anticaries activity of *S. chinensis* extract was reported by Vuong and Hoover in 2008. They observed that the plant extract inhibited sucrose-dependant biofilm formation by preventing glucan adhesion on tooth plane and glucosyl transferase activity.

Transdermal Delivery of Medicines

Arra *et al.* (1998) isolated a new film-forming material from *S. macrosperma* Sfor transdermal delivery of medicines like isosorbide 5-mononitrate, from the roots of the species.

Bio insecticidal Property

Several species belonging to the Celastraceae have been used in Chinese traditional medicine to protect against insect attack (Swingle *et al.* 1941, c.f. Deepa and Narmatha Bai, 2010). The plants produce various β-dihydroagarofuran sesquiterpene polyesters and pyridine alkaloids, which lead to their insect-feedant and insecticidal activities. Deepa *et al.* (2003, c.f. Deepa and Narmatha Bai, 2010) isolated a new compound with benzoid skeleton from the leaves of *S. beddomei* and an oxaza cyclohexane derivative from the nutrient stem callus of the same species in 2004. Both these compounds exhibited significant antifeedant and insecticidal activities, leading to 70-100% mortatility in cotton leaf worm, Spodoptera litura.

Salacia Tea

Based on a double blind test, Jayawardena *et al.* (2005) reported that herbal tea containing *S. reticulata* is an effective remedy for Type 2 diabetes. Han *et al.* (1999) reported anti-obesity and hypolipidaemic effects of Salacia tea and attributed it to the enhancing effect of caffeine on noradrenaline-induced lipolysis in adipose tissue and to the inhibitory action of some other substance in Salacia tea on pancreatic lipase activity. They also suggested that it may be used as an effective crude drug for the treatment of obesity and fatty liver caused by a high-fat diet.

As Food

The rind of the fruits of *S. fruticosais* sweet in taste and is consumed by the tribal communities of Pathanamthitta district (Binu, 2010).

Toxicity Evaluation

Salacia species are being increasingly consumed as a dietary supplement to prevent obesity and diabetes, in Japan, USA and other countries. In this context a few studies were made to evaluate the adverse effects of Salacia. Many of these studies were conducted on rodents and it was seen that consumption of Salacia species has no serious adverse effect. (Wolf and Weisbrode, 2003). No genotoxicity was found in reverse mutation assay and mouse micronucleus assay, and a weakly positive result was obtained for the chromosomal aberrations assay of Salacia root extract conducted by Flammang *et al.* (2006). But reproductive toxicity in the form of reduced survival and low birth weight of F1offspring was reported by Ratnasooriya et al. (2003). They cautioned that the use of the plant extract should be avoided by pregnant diabetic women. However, Jihong *et al.* (2011) observed no such reproductive toxicity for aqueous extract of *S. chinenesis*, "even at a remarkably high dosage level, 2000 mg/kg/day, in Sprague-Dawley rats".

Im *et al.* (2008) conducted DNA microarray analysis of the aqueous extract of *S. reticulata* and observed that the extract did not affect the expression of genes with known function such as those associated with stress response, transcription, translation, cell function, immune response and metabolism. Although the extract was noted to regulate the m-RNA levels of some genes related to energy metabolism, they concluded that it has "no significant acute" hepatotoxicity, thereby emphasizing the efficacy of Salacia species as a "functional food for good health".

General Medicinal Uses

The stem bark of *S. fruticosa* is considered useful in treating polyurea, diabetes, excessive thirst, discolored spreading patches on the skin, diarrhoea and fever. Root bark is used for treatment of gonorrhea, rheumatism and skin diseases (Prajapati, 2003; Jayakumar *et al*. 2010). Decoction of powdered root bark of *S. oblonga*, with sugar is used against itches, asthma, thirst, weakness and ear diseases, and possesses anti-inflammatory effects (Rama Rao, 1914; Ismail *et al*. 1997). The roots and stems are used in treating rheumatism, gonorrhea and skin diseases (Jayaweera, 1981).

The root decoction of *S. chinensis* is used as a tonic, blood purifier, in the treatment of diabetes, in amenorrhea and dysmenorrhea and veneral diseases (Prajapati, 2003; Jayakumar *et al*. 2010). The roots are also used in normalizing menstruation and invigorating circulation (Pengand Funston, 2008). Root bark may be boiled in oil or used as decoction or powder for the treatment of rheumatism, gonorrhea, itches, asthma, thirst and ear diseases (Gopalakrishnan *et al*. 1997). The stems are used as a laxative, for relaxation of myalgia and in diabetes (Matsuda *et al*. 2005). The water extract from the stem is used for treatment of back pain, and hence the stems are sold in the markets of Laos (Delang, 2007).

The roots of *S. reticulata* are acrid, bitter, thermogenic, astringent, anodyne, anti-inflammatory, depurative, emmenagogue, vulnerary, liver tonic and stomachic. They are useful in vitilated conditions of vata, diabetes, haemorrhoids, inflammation, leucorrhoea, leprosy, skin diseases, amenorrhoea, dysmenorrhoea, wounds, ulcers, Spowdered and taken with sugar cures rheumatism, gonorrhoea itches and swellings. Fruit pulp is edible. Sekiguchi *et al*. (2010) demonstrated that the powdered leaf of *S. reticulata* ameliorates rheumatoid arthritis in rats, by suppressing the production of degradative enzymes and osteoclastogenesis.

Conclusion

Although the genus Salacia is more popular for its antidiabetic potential, its members have over years proved to possess a wide range of medicinal activities ranging from antiobesity to anticancer efficacy. The auxiliary medicinal relevance of this genus includes hepatoprotective, anti-inflammatory, antioxidant, antimalarial, antimicrobial, anticaries and anticancer properties. The members are also used for treating cardiac problems, nephropathy, skin infections, rheumatism, asthma, ear diseases, veneral diseases, back pain, haemorrhoids, leprosy, wounds, ulcers, hepatopathy etc.

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