

## 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, colloturine, linoleic acid, salireposide, symplocoside, betasito-glycoside, symploveroside, benzoylsalireposide, 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, upto 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 Lodhra 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 cinchona bark and had been known at various times as "Ecorce de lautour", "China nova" and "China paraquatan" (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: Rodhra, Paittki Lodhra, Sabara Lodhra, Tirita
- Assamese: Mugam
- Bengali: Lodha, Lodhra
- English: Symplocos bark
- Gujrati: Lodhaz
- Hindi: Lodha
- Kannada: Lodhra
- Kashmiri: Kath
- Malayalam: Pachotti
- Marathi: Lodha, Lodhra
- Punjabi: Lodhar
- Tamil: Vellilathi, Vellilothram
- Telugu: Lodhuga
- Urdu: Lodh, Lodhpathani

**Synonyms (Nadkarni, 1954):** Lodhra, Akshibhaishajya, Rodhra, Shavaraka, Sthoolavalkala, Tirita, Tilva, Galava.

**Traditional uses (Kirthikar and Basu, 1999, Anonymous, 2006; Nadkarni, 1954; Raghunathan and Mitra, 2000):** The bark is astringent, expectorant, anti-inflammatory, febrifuge, 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
- Guna: Laghu, Ruksha
- Veerya: Sheeta
- Vipaka: Katu
- Doshaghna: Kaphapittashamaka
- Rogaghna: Shotha, Vrana, Netrabhishyanda, Karnasrava, Atisara, Jwara etc.
- Karma: Shothahara, Kushaghna, Chakshushya, Sara, Vranaropana etc.

**Siddha properties (Sharma *et al.*, 2000):**

- Siddha name: Vellilatthi, Velliloththiram, Thillakam
- Suvai (Taste): Thuvarpupu (Astringent)
- Veeriyam (Potency): Thatpam (Cooling)
- Vipakam (Transformation): Inippu (Sweet)
- Ceikai (Pharmacological action): Kuzhirchiundakki (Refrigerant), 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 for 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 6.5-12.5×3-4.3 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 obliquely 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,

Lodhra has been elaborated in detail due to its Pitta dosha and Kapha dosha pacifying activities i.e., it mitigates vitiated forces (doshas) of body. Lodhra 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 Rodhra.

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

According to Ayurveda, Lodhra 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. Lodhra 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 vagina. These officinal properties have made Lodhra as an authoritative herb to treat various health related disorders of mankind.

Table 1: Physical constituents of *Symplocos racemosa*

Parameters	Specification (%)
Total ash	12
Acid insoluble ash	1
Alcohol soluble extractive	9
Water soluble extractive	15



Fig. 1(a-c): *Symplocos racemosa* (a) Whole plant, (b) Fruit and (c) Bark

Table 2: Ayurvedic formulations of *Symplocos racemosa*

Formulation of Lodhra	Indication
Rodharasava (Lodhrasava)	Menorrhagia, leucorrhoea, skin diseases, bleeding piles, grahani (irritable bowel syndrome)
Pushyanuga churna	Dysmenorrhoea, irregular menstrual bleeding and excessive menstrual bleeding
Bruhat gangadhara churna	Diarrhoea, dysentery and colitis

**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 Abhrak bhasma, Asthisandhanaka lepa, Bhringaraj taila, Briha gangadhara, Chandanasava, Dashmularishta, Drakshadi kvath chuna, Gangadharchurna (vrihat), Grahanimihir taila, Irimedadi taila, Jatyadi taila, Jivantyadi ghrita, Kasisadi ghrita, Khadiradi gutika (mukharoga), Kumaryasava, Kunkumadi taila, Kutajastak kvath churna, Laghugangadhara churna, Lodhrasava, Nagarjunanjan, Nyagrodhadi churna, Pippaladyasava, Piyushvalli rasa, Prameha mihira taila, Pushyanug churna, Rodhrasava,

Sarivadyasava, Somnath ras, Srikhandasava, Tutthadi lepa, Ushirasava, Vastyamayantaka ghrita, Vidangarishta and Vimla vartti (Rao *et al.*, 2011).

#### PHYTOCHEMISTRY

**Chemical constituents:** Bark contains flavanol glucosides like symplocoside, symposide, leucopelargonidin 3-glucoside, ellagic acid, flavanol glycoside like rhamnetin 3-digalactoside, triterpenoids like 19  $\alpha$ -hydroxyarjunolic acid-3, 28-O-bis- $\beta$ -glucopyranosides, 19  $\alpha$ -hydroxyasiatic acid-3, 28-O-bis- $\beta$ -glucopyranosides, betulin, Oleanolic acid,  $\beta$ -sitosterol and  $\alpha$ -amyrin (Nagore *et al.*, 2012a; Badoni *et al.*, 2010). Apart from these chemical constituents the bark mainly contains alkaloids loturine, isoloturine and harmane (Fig. 2) (Ishida *et al.*, 2001). De Silva *et al.* (1979) reported oleanolic acid, Betulinic acid through petroleum ether extract and ellagic acid from methanol extract. Ali and Srivastava (1990) isolated three new triterpenes 28-hydroxy-20 $\alpha$ -urs-12, 18(19)-dien-3 $\beta$ -yl acetate,

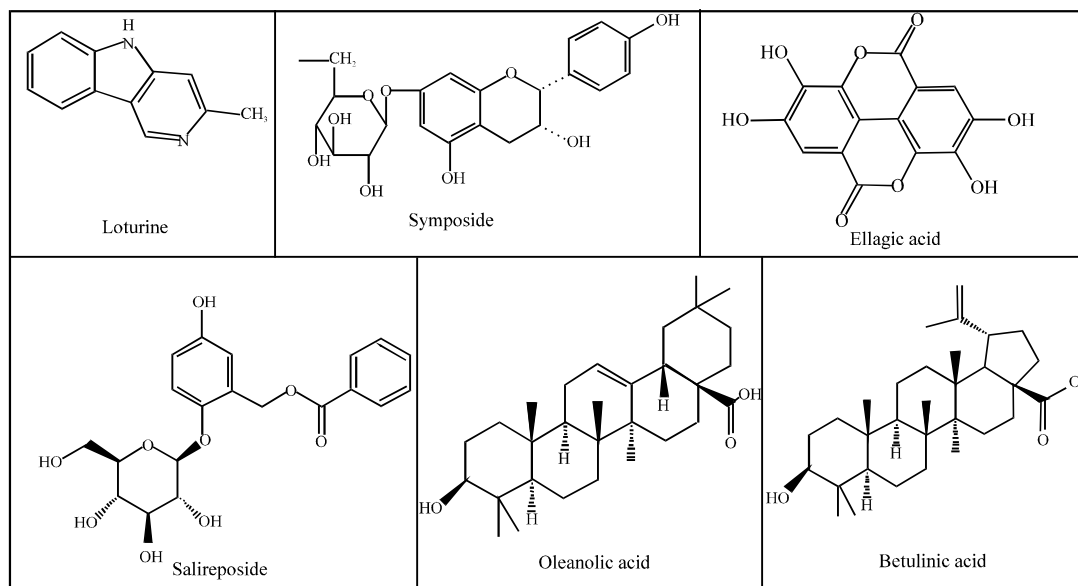


Fig. 2: Important chemical constituents of *Symplocos racemosa*

3-oxo-urs-20 $\alpha$ -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 benzoylsalireposide along 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  $\text{CHCl}_3$  upto 100% and followed by methanol. Ahmad *et al.* (2005) analysed the two new phenolic glycosides, *Symconoside A* and *Symconoside 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 (0:100) 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 ketochoaulmoogric acid, nonaeicosanol, triacontyl palmitate and methyl triacontanoate. 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  $\text{CHCl}_3$  with a gradient of methanol up to 100%. Ahmad *et al.* (2006) isolated one new C-glycoside, symcososide along with one known

compound sito-glycoside. Ahmad *et al.* (2007) separated two new phenolic glycosides of salirepin series, symplocuronic 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  $\text{CHCl}_3$  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 loturine 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 florescent background at  $R_f$  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 ( $r^2$ ) were calculated and found to be satisfactory. Nagore *et al.* (2012c) also developed new HPTLC method for the determination of gallic acid 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 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 aluminium 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*.

**Analgesic 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-ethylenzothiazoline-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., salireposide and benzoysalireposide 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 pneumonia*, *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,  $IC_{50} = 27183 \text{ ng mL}^{-1}$ ), HeLa (Human cervix cancer cell line,  $IC_{50} = 22861 \text{ ng mL}^{-1}$ ), Ethyl acetate extract was found to be less cytotoxic against HL 60 ( $IC_{50} = 117084 \text{ ng mL}^{-1}$ ), HeLa ( $IC_{50} = 137151 \text{ ng mL}^{-1}$ ). 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  $\alpha$ -chymotrypsin.

**Hepatoprotective activity:** Wakchaure *et al.* (2010) evaluated the ethanol extract of bark on carbon tetrachloride (CCl<sub>4</sub>)-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 CCl<sub>4</sub>-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<sup>-1</sup> 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 *Symplocos racemosa* in uterine disorders.

**Lipoxygenase and urease inhibitory activity:** Lipoxygenase 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 ketochoaulmoogric acid, nonaecosanol, triacontyl palmitate and methyl triacontanoate using *in vitro* lipoxygenase and urease inhibition assay. The result indicate that 1-ethyl brachiose-3'-acetate and triacontyl palmitate displayed the inhibitory potential against lipoxygenase and urease enzyme. Lodhi *et al.* (2007) isolated triacontanyl palmitate from n-hexane soluble fraction of bark and investigated the urease inhibitory activity by urease inhibition assay. Triacontanyl palmitate 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 *Symplocos racemosa* inhibited phosphodiesterase I activity. Choudhary *et al.* (2004) performed phosphodiesterase I inhibitory activity of benzoyl salireposide and salireposide isolated from *Symplocos 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 symplomoside, symponoside, symplomoside, symploveroside, benzoylsalireposide and salireposide have phosphodiesterase and thymidine phosphorylase-inhibiting activities. Ahmad *et al.* (2006) investigated butyrylcholinesterase inhibitory activity of symcososide isolated from bark of *Symplocos racemosa*.

## CONCLUSION

The scientific research on *Symplocos 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 *Symplocos racemosa* is dependent on geographical locations and seasons. A detailed and systematic study is required for identification, cataloguing 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.

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