Phytopharmacological Profile of Symplocos racemosa: A Review

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ABSTRACT
Background: Symplocos racemosa Roxb. is an evergreen Ayurvedic plant widely distributed in the tropics and subtropics of Asia, Australia and America. Results: This weed possesses a wide range of ethnomedicinal uses including treatment for dysentery, bowel complaints, inflammations, vaginal discharges, abortion and miscarriages, snake bites. A wide range of bioactive compounds including flavonoids, tannins, loturine, loturidine, coluatorine, hinoic acid, salireposide, symplocosside, betasito-glycoside, symploverside, benzoylesterigoside, salireposide etc. have been isolated from this plant. Conclusion: Modern phytochemical, pharmacological investigations showed that the crude extracts and isolated compounds from Symplocos racemosa possess many kinds of biological functions. The present review summarizing the research works undertaken till date, on this plant in order to provide sufficient baseline information for future research and for commercial exploitation.

Key words: Symplocos racemosa, ethnomedicinal uses, bioactive, inflammations

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INTRODUCTION
In the current scenario, focus on plant research has increased all over the world and a large body of evidence has collected to show the immense potential of medicinal plants used in various traditional systems (Bora and Sharma, 2011; Deoda et al., 2012). Symplocos racemosa is a small, evergreen tree, up to 6-8.5 m tall found in the plains and lower hills throughout North and East India, ascending in the Himalayas up to an elevation of 1400 m, Bengal, Assam and Chota Nagpur (Sharma et al., 2000). Symplocos is a genus of flowering plants in the order Ericales, containing about 250 species native to Asia, Australia and the Americas. About 68 species are found in India, of which only a few are of economic importance (Rao et al., 2011). In Sanskrit this tree was known as Lodhraj meaning "propitious" and "Tilaka" because it was used in making the Tilaka mark on the forehead (De Silva et al., 1979). In Europe it was formerly looked upon as a chincha bark and had been known at various times as "Ecorce de laoutour", "China nova" and "China paraguayen" (Watt,1972). This study provides a review of the botany, chemical composition, biological activity, toxicology and traditional and contemporary use of Symplocos racemosa. Furthermore, a preliminary comparison of application Lodhra in folk medicine with its pharmacological activity is made.

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Taxonomical classification (Sharma et al., 2000; CSIR, 1956):
- Kingdom: Plantae
- Division: Magnoliophyta
- Class: Magnoliopsida
- Order: Ericales
- Family: Symplocaceae
- Genus: Symplocos

Vernacular names (Kirthikar and Basu, 1999):
- Sanskrit: Rodhraj, Paitki Lodhraj, Sabara Lodhraj, Tirita
- Assamese: Mugam
- Bengali: Lodha, Lodhra
- English: Symplocos bark
- Gujrati: Lodhaz
- Hindi: Lodha
- Kannada: Lodhara
- Kashmiri: Kath
- Malayalam: Pachotti
- Marathi: Lodh, Lodhraj
- Punjabi: Lodhar
- Tamil: Vellilatii, Vellilothram
- Telugu: Lodhugha
- Urdu: Lodh, Lodhpathi

Traditional uses (Kirthikar and Basu, 1999, Anonymous, 2006; Nadkarni, 1954; Raghunathan and Mitra, 2000): The bark is astringent, expectorant, antiinflammatory, efibrug, haemostatic, stomachic, constipating and suppurative. It is useful in eye diseases, spongy and bleeding gums, asthma, bronchitis, dropsy, arthritis, ulcers, tumours, leprosy, skin diseases, acne and pimples, fever, haemorrhages, menorrhagia, dyspepsia, flatulence, leucorrhoea, diarrhoea, dysentery, hepatic disorders, chyluria (filarial), elephantiasis, haemorrhoids, baldness, scrofula, ear diseases and gonorrhoea.

Ayurvedic properties (Raghunathan and Mitra, 2000):
- Rasa: Kashaya
- Gunas: Laghu, Ruksa
- Veerya: Sheeta
- Vipak: Katu
- Doshaghnata: Kaphapittashamaka
- Rogaghnata: Shotha, Vrana, Netrabhashyanda, Karnasrava, Atisara, Jwara etc.
- Karma: Shothahara, Kushaghna, Chakshushya, Sara, Vranaropana etc.

Siddha properties (Sharma et al., 2000):
- Siddha name: Vellilathithi, Velliloththiram, Thillakam
- Suva (Taste): Thuvapppu (Astringent)
- Veeriyam (Potency): Thatpam (Cooling)
- Vipakam (Transformation): Iniippu (Sweet)
- Ceikai (Pharmacological action): Kuzhirchinthadakkii (Refrgerant), Natchari (Antidote)
- Gunam (Uses): Used in Ascitis and Bone disorders

Dose (Raghunathan and Mitra, 2000):
- 3-5 g of the drug in powder form
- 20-30 g of the drug in decoction

Part used: Bark, leaves, fruit.

PHARMACOGNOSTIC STUDY

Macroscopic study (Sharma et al., 2000; Kirthikar and Basu, 1999; Nadkarni, 1954):
- Leaves: Leaves simple, alternate, spiral; petiole upto 1.5 cm long, planoconvex in cross section, glabrous; lamina 6.5-12.5x3-4.3 cm, oblanceolate to narrow elliptic, apex narrowly acuminate, base acute to attenuate, margin serrate and slightly recurved, glabrous, midrib canaliculate above; secondary nerves 6-12 pairs; tertiary nerves oblique quite distantly percurrent (Fig. 1)
- Fruit: Drupe, ellipsoid or oblong, ca. 1.5 cm long; seeds 1-2 (Fig. 1b)
- Bark: Bark greyish, lenticellate; blaze cream (Fig 1c)

Microscopic study (Raghunathan and Mitra, 2000): Transverse section of mature bark shows a wide cork of thin-walled, rectangular cells, cork cambium 1-3 layered, secondary cortex consists parenchymatous cells towards outer side and rounded cells towards inner side, a number of stone cells scattered throughout the region having highly thickened walls with distinct pits, prismatic and cluster crystals of calcium oxalate and starch grains, mostly simple present in a number of cortical cells. Secondary phloem wide consisting of sieve elements, phloem parenchyma, phloem fibres and stone cells, medullary rays.

Physical constituents (Sharma et al., 2000): Physical constituents are mentioned in Table 1.

Importance of Lodhra in Ayurveda (Raghunathan and Mitra, 2000; Chumekar, 2010): In Ayurvedic texts, Lodhara has been elaborated in detail due to its Pitta dosha and Kapha dosha pacifying activities i.e., it mitigates vitiated forces (doshas) of body. Lodhara cleans the wound, arrests bleeding and initiate fast healing process of wound. Due to the Rodhaka (arresting) property of plant it is also called as Rodhara.

Since, thousands of years, Lodhara has been used safely to treat many GI tract disorders. Lodhara bark is acrid, digesting and astringent to bowels. Due to its Grahi (anti-diarrheal) property it is commonly used to treat Atisara (diarrhoea). Lodhara has also been used as Sheet Virya (cool potency), Laghu (light quality), Netralikakar (beneficial for eyes) and Rakta dosh Nashaka.

According to Ayurveda, Lodhara reduces fever and cures the spongy gums/bleeding. It is useful to treat skin diseases (such as leprosy), dropsy and liver complaints. It has been considered as drug of choice in the treatment of gynecological disorders. Lodhara has been used to cure the menorrhagia, leucorrhoea (excessive discharge from vagina) and other menstrual disorders. It is also useful in abortions and miscarriages and for ulcers of vaginal. These official properties have made Lodhara as an authoritative herb to treat various health related disorders of mankind.

Table 1: Physical constituents of Syzygium cumini

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Specification (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ash</td>
<td>12</td>
</tr>
<tr>
<td>Acid insoluble ash</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol soluble extractive</td>
<td>9</td>
</tr>
<tr>
<td>Water soluble extractive</td>
<td>15</td>
</tr>
</tbody>
</table>
Table 2: Ayurvedic formulations of Symplocos racemosa

<table>
<thead>
<tr>
<th>Formulation of Lodhra</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rodhazava (Lodhrasava)</td>
<td>Menorrhagia, leucorrhoea, skin diseases, bleeding piles, grahami (irritable bowel syndrome)</td>
</tr>
<tr>
<td>Pushyanuga churna</td>
<td>Dysmenorrheoa, irregular menstrual bleeding and excessive menstrual bleeding</td>
</tr>
<tr>
<td>Brahatangadhi churna</td>
<td>Diarrhoea, dysentery and colitis</td>
</tr>
</tbody>
</table>

**Ayurvedic formulations:** Some important formulations which contains Lodhra as an important ingredient are mentioned in Table 2. Other some formulations which contain Lodhra as important ingredients are Ashbrak bhasma, Asthisandhanaka lepa, Bhringaraj taila, Briha gangadhara, Chandanasava, Dashmularishta, Drakshadi kvath churna, Gangadharchurna (vrihat), Grahanimirih taila, Irmedadi taila, Jatyadi taila, Jivanti ghirita, Kasisadi ghirita, Khadiradi gutika (mukharoga), Kumaryasava, Kunkumadi taila, Kutajastak kvath churna, Laghugandhvahara churna, Lodhrasava, Nagarjunyanjan, Nyagrodhi churna, Pippaladyasava, Piyushvali rasa, Prameha mihira taila, Pushyanug churna, Rodhrasava, Sarivadyasava, Somnath ras, Srikhandasava, Tutthadi lepa, Ushirasava, Vastamayantaka ghirita, Vidangarishta and Vimla varti (Rao et al., 2011).

**PHYTOCHEMISTRY**

**Chemical constituents:** Bark contains flavanol glucosides like symposocide, symposide, leucopelargonidin 3-glucoside, ellagic acid, flavonol glycoside like rhamnetin 3-digalactoside, triterpenoids like 19 α-hydroxyarjumonic acid-3, 28-O-bis-β-glucopyranosides, 19 α-hydroxyasiatic acid-3, 28-O-bis-β-glucopyranosides, betulin, Oleanolic acid, β-sitosterol and α-amyrin (Nagore et al., 2012a; Badoni et al., 2010). Apart from these chemical constituents the bark mainly contains alkaloids loturine, isoloturine and harmiace (Fig. 2) (Ishida et al., 2001). De Silva et al. (1979) reported Oleanolic acid, Betalinic acid through petroleum ether extract and ellagic acid from methanol extract. Ali and Srivastava (1990) isolated three new triterpenes 28-hydroxy-20α-urs-12, 18(19)-dien-3β-y1 acetate,
Fig. 2: Important chemical constituents of *Symplecos racemosa*

3-oxo-urs-20α-12, 18(19)-dien-28-oic acid and 24-hydroxyolean-12-en-3-one together with the known triterpenoids betulin and oleanolic acid (Ali and Srivastava, 1990). Ahmad *et al.* (2003) isolated phenolic glycoside named benzoylepisareposide along with five known compounds i.e., salireposide, b-amyrin, oleanolic acid, b-sitosterol and b-sitosterol glycoside (Fig. 2). They used methanolic extract for obtaining residue. The whole residue was extracted with hexane, chloroform, ethyl acetate and butanol. The ethyl acetate extract was subjected to CC over a silica gel column using hexane with gradient of CHCl₃ up to 100% and followed by methanol. Ahmad *et al.* (2005) analysed the two new phenolic glycosides, *Symposide A* and *Symposide B*. In which methanolic extract dissolved in water and partitioned successively with n-hexane, chloroform, ethyl acetate, n-butanol. Then ethyl acetate fraction was subjected to VLC over plate-silica with gradient of hexane and chloroform (9:10) and followed by methanol up to 0-100%. Abbasi *et al.* (2005) isolated new ethyl substituted glycoside, 1-ethyl brachiose-3′-acetate along with four known compounds ketocholemoenic acid, noaeicosanol, triacetyl palmitate and methyl triacanatoate. They dissolved methanolic extract in water and partitioned with hexane, chloroform, ethyl acetate and n-butanol successively. The butanol soluble fraction was subjected to column chromatography over a silica gel column using CHCl₃, with a gradient of methanol up to 100%. Ahmad *et al.* (2006) isolated one new C-glycoside, syncososide along with one known compound sito-glycoside. Ahmad *et al.* (2007) separated two new phenolic glycosides of salicine series, symplocrine acid and symplocemoside. They dissolved methanolic extract in water and partitioned with hexane, chloroform, ethyl acetate and n-butanol successively. The n-butanol extract was subjected to column chromatography over silica gel using CHCl₃, with gradient of methanol up to 100%. Rashid *et al.* (2008) reported three new benzyl derivatives, locoracemosides A, B and C from n-butanol soluble (Fig. 2). Vijayabaskaran *et al.* (2010a) isolate new phenolic glycoside i.e., 3, 5-dihydroxy-2-(hydroxyl methyl)-6-(3, 4, 5-trimethoxy phenoxy) tetrahydro-2H-pyran-4-yl, 4-hydroxy-3-methoxy benzoate. In which, ethanolic extract was eluted with isoamyl alcohol: Acetic acid: Water (1:1:2) to afford compound as a brown solid. It was recrystallized from hexane to afford that phenolic compound.

**Standardization by sophisticated instrument:**

Nagore *et al.* (2012a) developed new HPTLC method for the determination of turmeric in different bark extracts. They developed HPTLC aluminium plates pre-coated with silica gel 60 F254 in ascending order into twin trough glass chamber previously saturated with mobile phase consisting of chloroform: acetonitrile: triethylamine (7:5:2 v/v/v). Loturine was appeared as bluish colored chromatographic zones on a fluorescent background at Rf value 0.60 min. Detection and quantification were performed by densitometry at...
280 nm (Chunekar, 2010). Nagore et al. (2012b) developed RP-HPLC method for estimation and quantitative determination of Loturine. The RSD and correlation coefficient (r²) were calculated and found to be satisfactory. Nagore et al. (2012c) also developed HPTLC method for the determination of gallic acid in different bark extracts. They developed HPTLC aluminum plates pre-coated with silica gel 60 F254 in ascending order into twin trough glass chamber previously saturated with mobile phase consisting of toluene: ethyl acetate: formic acid: methanol (8: 8: 4: 2 v/v/v/v). Gallic acid was appeared as dark brownish colored chromatographic zones at Rf value 0.70. Kumar et al. (2006) developed new HPTLC method for the determination of harmine in different bark extracts. They developed HPTLC aluminum plates pre-coated with silica gel 60 F254 in ascending order into twin trough glass chamber previously saturated with mobile phase consisting of toluene: ethyl acetate: methanol (6:2:2 v/v/v). Detection and quantification were performed by densitometry at 324 nm.

PHARMACOLOGICAL ACTIVITY

**Anti-acne effect:** Kumar et al. (2007) investigated the anti-acne activity of ethanolic extracts of *Symplocos racemosa* bark by disc diffusion and broth dilution methods. The results from the disc diffusion method showed that these medicinal plants could inhibit the growth of Propionibacterium acnes.

**Analgesc and anti-inflammatory activity:** Sharma et al. (2013) estimated the analgesic activity of ethanolic and aqueous extract of bark by formalin induced paw licking and tail flick models and anti-inflammatory activity by carrageenan induced hind paw edema model. Their results revealed that ethanolic extract significantly suppress the inflammation than aqueous extract. Vijayabaskaran et al. (2010a) also investigated the anti-pyretic activity of bark ethanolic extract against brewer’s yeast induced pyrexia. From the study it was evident that ethanolic extract has antipyretic activity.

**Antioxidant activity:** Devmurari (2010a,b) tested the Antioxidant activity of ethanolic extract of leaves and flowering top by measuring the level of lipid peroxidation, glutathione (GSH), superoxide dismutase (SOD), catalase and protein content. The extract showed significant activities in all antioxidant assays by reducing lipid peroxidation, superoxide dismutase and catalase activity.

Vijayabaskaran et al. (2012b) examines the antioxidant activity of ethanolic extract of bark by DPPH (2, 2-diphenyl-1-picrylhydrazyl), nitric oxide, hydroxyl radical and ABTS [2, 2'-azinobis-(3-ethylthiazolone-6-sulfonic acid)] assay method. Their results indicated that the ethanolic extract showed potent antioxidant activity against ABTS assay method.

Ravichandran et al. (2005) also mentioned that the principle constituents of *Symplocos racemosa* i.e., salireoside and benzoylsalireposide have potent antioxidant activity.

**Anthelmintic activity:** Rao et al. (2011) evaluated anthelmintic activity of petroleum ether, chloroform and ethanol extract of bark on adult Indian earthworms, *P. posthuma*. The present investigation reveals that the ethanolic extract was endowed with potent anthelmintic property as compared to other extract.

**Anti-angiogenic activity:** Hussain et al. (2009) have reported the anti-angiogenic activity of (1) Symplocoside and (2) Symponoside, glycosides isolated from the bark. Their results revealed that both isolated glycosides inhibit Thymidine Phosphorylase (TP) activity and associated angiogenesis.

**Antibacterial activity:** Devmurari (2010c) assessed the antibacterial activity spectrum of petroleum ether and ethanolic bark extract which were used against three Gram positive bacteria, *Staphylococcus aureus*, *Enterococcus faecalis*, *Bacillus cereus* and three gram negative bacteria *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*. Ethanolic extract of *Symplocos racemosa* Roxb. possess good antibacterial activity as compare to petroleum ether. In one of their experiments, it also exhibited that *Symplocos racemosa* Roxb. has poor antibacterial activity against gram negative micro organism like *P. aeruginosa* and *E. coli*.

**Anticancer activity:** Raval et al. (2009a) evaluated the chloroform, butanol and ethyl acetate bark extracts for their cytotoxic activity determined using the XTT salt based cytotoxicity assay in 96-micro plate format against one leukaemia and one cervical cancer cell line. They reported that the butanol extract have highest cytotoxicity activity against HeLa cell line.

Raval et al. (2009b) also found butanolic extract as cytotoxic against HL 60 (Human leukemia cell line, IC₅₀ = 27183 ng mL⁻¹), HeLa (Human cervix cancer cell line, IC₅₀ = 22861 ng mL⁻¹). Ethyl acetate extract was found to be less cytotoxic against HL 60 (IC₅₀ = 117084 ng mL⁻¹), HeLa (IC₅₀ = 137151 ng mL⁻¹). Chloroform extract displayed no cytotoxicity against both cell lines.
Alzheimer's disease: Rashid et al. (2008) isolated three new benzyl derivatives; locoracemosides A, B and C from n-butanol soluble extract from bark have in vitro inhibitory activity against α-chymotrypsin.

Hepatoprotective activity: Wakchaure et al. (2010) evaluated the ethanol extract of bark on carbon tetrachloride (CCl₄)-induced hepatic damage in rats. Ethanol extract showed significant dose-dependent restoration of serum enzymes, bilirubin, albumin, total proteins and antioxidant levels. Significant improvement was observed in liver (morphological and histopathological). Therefore, it is an effective hepatoprotective agent in CCl₄-induced hepatic damage and has potential clinical applications for treatment of liver diseases.

Female reproductive disorders: Saraswathi et al. (2012) evaluate the ethanolic extract of bark in treating female reproductive dysfunctions. Cold restraint stress (4°C for 3 h day⁻¹ for 28 days) was used as stressor to induced changes in reproductive dysfunctions. From the experimental studies, Ethanolic extract of bark at two different doses showed promising result in treating female reproductive dysfunctions induced by cold restraint stress. Bhutani et al. (2004) analyzed the in vivo effect of aqueous extracts of bark on serum FSH and LH levels in immature female rats under basal conditions. Aqueous extract on oral administration significantly stimulated serum FSH level (p<0.016) along with the rise in serum LH level (p<0.001). Swarup and Umadevi (1998) also mention the usefulness of Smpylos racemosa in uterine disorders.

Lipoxygenase and urease inhibitory activity: Lipoxigenase and urease participates in the development of kidney stones, pyelonephritis, peptic ulcers and other disease states. Abbasi et al. (2005) assessed the activity of 1-ethyl brachiose-3'-acetate along with four known compounds ketochaulmoogric acid, nonaeicosanol, triacetyl palmitate and methyl triacantanoate using in vitro lipoxigenase and urease inhibition assay. The result indicate that 1-ethyl brachiose-3'-acetate and triacetyl palmitate displayed the inhibitory potential against lipoxygenase and urease enzyme. Lodhi et al. (2007) isolated triacantanol palmitate from n-hexane soluble fraction of bark and investigated the urease inhibitory activity by urease inhibition assay. Triacantanol palmate inhibited the urease enzymes in a concentration-dependent manner.

Peptic ulcer disease: Krishna et al. (2013) have reported the possible anti-ulcerogenic activity of aqueous and ethanolic extracts of bark. They use the pylorus ligated and aspirin induced models for evaluation of activity. The aqueous and ethanolic extracts have reduced ulcer index more significantly in pylorus ligation than aspirin induced models.

Phosphodiesterase, thymidine phosphorylase and butyrylcholinesterase inhibiting activity: Gomes et al. (2010) mentioned that benzoylsalireposide and salireposide isolated from Smpylos racemosa inhibited phosphodiesterase I activity. Choudhary et al. (2004) performed phosphodiesterase I inhibitory activity of benzoyl salireposide and salireposide isolated from Smpylos racemosa. They used phosphodiesterase I enzyme from snake venom and human nucleotide pyrophosphatase phosphodiesterase-1. Result indicates that both isolated compound have phosphodiesterase I inhibitory activity. Abbasi et al. (2004) also mentioned that symplecomoside, symponoside, symplososide, symploverside, benzoylsalireposide and salireposide have phosphodiesterase and thymidine phosphorylase-inhibiting activities. Ahmad et al. (2005) investigated butyrylcholinesterase inhibitory activity of symcososide isolated from bark of Smpylos racemosa.

CONCLUSION
The scientific research on Smpylos racemosa suggests a huge biological potential of this plant. It is strongly believed that detailed information as presented in this review on the phytochemical and various biological properties of the extracts might provide detailed evidence for the use of this plant in various indications. The phytochemical variations and efficacy of the medicinal values of Smpylos racemosa is dependent on geographical locations and seasons. A detailed and systematic study is required for identification, cataloging and documentation of plants which may provide a meaningful way for promoting traditional knowledge of the medicinal herbal plant. Also clinical study on each pharmacological activity is needed to have efficacy and safety data. There is need of further research to provide scientific base for possible role of this plant to treat diseases such as HIV, diabetes, arthritis and skin disease.

REFERENCES


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