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Research Article

Salacia sps.: A Source of Herbal Drug for Several Human Diseases and Disorders

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ABSTRACT

Salacia sps is prominent plant in the domain of medicinal plant with varied benefits for several ailments. *Salacia sps* contains abundant range of phytochemicals (secondary metabolites) like Salacinol, Katnanol, Mangiferin, Poly phenolic, Tannins and many more *Salacia sps* possess Antimicrobial, Antifungal, Antimalarial, Anticancer, Antiobesity, Antidiabetic properties etc. *Salacia sps* has been found to offer high potency of biological owing to the bioavailability and safety. These properties are helpful in the formulation of drug and also potentially offer significant nutritional and dietary benefits. This review focuses on the biodiversity, plant characteristics, phytochemicals, ethno pharmacological properties, *in vitro* and clinical trials including the product developments as well as manufacture. Further research would lead to validation of the claims which will have far reaching benefits to mankind.

Keywords: Salacia Sps, phytochemicals, antioxidants, ethnopharmacology, anti-inflammatory, anti-microbial

INTRODUCTION

India is known for plant based medicines from ancient times in the form of Ayurvedic, Unani and Siddha systems. Plant based medicine are employed for curing many diseases owing to their bioactive secondary metabolites of therapeutic importance[1]. They are used in management of several disease conditions like respiratory disorder, chronic fever, cold, cough, malaria, dysentery, diarrhea, arthritis, skin diseases, convulsions, diabetes, trauma and in treatment of internal organ, hepatic, vessel and immunologic disorders[2]. The phytochemicals of medicinal plants are being exploited in industrial production of pharmaceuticals, perfumes, cosmetics and food ingredients[3]. Over 90% of the medicinal herbs are obtained from plants collected from wild. Eighty per cent of the world population depends on the plant based medicines valued to the extent of 27 billion US Dollar yearly. India alone uses 7500 sps of plants for practice in herbal medicines and in that 90% plants are used in formulations[4]. One such plant is *Salacia* sps belonging to Celastraceae. It is a versatile plant used in treating variety of diseases and disorder confronting human lives. We have recently reviewed antidiabetic and antiobesity properties of this wonder plant[5]. In this review we present details of several curative properties based on the extensive literature survey of experimental data from published literature to bring out the perspectives providing the promises and prospects of *Salacia* as a herbal drug and pharmaceutical.

Ethnopharmacology of Salacia sps

This plant has been used in herbal formulation in India, China and several eastern countries and South America. In Vietnamese ancient drugs, the roots and stems of this sps are used for treatment of back-ache, rheumatism and depression[6]. In Laos, the water extracts of stems and bark of *S. chinensis* are used for treatment of back pain and additionally used as a liver tonic[7]. *S. reticulata* is extremely effective in cases of rheumatism, skin diseases, inflammations, menstrual disorders and spermatorrhoea. The roots are thermogenic, diuretic, acrid, bitter, astringent and anodyne. They are helpful in vitiated conditions of *vata* (a polygenic disorder, described in Ayurveda), hemorrhoids, rheumatism, gonorrhea, leucorrhoea, leprosy, amenorrhea, dysmenorrhoea, wounds, ulcers, hyperhydrosis, hepatopathy, dyspepsia, flatulence, and amenorrhea, antiparasitic, asthma, athletic endurance, cancer, painful menstruation, gonorrhea, cardiopathy, high steroid alcohol, itching, leukemia, metabolic disorders, muscle and joint disorders, obesity, rheumatism, skin diseases, swelling, antibacteria, anti-inflammatory and antioxidant etc.

General description of Salacia sps

Plant; Large, straggling, woody shrub with dichotomous branching.

Leaf: simple, opposite, ovate oblonga, acuminate, elliptic-oblong, base acute, apex abruptly acuminate, prominent beneath glabrous and shining

Flower: bisexual, 2-8 clustered in leaf axils, greenish white to greenish yellow, calyx lobes entire, anthers dehiscing transversely.

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Fruits: globules, pinkish orange, tubercular, pinkish - orange when ripe.
Seeds: are 1-4 almond like contain immersed in deep pulp.
Root bark: golden color
It is a shade loving plant – hence grow luxuriously in forest areas. It can be fully-grown in coconut feather palm and also the different plantations. It will climb the tree if it gets shelter otherwise it grows as a woody plant of 6 -7 feet height.

Distribution

Salacia sps are widespread in tropical climatic zone as well as in South America, East Asia, and predominantly in Indo- China region [8]. It is found in Vietnam, Malaysia, Indonesia, Asian countries like India and SriLanka. *S. oblonga* are found in countries viz., India, China, Vietnam, Malaysia, Indonesia and different Asian countries [9]. *S. chinensis* is found in Asian countries in viz., Sri Lanka, Burma, Thailand, Indo-china, China and Asian nation[10]. *S. reticulate* and *S. macrosperma* is found in India and SriLanka. *S. reticulata* is known to be a woody plant with achromatic branches found in southern India especially in Tamil Nadu and Kerala. *S. brunoniana* is distributed in different geographical regions in India. *S. fruticosa* and *S. beddomei* is predominant in Kerala,in Southern India; *S. prenoides* and *S. madagascariens* are found in Madagascar; *S. hainanensis* in China; *S. petenensis* in Central America; *S. cordata* in Bolivia; *S. crassifolia* in Brazil;. *S. impressifolia* in South America; S. *alwynii* in Venezuela; *S. elliptica* in Brazil; *S. gerrardii* in Republic of South Africa; *S. grandifolia* in Brazil; *S. lehmbachii* in African nation, and *S. arborea* in Brazil. In India 21 sps of *Salacia* are found[11].

Propagation

Salacia plant is generally propagated through seeds, stem cutting and root cuttings. Seeds from well –ripened fruits, are germinated in 21-30 days of the sowing. These seedlings are planted in main field when they are 2-3 months old. Stem cuttings of 10-15cm with 3-4 nodes are dipped in cow dung suspension to hasten the rooting process. Such treatment results in establishment of the plants in 40-50 days[12].

Harvesting and yield

Roots are harvested only after 3year completion in the field. Root knots appear circular when roots are cut, which is an indication of maturity of roots.

Plant tissue culture

This plant is recalcitrant in tissue culture and generally very difficult to grow in *in vitro* conditions. However Deepa *et al.*[13] has standardized a tissue culture protocol for *S. beddome* from nodal explants for *in vitro* propagation through axillary bud proliferation on 1/2 strength MS Medium with BAP (1 mg /L). The addition of IAA (1mg/L) to an equivalent medium resulted in shoot elongation. For initiation of roots the small shoots were cultured on ½ strength MS medium with the addition of IBA (10 mg/L) and NAA (10 mg/L) and incubated in dark for seventy two hours. The small shoots with root primordia could also be transferred to ½ strength basal MS media for root elongation. Dhanasri *et al.*[14] showed a most effective shoot multiplication in MS media with supplementation of BA and IAA (3.5 and 0.5mg/mL, respectively) for *S. reticulata*. Jaykumar *et al.*[15] standarized a protocol for *S.Chinensis* shoot multiplication and elongation in MS media with BAP(2.mg/lt), NAA(0.8mg/lt) and additive such as ascorbic acid (100mg/It).Roots were induced in ½ MS with IBA (1.5mg/lt). The multiplied plants doesn't show any genetic instability and variation in RAPD, ISSR assay. Mangiferin identification and Quantification performed by using RP HPLC for every regeneration stages. Nayana *et al*[16] demonstrated that *S. reticulata* plants can be conserved through vegetative propagation by planting the plants in pots containing a mixture of top soil and composts in the ratio of 1:1. Similarly Deepak *et al*[17] showed that *S.oblonga* plants can be conserved vegetativly by Stem cutting . The maximum shooting response were found in 200ppm IBA treated plants.

Phytochemical Composition of Salacia

Phytochemicals present in the *Salacia* sps are salacinol, katnanol, mangiferin, manferin glucoside. Proanthocyanidins, epicatechin, epigallocatechin, gallate catechins, diterpenes, eudesmane type sesquiterpenes, friedelane, norfriedelane, glycosides, Neosalacinol , Neokotalanol, Quinonemethide, 15 α hydroxy friedeelan 3 one, Lehmbachol C, Lehmbachol D, Pristimerin, Lehmbachol A, Dicatone, Dulcitol, tannin, Salacenonal, Alpha glucosidase inhibitors, catechins, friedooleanaes, quinonemethides, gutta-percha, mangiferin, canophyllol, 3β-sitosterol, pristimerin, epi-kokoondiol, salacenonal, salaciquinone, iguesterin, neosalacinol, neokatalanol, 3-oxofriedelane, 3β-hydroxyfriedelane, 3β-stearyloxyurs-12-en, 3β-stearyloxyolean-12-en , 3,4-*seco*-friedelan-3-oic acid , 28-hydroxy-3-oxofriedelane (canophyllol), 1,3-dioxo-16α-hydroxyfriedelane, 16α-hydroxy-3-oxofriedelane, 30-hydroxy-3-oxofriedelane, 16α, 28-dihydroxy-3-oxofriedelane, 3,16-dioxofriedelane, β-sitosterol, 28-hydroxy-3-oxofriedelane, 3β-Stearyloxyurs-12-en, 3β-stearyloxy-olean-12-en, gutta-percha, 3,4-*seco*-friedelan-3-oic acid, palmitic acid , β-sistosterol glucoside , ethyl glucopyranoside,1,3-dioxo-16α-hydroxyfriedelane, 16α-hydroxy-3-oxofriedelane, 30-hydroxy-3-oxofriedelane, celasdin B, methyl 2,4-dihydroxy-3,6-dimethylbenzoate and 3,16-dioxofriedelane[18, 19, 20, 21, 22, 23,24, 25,26,27].

Zhang *et al.*[19] isolated sixteen compounds from *S. prinoides*, including seven triterpenes: lupeol, Lup-20(29)-en-3beta,30-diol, 30-Hydorxylup-20(29)-en-3-one,3, 22-dioxo-29-normoretane , Ursolid acid , beta-Sitosterol , beta-Daucosterol ; Four flavanoids: Quercetin , Quercet-i n-3', 4'-dimethyl ether , Isorhamneti n , Kaempferol -4'-methyl ether; Three Phenolic acids: Gallic acid , Ethylgallate , Egallic acid ; Two Fatty series: Hentri acontanol , Hentri acontan-12-ol Further Zhao *et al.,*[28] isolated 18 compounds from *S. amplifolia* . It included 13 triterpenes, three simple phenolics, one polyol and one chromanone. Quinonemethides serve as taxonomic markers for Celastraceae family. Carvalho et al.[29] found a new quinonemethide triterpene named as salacin in the root bark of *S campestris*. Salacin was identified on the basis of NMR-spectral and mass spectrometric analysis.

These isolate showed a potent antioxidant activity towards DPPH. Duarte *et al.*[18] isolated nearly 20 constituents from *S. elliptica* i.e. two polyols, xanthone, long chain hydrocarbons mixture, one polymer, two steroidal compounds, one carboxylic acid, one aromatic ester and eleven pentacyclic triterpenes. New triterpene called 1, 3-dioxo-16α-hydroxyfriedelane was identified and its chemical structure was configured through ^{1}H and ^{13}C NMR including 2D experiments (HMBC, HMQC, COSY and NOESY). Gao *et al.*[20] isolated four new and four known constituents from methanol extracts from the roots of *S. hainanensis* ,two lupane derivatives, 3α,28-dihydroxy-lup-20(29)-en-2-one and 3α-hydroxy-lup-20(29)-en-2-one, two friedelane derivative, D:A-friedo-oleanane-7α,30-dihydroxy-3-one, and a novel natural product, 2,3-seco-lup-20(29)-en-2,3-dioic acid , along with known compounds. The spectral analysis done by 2D NMR and high-resolution mass spectra experiments data help to establish structures. All Constituents showed a inhibiting activity on α-glucosidase than the positive control (Acarbose, IC_{50}= 5.83 μM). Adumanya et al.[30] have isolated 38 essential oils in chloroform leaf extract of S. *senegalensis* in them only 7 essential oils have potent medicinal property they are Alpha Terpinene, Germacrene D, Alpha Pinene, Alpha Caryophyllene,Linalool, Cymene, and Carvacrol.

Beneficial effects

Anti inflammatory effects

Yoshikawa *et al.*[31] showed an anti-inflammatory activity on CCl4 induced rats and evaluated antioxidant potentials and total phenolic contents of S. *reticulate* hot and alcohol extract. They suggested that phenols present in the *S. reticulate* extracts was responsible for anti-inflammatory activity. Further, Ramamoorthy *et al.*[32] showed that chloroform and hexane extracts of *S. reticulate* root exhibit anti-inflammatory activity; however chloroform extract was found to be more potent. It exhibited anti-inflammatory activity against the carragenan induced paw edema which can be attributed to the presence of coumarins, glycosides, carbohydrates and phytosterols present in the extract.

Antioxidant effects

Navneet *et al.*[33,34] have demonstrated that the hydro alcoholic extract of *S. oblonga* root bark possess antimutagenic properties with result against the cyto-nuclear injury caused by mitomylin-c(MMC). The extract prevented the incidence of micronuclei formation elicited by the clastogen and additionally reduced the formation of DPPH radical as a antioxidant property.

Vellosa *et al.*[35] who studied the crude alcohol extract of *S. campestris* root bark which exhibited antioxidant and anti-radical property. Krishnakumar *et al.*[36] evaluated the antioxidant properties by employing streptozotocin model of rats by oral administration of extract of *S.oblonga* (250 mg/kg/body weight/day). The significant increase of antioxidant enzymes viz., catalase, superoxide mutase, and glutathione peroxidase and glutathione reductase were observed in the heart tissue of diabetic animals upon treatment with *S.oblonga* extract.

Subhasree *et al.*[37] have investigated the hydroalcoholic extracts of S. *oblonga, S. reticulata and S. roxburghii* for antibacterial and antioxidant activity. However, *S. oblonga* has been reported to have the highest antibacterial activity. Chavan et al[38] have described that *S. chinensis* fruit pulp had antioxidant property due to high polyphenolic and flavonoid content in it.

Alternative pharmacological activities of Salacia extracts

Huang *et al.*[39] investigated the liquid extracts of roots of *S. oblonga* which improved hepatic steatosis by activation of PPAR-α. Analysis when applied on Zucker diabetic fatty (ZDF) rat. Extract of *S.oblonga* roots increased hepatic expression of PPAR-α, ribonucleic acid and macromolecule, and carnitine palmitoyltransferase-1 and acyl-CoA enzyme mRNAs in ZDF rats. *In vitro, S. oblonga* roots extract and its main constituent- mangiferin activated PPAR-α luciferase activity in human embryonic urinary organ 293 cells and compound protein enzyme ribonucleic acid expression and accelerator activity in THP -1 differentiated macrophages. These effects were fully smothered by a selective PPAR-α antagonist MK-886. This study showed that *S.oblonga* roots extract functions as a PPAR-α matter, which supplies mechanism for improvement of hepatic steatosis in polygenic disorder and fat.

Ratnasooriya *et al.*[40] conducted an experiment on female rats by oral administration of *S. reticulate* extract and observed the pups were having low weight which would influence the neurocognitive deficiencies, Neuro behavioural effects and mortality. They further suggested that *S. reticulate* should not be given to female diabetic patients during pregnancy period due to possible toxic influence on the fetus.

Govindaraj *et al.*[41] showed, anti mutagenicity and genotoxicity activity for Mangiferin isolated from *S. chinensis* in *Salmonella typhimurium* strain. Nathiya *et al.*[42] reported the neuroprotective and inhibitor effects of hydro alcoholic extract of root bark of S. *oblonga.* Neurotoxicity and oxidative stress was induced in normal rats by administration of aluminiun chloride (300 mg/kg body weight oral). The action of *S. oblonga* extracts on tissue and bodily fluid inhibitor markers were ascertained. With reference to inhibitor activity, extract exhibited a significant result showing augmented result of accelerator enzyme and non-enzymatic parameters viz, CAT, SOD, GST, GSH and therefore the LPO level was considerably attenuated on treatment with *S. oblonga* extracts. The blood and cortex Acetylcholine esterase (AchE) level were considerably attenuated in *S. oblonga* extracts treated rats that indicates the decrease in aluminum chloride induced neurotoxicity. They indicated that *S. oblonga* extracts exhibit the neuro-protective and inhibitor activity through modulating of oxidative stress.

Sekiguchi *et al.*[43] conducted an experiment on DBA/1 J mice, and divided the mice into 3 groups. Group A as control, group B received collagen antibody induced arthritis (CAIA) and group C received both CAIA and *S.reticulata* leaf extract. After 24 days they observed decrease in the amount of ribonucleic acid coding receptor-activator of nuclear factor Kappa B ligand (RANKL),

matrixmetalloprotinase-2(MMP-2), matrix metalloprotinase-3(MMP-3), cathepsin K and c-fos and they exhibited its beneficial effects for the rheumatoid arthritis disease related to osteoclastogenesis.

Venkatasubramanian *et al.*[44] have conducted studies on animals and humans on dehydrated *S. prinoides* and soybean plant flour deprived beneficial effects. So, they argued that dehydrated *S. prinoides* will be useful as a food supplement for diabetic management.

Table 1: Major Photochemicals isolated from *Salacia* Sps

Name of compound	Molecular formula	Melting point	Extract color	Reference
Salacinol	$C_9H_{18}O_9S_2Na$	187–189 ˚C	Colorless prisms	51
Neosalacinol	$C_9H_{18}O_6S$			52
Mangiferin	$C_{19}H_{18}O11$	271- 274 ˚C	Yellow powder	53
Kotalagenin-16-acetate	$C_{32}H_{51}O_5$		White powder	54
15α-hydroxy-24-nor-friedel-5-ene-1, 3 –dione	$C_{29}H_{44}O$	284- 285 ˚C	White powder	55
Salasol A	$C_{28}H_{36}O_{10}$		White powder	25
Salasol B			White powder	51
Salasone A	$C_{30}H_{48}O_3$		White powder	25
Salasone B	$C_{30}H_{48}O_3$		White powder	25
Salasone C	$C_{30}H_{50}O_3$		White powder	25
Salasone D			White powder	26
Salasone E			White powder	26
Salaquinone A	$C_{28}H_{34}O_5$		Amorphous powder	25
Salaquinone B	$C_{28}H_{36}O_5$		Amorphous powder	26
Salaterpene A	$C_{35}H_{41}O_{12}$	190–191^{0}C	colorless crystal	56
Salaterpene B	$C_{37}H_{42}O_{12}$	204–205^{0}C	colorless crystals	56
Salaterpene C	$C_{33}H_{38}O_{10}$	279–280^{0}C	colorless crystals	56
Salaterpene D	$C_{37}H_{39}O_{10}$	216–217^{0}C	colorless crystals	56
Lehmbachol A	$C_{31}H_{30}O_9$		Amorphous yellowish powder	24
Lehmbachol B	$C_{31}H_{30}O_9$		Amorphous yellowish powder	24
Lehmbachol C	$C_{31}H_{30}O_9$		Amorphous yellowish powder	24
Lehmbachol D	$C_{26}H_{26}O_8$		Amorphous yellowish powder	24
28-hydroxy-3-oxo-30-lupanoic acid	$C_{30}H_{48}O_8$	285-287^{0}C	White powder	21
3-oxo-lupane-30-Al	$C_{30}H_{48}O_2$	224-225^{0}C	White crystals	21
29-nor-21α-H-hopane-3,22-dione	$C_{29}H_{46}O_2$	272-273^{0}C	White crystals	21
21α-H-hop 22(29)-ene-3β,30-diol	$C_{30}H_{50}O_2$	246-247^{0}C	White crystals	21
Betulin	$C_{30}H_{50}O_2$	217-218^{0}C	White crystals	21
7α,21α-dihydroxyfriedelane-3-one	$C_{30}H_{50}O_3Na$	272-273^{0}C	Colorless plates	22
7α,29-dihydroxyfriedelane-3-one	$C_{30}H_{50}O_3K$	325–327^{0}C	Colorless crystals	22
21α,30-dihydroxyfriedelane-3-one		285–286^{0}C	Colorless needles	22
21α,30-Dihydroxyfriedelane-3-one diacetate	$C_{34}H_{54}O_5$	175-178^{0}C	Colorless crystals	22
2,3-Seco-20(29)-lupene-3-acetoxy-2-oic-acid (salacinin A, 1)	$C_{32}H_{52}O_4$		White amorphous powder	57

Table 1: Major Photochemicals isolated from *Salacia* Sps

Name of compound	Molecular formula	Melting point	Extract color	Reference
21α-Hydroxyfriedel-1-ene-3-one (salacinin C, 3)	$C_{30}H_{48}O_2$		White amorphous powder	57
3β,28-dihydroxylup-20(29)-en-2-one (salacinin B, 2)	$C_{30}H_{48}O_3$		White amorphous powder	57
polyhydroxylated cyclic 13-membered sulfoxide	$C_{12}H_{24}O_9S$		Colorless amorphous solid	58
Foliachinenoside E	$C_{21}H_{36}O_8$		Colorless amorphous powder	23
Foliachinenoside F	$C_{21}H_{36}O_8$of 2		Colorless amorphous powder	23
Foliachinenoside G	$C_{18}H_{32}O_8$of 3		Colorless amorphous powder	23
FoliachinenosidesH	$C_{16}H_{28}O_{10}$ for **4**,		Colorless amorphous powder	23
Foliachinenosides I	$C_{16}H_{30}O_{10}$ for **5**		Colorless amorphous powder	23
Foliasalacioside J	$C_{19}H_{34}O_8$of **6**		Colorless amorphous powder	23
Foliasalacioside K	$C_{19}H_{34}O_9$		Colorless amorphous powder	23

Table 2: Biological activities related to *Salacia* plants

S. No	Biological activity	Extract type	Model system	Reference
1	Nephroprotective activity	The ethanolic extract of *S. oblonga*	Rats Acetaminophen (200mg/kg and 500mg/kg)	59
2	Antiplasmodial activity	Extracted from seeds of S.*longipesvar. Camerunensis*	*in vitro* against *Plasmodium falciparum* chloroquine-resistant strainW2 (Ic_{50} valve 2.28 μg/ml)	56
3	Anti-inflammatory activity	*S. oblonga* root bark powder	male albino rats (1gm/Kg)	60
4	Reproductive perform Activity	*S. chinensis* Extract	Sprague–Dawley male and females rats (500-2000mg/kg/day)	61
5	Hypotensive activity	*S. oblonga* Stem ethanolic extract	Female Wistar rats (4-120 mg/kg) in vitro experiments (0.01-0.3 mg/ml)	62
6	Anticancer activity	Eight triterpenoids isolated from *S. chinensis*	Four neoplastic cell lines Hep-G2, LU, KB, and MCF-7 (1 and 10 μg/ ml)	22
7	Hepatoprotective activity	*S. chinensis* Root extract	Wistar strain of albino rats (50-5000mg/kg b.w.)	63
8	Antioxidant activity	Aqueous- Methanolic *S. oblonga* extract powder	*in vitro* assays H2O2 Scavenging activity IC50 values 380 (μg/ml) Superoxide Radical Scavenging activity IC50 values 186 (μg/ml) NO-Radical Scavenging activity IC50 values 690 (μg/ml)	64
9	Genotoxic and oxidative stress efficiency activity	*S. oblonga*	Wistar albino rats (3gm/kg/day)	65

Table 2: Biological activities related to *Salacia* plants

S. No	Biological activity	Extract type	Model system	Reference
10	Genotoxic, cytotoxic, antigenotoxic, and anticytotoxic effects	*S. crassifolia* stem bark extract	young male adult (outbred mice (*Mus musculus*, Swiss Webster) 50, 100, or 150 mg/kg	66
11	gene expression profiles	*Salacia* plant extract powder	male rats, Sprague Dawley	67
12	Studied immunomodulatory effect	*Salacia chinensis* water extract	Random bred Swiss albino rats 1mg/kg	68
13	**A**ntioxidant activity	*S. pallescens*	DPPH Radical scavenging assay One mg /ml methanol extract	69
14	Antiplasmodial activity	*S. senegalensis fresh leaves extracts*	Swiss albino mice infected with *Plasmodium berghei* (5000 mg per kg body weight)	70
15	Antimicrobial assay	*S. oblonga* aerial and root ethanol extracts	*In vitro* assay (1mg/ml)	71
16	Anti-Abortificient Activities	Aqueous root extract of *S. lehmbachii*	Wistar rats. (0.5 × 10 mg/ml)	72
17	Antifibrogenic activity	aqueous extract *S.Oblonga*	Zucker diabetic fatty (100 mg/kg, p.o., 6 weeks)	73
18	Antidiabetic	*Salacia parviflora* extract	84 type-2 diabetes patients	74
19	metabolic diseases, including diabetes and obesity.	*S. reticulate* hot water extract	Tsumura Suzuki obesity diabetes (TSOD) mice (spontaneous obese type II diabetes model mice)(0.3 or 1.0%,)	75
20	Antimicrobial Activity	ethanolic and aqueous extracts of *Salacia chinensis*	*In vitro* assay (250,500,750,1000,1250µg)	76
21	Antidiabetic and Hypolipidemic activity	Hydroalcoholic root extract of *S. Oblonga*	Albino rats of the Wistar strain STZ induced diabetic rats 50mg/Kg body weight, (50 mg/Kg and 100mg/ml)	77
22	Hematological changes activity	Hydroalcholic powder extract of *Salacia oblonga* for biochemical changes and heamatological studies in normal	White Albino Wistar Female Rats induced aluminum (200mg/Kg and 400mg/Kg)	78
23	Nephrop	*Salacia Chinensis* powder	Patients 2 groups with 15 patients each *Salacia Chinensis* 1000 mg twice-a-day.	79
24	Hypoglycemic activity	hydro alcoholic extract of roots and stems of *Salacia chinensis* Linn.	30 healthy volunteers (1000 mg extract of *Salacia chinensis*)	80
25	Antidiabetic Activity	Leaf and stems extract of *S.reticulata*	1.0mg of extract type 1 diabetic male DDY mice	81
26	α-Glucosidase inhibition activity	*S. chinensis* aqueous extraction methanolic extraction	*In vitro* assay	82
27	Oxidative stress,	The hydro alcoholic extract of *S. oblonga*	Wistar strain male albino rats induced by aluminum chloride(300 mg/kg b.w.)(67mg/kg b.w.)	83

Table 2: Biological activities related to *Salacia* plants

S. No	Biological activity	Extract type	Model system	Reference
28	Antioxidant activity	Methanolic-Aqueous (roots and stems) extract powder of *S. oblonga*	*In vitro* assay	84
29	Antioxidant and Cytotoxicity activity	*S.oblonga* extracts from roots and stem	*In vitro* assay (10 - 75µg/ml)	85

Table 3: Some representative patents based on *Salacia*

Title	Patent no	Reference
Foodstuff comprising an extract of a plant of the genus *Salacia* and Flavonoid	US 8,226,991 b2	86
Foodstuff of tablets or capsules	US 8,241,677 b2	87
Agent for reducing intestinal toxic bacterium and food or pharmaceutical preparation comprising the same	US 2010/0261784 a1	88
Mineral absorption accelerator and iron deficiency anemia Improver of food composition	US 2011/0052732 a1	89
Matrix metalloprotease (mmp) production inhibitor	US 2011/0217391 a1	90
An organoleptically enhanced salacia plant extract and a process thereof (minora)	WO 2008136013 A1	91
Primary bile acid and secondary bile acid generation regulator	US 2012/0276229 a1	92
Dietary supplement for promoting wellness and weight loss and methods of administering the same	US 8114445 B2	93
Nutraceutical formulation for treatment of diabetes	Neutraceutical formulation for treatment of diabetes US 20140186466 A1	94
Body weight gain suppressing Composition and food product Comprising the same	US 2012/0276081 A1	95
A synergistic ayurvedic / functional food bioactive composition (cincata)	WO 2008142702 A1	96

Ruphin *et al*.[45] have reported for the first time that the stem barks of *S. leptoclada* acetone extract posses' cytotoxic and antiplasmodial activity. Skiguchi *et al.*[46] have investigated the potentiality of *S. reticulata* leaves to inhibit *in vitro* the interleukin-1β (IL-1β)-activated proliferation synoviocyte-like cell line derived from arthritis model mice. They showed that the residual water fraction of the *S. reticulata* leaf extract was concerned within the inhibition of IL-1β-activated cell proliferation and regulation of ribonucleic acid expression in MTS-C H7 cells. They explain that *S. reticulata* leaves will have an effect on the functions of IL-1β-activated MTS-C H7 cells. They hypothesized that active ingredients may be 3KD peptides. It was concluded that *S. reticulata leaves* seem to possess a potential as functional food for the management of rheumatoid arthritis.

Bacteriocide and Antifungal Activity

Venkateshvarlu *et al.*[47] showed that ethanolic extract of roots of *S. macrosperma* exhibit antimicrobial activity *in vitro*. The extracts were analyzed for antimicrobial and antifungal activity. Both chloroform and benzene fraction showed antifungal and antimicrobial activity in dose dependent manner against E. *coli, B. subtilis* and *A.niger*. Rao and Giri[48] also reported that S.*oblonga* ethyl acetate extract has antimicrobial activity against Gram positive (*Staphylococcus aureus, S. epidermidis, E. faecalis, B subtilis, L monoextogener*) and Gram negative pathogenic strain (*Klebsiella pneumoniae, E. aerogenes, E. cloake, P. aeruginasa, E coli, S typhimurium*). Further, Rao and Giri[49] investigated anti-microbial activity of *S.oblonga* aerial part (stem and leaves) and roots ethyl acetate extracts towards the pathogen bacteria gram positive bacterium(*S. epidermidis, E .faecalis and B.subtilis*) and gram negative bacterium(*E.coli, S.typhi, E. cloacae, P aeruginosa and K.pneumonia*).the root extract of *S.oblonga* showed highest zone of inhibition than aerial part against *B,subtilis*).

Choudhary *et al.*[50] conducted antimicrobial and anti fungal activity of chloroform and methanolic extracts of *S. reticulata* Gram positive and Gram negative bacteria; and fungi. Both demonstrated inhibition towards all microorganisms employed in the test, but chloform extracts show significant activity followed by methanol extract. *S. aureus, Bacillus subtilis, Pseudomonas aeurginosa and Escherichia* coli were employed in bactericide activity testing and *Cryptococcus neoformans, Candida tropicalis, Monilia albicans* and *Epidermophyton floccosum* were employed in antifungal activity.

Companies providing products

These are several companies around the world in India and abroad that are involved in product development and formulations related to *Salacia* Viz., Natural remedies Pvt Ltd, Metropolis, Prakruti remedies Pvt ltd, Sheethaiiyam, Konark seasoner and Health Care, Xioan DwBiology (China), M/s Varanasi Bio Research Pvt. Ltd, Sanjivini Herbals, Nutra, Ayurveda Kothala Himbutu Association (Japan), Pioneer Enterprises, Phytodiabcare, Natural Herbs, Seasoner Remedies, Seasoner Drugs and Supplements.

CONCLUSION

Herbal medicine is gaining popularity in various parts of the world. *Salacia* is a versatile medicine plant in India and elsewhere. In an earlier review (5), we had dealt with antidiabetic and antiobesity properties of *Salacia*. Here we have compiled exhaustive information of a several other pharmacological effects and discussed them. However, some of the anecdotal claims need further validation. Already several, *Salacia* based, formulations are available in the international markets. Predominantly, it is being used as herbal drug for antioxidants, antimicrobial, anticancer properties. This review provides information to international researchers, to take up advanced scientific research to add value to existing knowledge which could stimulate many more product developments. However from biodiversity angle there is need for conservation and sustainable utilization of germplasm, for which plant tissue culture method needs to be adopted extensively. There is need to adopt technique of genetic marker and molecular characterization to solve the problem of species differentiation for authentic identification. Phytochemical finger print is also required to study potentiality to produce desired metabolites and also for identifying chemotypes. There seem to be a necessity of in depth research in exploring the potential of *Salacia* for various medicinal uses.

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CONFLICT OF INTEREST

There is no any conflict of interest by any one of the authors.

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