

Review Article

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## *Symplocos paniculata* Miq. - A Review

G. Kusuma<sup>1</sup>, B. Vijaya Kumar<sup>2</sup> and S. Chitra<sup>3\*</sup>

<sup>1</sup>Research Officer (Ay.) /Scientist-2, Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute, CCRAS, Ministry of AYUSH, Govt. of India, A.A. Hospital Campus, Arumbakkam, Chennai-600 106, Tamil Nadu, India

<sup>2</sup>Department of Chemistry, Vel Tech High Tech Dr. Rangarajan Dr. Sakunthala Engineering College, Avadi, Chennai-600 062, Tamil Nadu, India

<sup>3</sup>Assistant Director (Biochemistry), Captain Srinivasa Murthy Regional Ayurveda Drug Development Institute, CCRAS, Ministry of AYUSH, Govt. of India, A.A. Hospital Campus, Arumbakkam, Chennai-600 106, Tamil Nadu, India

**\*Corresponding author.**

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### ABSTRACT

Historically plants have played an important role in medicine. Medicinal herbs are moving from fringe to mainstream use with a greater number of people seeking remedies. Through observation and experimentation, human beings have learnt that plants promote health. The use of these herbal remedies is not only cost effective but also safe and almost free from serious side effects. The genus *Symplocos* has been reviewed for its chemical constituents and biological activities including traditional importance of some common species. *Symplocos paniculata* is an evergreen Ayurvedic plant, with wide range of ethno medicinal uses including treatment for dysentery, bowel complaints, inflammations, snake bites, vaginal discharges and miscarriages. From various literatures the crude extracts of *S. paniculata* possess different kinds of biological functions studied by researchers through phytochemical, pharmacological and biochemical investigations.

### Introduction

The genus *Symplocos* consists of almost 300–500 species. These plants are distributed in tropical and subtropical area in Asia, Malaysia, and America<sup>1</sup>. In recent years, an extensive work in chemistry and pharmacology on the genus *Symplocos* has been recorded. *Symplocos* is one of the most selected genera having potential medicinal values. Two species in the genus *Symplocos* namely *Symplocos paniculata* Miq. and *Symplocos racemosa* Roxb. are widely used in Ayurveda and are known as Pattika

lodhra and Savara lodhra respectively in Sanskrit. Savara lodhra- *S. racemosa* is extensively used in therapeutics for various diseases whereas Pattika lodhra- *S. paniculata* is less known among Ayurvedic fraternity though mentioned in various classical texts of Ayurveda. The properties of *S. paniculata* are the same as those of *S. racemosa*; but of the two species *S. paniculata* is the better therapeutically<sup>2</sup>. The presence of easily separable plates (Pattika) of tissues in the inner bark<sup>3</sup> (Fig.1) and due to its thick nature (Sthulavalkalah in Sanskrit), *S. paniculata* got the name Pattika lodhra. Other than the thick nature

of the bark the synonyms do not give any indication that may help to identify the botanical source of

*S.paniculata*<sup>4</sup>. Pattika lodhra is commonly known as Asiatic Sweet leaf, Sapphire berry (Fig.2).



**Fig. 1:** Stem bark of *Symplocos paniculata*.



**Fig. 2:** Fruiting and flowering branches of *Symplocos paniculata*.

Certain Ayurvedic formulations like Nyagrodhadi Kwatha churna contain both Savara lodhra and Pattika lodhra as ingredients. The knowledge about Pattika lodhra is absolutely necessary as it throws light on its identity which will be useful further in

authenticating the drug in drug standardization. *S. paniculata* Miq is sold in the market under the name Lodhra. The common names of *S. paniculata*<sup>2</sup> and its 14 accepted scientific synonyms<sup>5</sup> are given in Tables 1 and 2.

**Table 1.** Vernacular names of *S. paniculata*.

S. No.	Name of the Place / Language	Vernacular Names
1.	Basharh	Lojh
2.	Burma	Daukyat
3.	Jaunsar	Lodh, lodra
4.	Kumaon	Lodh
5.	Punjab	Laudar, Lodar, Lodh, Loj, Loja, Lu, Pathani
6.	Sind	Lodh, Lodur, Pathani
7.	Hindi	Ludh
8.	Sanskrit	Akshibheshaja, Bahulatvacha, Brihaddala, Brihadvalka, Brihatpatra, Galava, Jirnabudhna, Jirnapatra, Kramuka, Lakshaprasada, Lakshaprasadana, Lodhra, Patti, Pattikakhya, Pattikalodhra, Shabara, Shirnapatra, Shvetalodhra, Sthulavalkala, Valka, Valkalodhra

**Table 2.** Accepted scientific synonyms for *Symplocos paniculata* Miq.

S. No.	Scientific Synonyms
1.	<i>Cotoneaster coreanus</i> H. Lév.
2.	<i>Myrtus chinensis</i> Lour.
3.	<i>Palura chinensis</i> (Lour.) Koidz.
4.	<i>Palura chinensis</i> var. <i>pilosa</i> Nakai
5.	<i>Palura sinica</i> (Ker Gawl.) Miers
6.	<i>Prunus mairei</i> H.Lév.
7.	<i>Prunus paniculata</i> - Thunb.
8.	<i>Symplocos chinensis</i> – (Lour.) Druce.
9.	<i>Symplocos chinensis</i> var. <i>vestita</i> (Hemsl.) Hand.-Mazz.
10.	<i>Symplocos crataegoides</i> Buch.- Ham. ex D. Don
11.	<i>Symplocos hunanensis</i> Hand.-Mazz.
12.	<i>Symplocos simaoensis</i> Y. Y. Qian
13.	<i>Symplocos sinica</i> var. <i>vestita</i> Hemsl.

## Distribution

*S. paniculata* is distributed in Himalaya up to 9,000 feet from the Indus to Assam, Khasia hills, upper and lower Burma, Punjab occurring in high altitudes between 600 and 2,400 m<sup>2,6</sup>.

## Morphology

*S. paniculata* is a large deciduous shrub or medium sized tree of 12 m in height. Young branches more or less pilose. Leaves are membranous of around 5-10 cm long, elliptic or ovate-elliptic, acute or acuminate, rounded or cuneate at the base, usually deeply serrate towards the apex, under surface usually pilose especially on the midrib, but sometimes quite glabrous, nerves are prominent situated beneath the petioles are of 5 mm in length. Flowers are pedicelled, white turning yellow, fragrant, arranged in cymose corymbs on elongate terminal and axillary panicles, those of the lateral branches often few and with longer pedicels; bracts small, linear, caduceous. Calyx-tube obconic, glabrous, more or less pilose; lobes rounded or lanceolate and acute, ciliate. Wood-white, soft to moderately hard, close grained, liable to twist and split when seasoning. Corolla three times longer than the calyx 5 in number. Stamens are 20-60 in number, equaling the corolla in length; filaments connate in 5 bundles. Ovary usually 2-celled, glabrous or hairy. Fruits are of 3-8 mm in size, globose or ovoid, crowned with the remains of the calyx-limb, fruits blue and turned black on ripe, usually one seeded<sup>2</sup>.

Flowering time of the plant is around May-June and fruiting season is during October-December<sup>7</sup>. The useful part of the plant is reported to be bark.

## Cultivation

Cultivation of *S. paniculata* requires an acid soil and a sunny position. Succeeds in a sunny position in any well-drained fertile neutral to acid soil<sup>8, 9</sup>. These plants are hardy to about -10° C, though it can survive in quite harsh winters but they need a warm, sunny protected position and a hot summer if they are to fruit well<sup>9, 10</sup>. Being self-sterile, it requires cross-pollination with a different plant in the same species if seed and fruit are to be produced. Plants in this genus are notably resistant to honey fungus. *Pidorus euchromioides* Walker (Lepidoptera; Zygaenidae) is a significant defoliator of Chinese sweet leaf, *S. chinensis* (Symplocaceae),

in Nanchang Jiangxi Province, People's Republic of China<sup>11</sup>. Overwintering larvae hibernate underground litter and become active just as the leaf buds of the host plant, *S. chinensis*, are opening, usually in early April and cause damage to the tender buds in early spring<sup>12</sup>.

## Propagation

Seed-best sown in a cold frame as soon as it is ripe. Stored seed requires stratification and is best sown in a cold frame in late winter; it can take 12 months to germinate<sup>10</sup>. Prick out the seedlings into individual pots when they are large enough to handle and grow them on in the cold frame for their first winter. Plant out in late spring or early summer. Cuttings of half-ripe wood, 7-10 cm with a heel, July/ August in individual pots in a cold frame. Roots are formed in about 4 weeks<sup>9, 13</sup>.

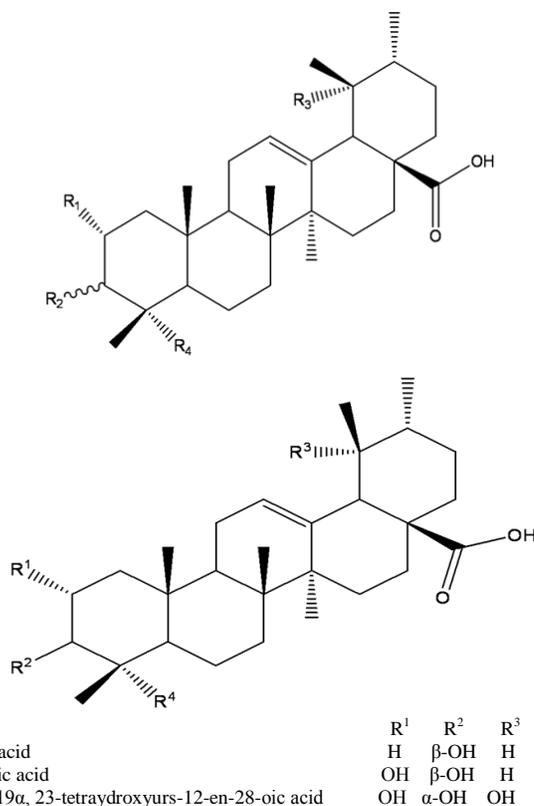
## DNA bar coding of *S. paniculata*

The consortium for the Barcode of Life (CBOL) in the 2009 has recommended *rbcL*, *matK* and *psbA-trnH* as the core DNA markers in the identification of plant species. The ribulose-1, 5-bisphosphate carboxylase large subunit (*rbcL*) and maturase K (*matK*) for *S. paniculata* has been sequenced and stored at the National Center for Biotechnology Information (NCBI) under the accession numbers GenBank: HQ427234.1 and GenBank: HQ427378.1 (Unpublished). The *psbA-trnH* intergenic spacer and partial sequence for the internal transcribed sequence (*ITS2*) of *S. paniculata* has been used for the study of phylogenetic analysis of Asian *Symplocos* (*Symplocaceae*) based on nuclear and chloroplast DNA sequences. These sequences are stored in GenBank: AB115370.1 and AY336263.1<sup>14</sup>. These sequences will be used in the identification of *S. paniculata*.

## Chemical Constituents of *S. paniculata*

The plants of genus *Symplocos* contain a variety of constituents viz. terpenoids, flavonoids, lignans, phenols, steroids, alkaloids, iridoids, and many

others<sup>15</sup>. Ursolic acid, corosolic acid and 2 $\alpha$ , 3 $\alpha$ , 19 $\alpha$ , 23-tetrahydroxyurs-12-ene-28-oic acid (Figs. 3 and 4)<sup>16</sup>, flavonoids<sup>17</sup> are reported to be present in *S. paniculata*. Besides some triterpenoids, triterpenoid saponins<sup>18</sup>, flavanol glycosides<sup>19</sup>, iridoid glycosides<sup>20</sup> and lignan glycosides<sup>21</sup>, isolated from *Symplocos* genus.



**Figs. 3 & 4:** Structures of ursolic acid, corosolic acid and 2 $\alpha$ , 3 $\alpha$ , 19 $\alpha$ , 23-tetrahydroxyurs-12-en-28-oic acid.

## Seeds

The seeds of *S. paniculata* contain 21% protein and 52% of oil on dry basis. The fatty acid composition of the oil contains 6% saturated fatty acids, 53% oleic and 36% linoleic acid<sup>22</sup>.

## Root

The butyl alcohol extract of root of *S. chinensis* exhibited six new triterpenoid saponins. Their structures were established as symplocosides A to F<sup>23</sup> (Fig.5). Symplocoside A (Fig.6) was obtained as a white amorphous powder and had a

molecular formula of  $C_{63}H_{100}O_{23}$  which was determined from its positive ion High-resolution electro spray ionisation mass spectrometry (HRESIMS) and confirmed by  $^{13}C$  Nuclear

Magnetic Resonance and Distortionless Enhancement by Polarization Transfer (DEPT) analysis and other fractions such as G-K have more significant functions (Fig.7).

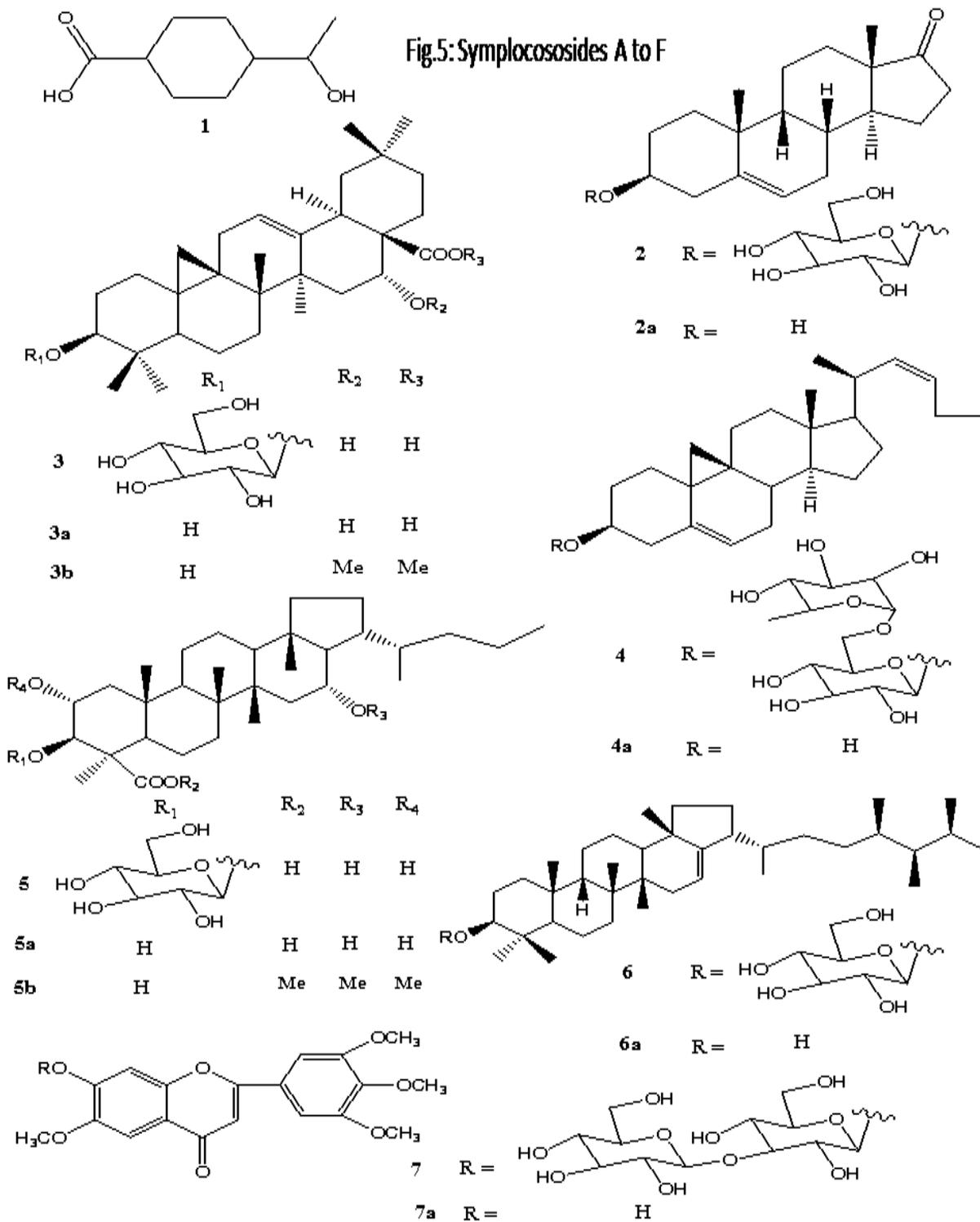
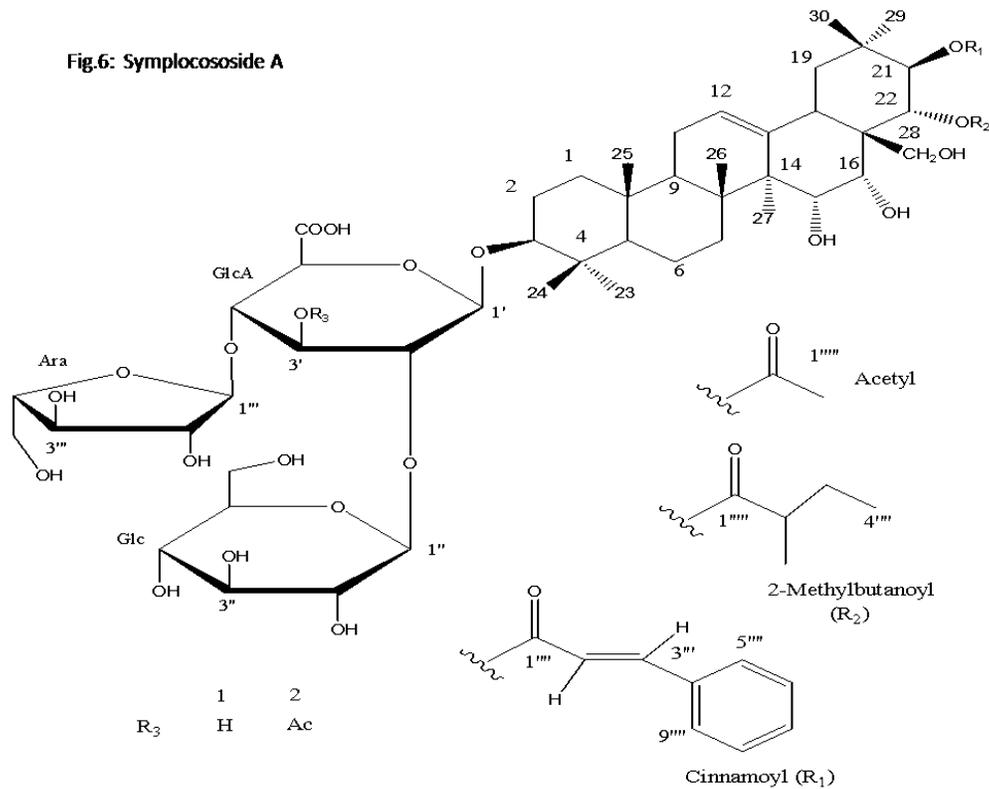
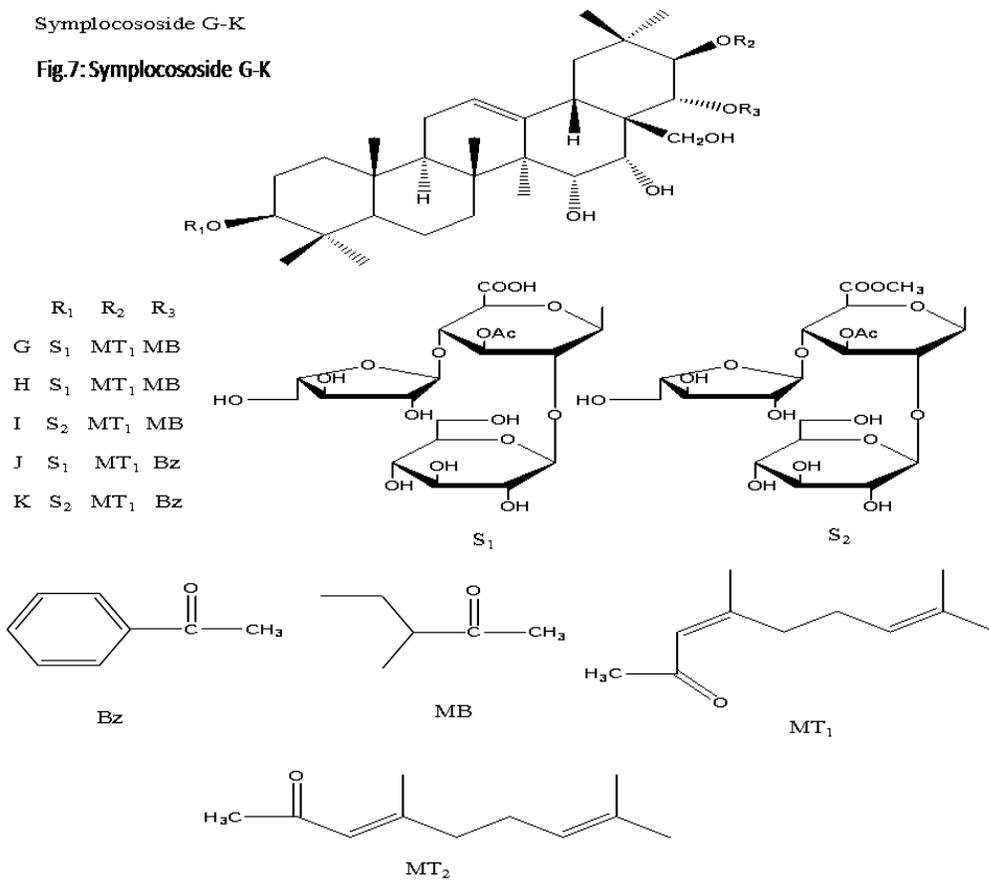


Fig.6: Symplocoside A



Symplocoside G-K

Fig.7: Symplocoside G-K



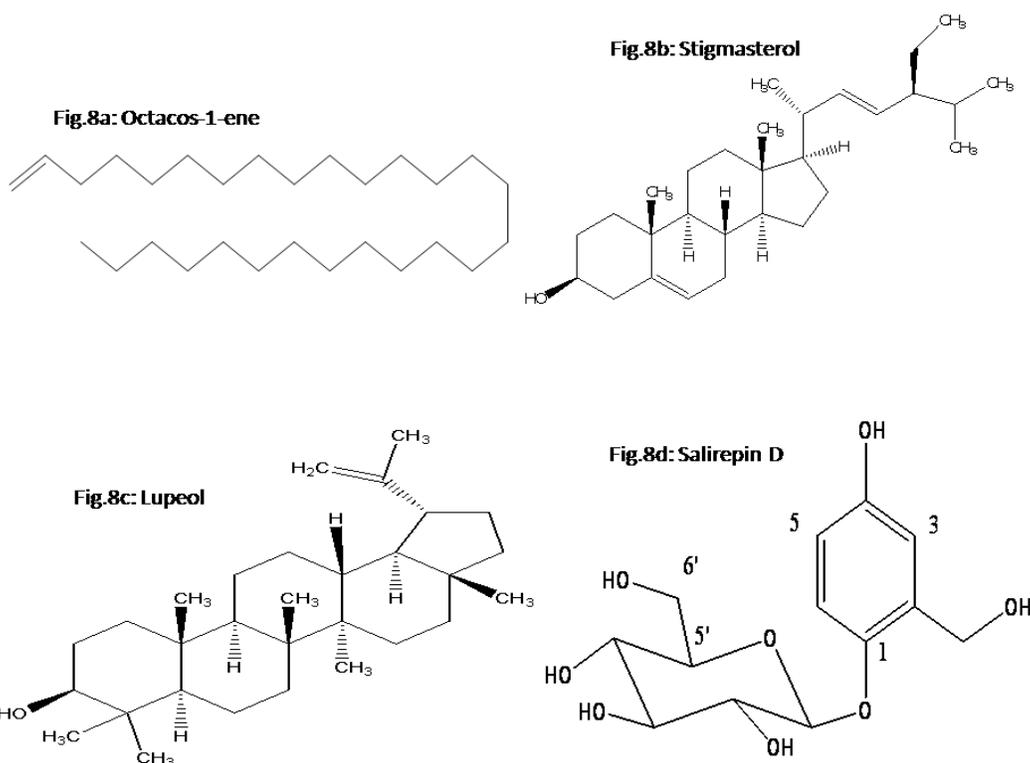
## Leaves

The leaves of *S. paniculata*, yielded 4 compounds (Fig.8) namely octacos-1-ene (8a), stigmasterol (8b) and lupeol (8c) and salirepin D (8d) on solvent extraction<sup>24</sup>.

## Stem bark

The stem bark of the plant afforded seven compounds, 4-(8-hydroxyethyl) cyclohexan-1-oic

acid; androst-5 (6)-ene 17-one 3 $\beta$ -O - ( $\beta$ -D-glucopyranoside); 9 $\beta$ , 25-cyclo 3 $\beta$ -O-( $\beta$ -D-glucopyranosyl)-echinocystic acid; 9 $\beta$ , 19-cyclo 24-methylcholan-5, 22-diene 3 $\beta$ -O-{ $\beta$ -D-glucopyranosyl (1 $\rightarrow$ 6)  $\alpha$ -L-rhamnopyranoside}; 30-ethyl 2 $\alpha$ ,16 $\alpha$ -dihydroxy 3 $\beta$ -O-( $\beta$ -D-glucopyranosyl) hopan-24-oic acid; 32, 33, 34-trimethyl-bacteriohopan-16-ene 3-O- $\beta$ -D-glucopyranoside and flavone 3', 4', 5', 6-tetramethoxy 7-O- $\beta$ -D-glucopyranosyl (1 $\rightarrow$ 3)  $\beta$ -D-glucopyranoside<sup>25</sup> (Fig.9).



## Medicinal uses

The members of genus *Symplocos* are gaining popularity due to their diverse biological activities and are well known for their traditional uses in the treatment of various diseases like leprosy, gynaecological disorders, ulcers, leucorrhoea, menorrhagia, malaria, tumefaction, bacterial diseases, diarrhoea, dysentery, eye diseases, hemorrhagic gingivitis, nephritis, bowel complaints, enteritis, snake bite and detoxification, particularly for anti-HIV, anti - tumor, and phosphodiesterase inhibitory activities<sup>2,26-30</sup>. The

juice of the bark is applied externally to sprains and muscular swellings<sup>31</sup>. The important preparations using the drug are Nyagrodhadi Kwatha Curna<sup>32</sup>.

## Ethno-veterinary use

The plant forms an ingredient of a herbal animal health product, NEBLON, useful in scours and non specific diarrhea in cattle and sheep. LD<sub>50</sub> studies on Neblon indicated that it is free from any toxic effect. The spasmolytic activity of neblon for reducing intestinal peristalsis was comparable to standard drugs, atropine sulphate

and its analogue, tropanyl<sup>33</sup>.

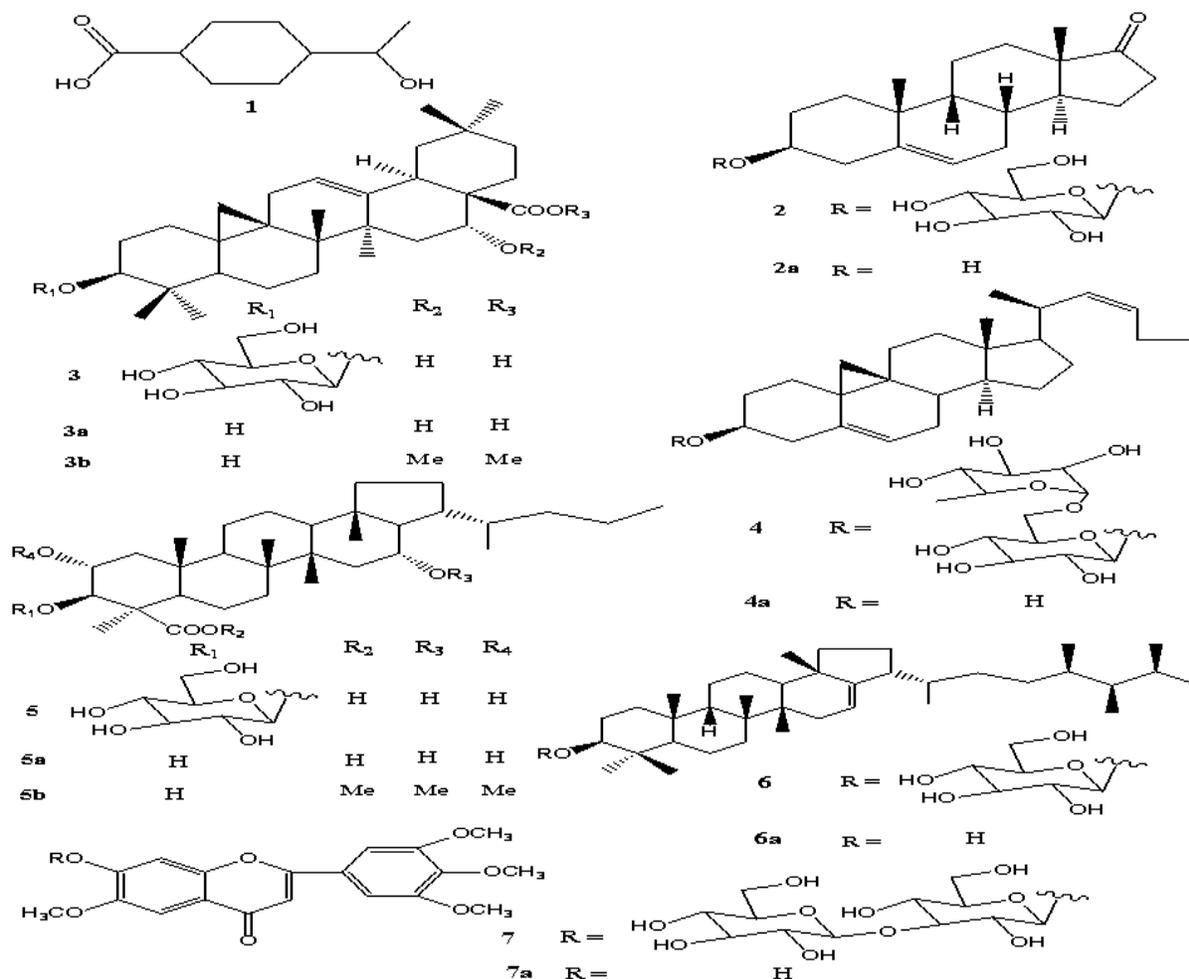
## Toxicology

*S. chinensis* is a toxic herb distributed in southern China<sup>29</sup>. When used in large quantity it causes dizziness, chest oppression and gastrointestinal disorder<sup>38</sup>.

## Other uses

Fruit is the edible part. It is cooked. Used in Jams, jellies and sauce<sup>34, 35</sup>. It is used as a dye, mordant and wood. A yellow or red dye is obtained from the leaves and bark. Leaves serve as fodder for sheep and goats and it is recommended for turning and for carving if properly seasoned<sup>31, 36-37</sup>.

Fig.9: Structures of seven compounds from stem bark



## Pharmacological activities

### Anti cancerous activity

Terpenoids are the major constituents within the genus *Symplocos* and most of them exhibit anti-proliferative effects<sup>15,30</sup>. Six triterpenoid saponins, symplocosides A-F isolated from *S. chinensis*, shown to have anti-proliferative activity. Among

them, symplocoside A exhibited activity against KB, HCT-8, A 549, BGC-823, and HELF cells<sup>39</sup>. Ursane-type triterpenes, in particular ursolic acid and corosolic acid, have been reported to possess a anti-tumor and anti-angiogenic activities<sup>40-41</sup>. The Ethyl alcohol soluble extract exhibited significant cytotoxic activities and four triterpenoids (Fig. 10a-10d) have been found from this fraction<sup>28</sup>.

An ursane triterpenoid, 2 $\beta$ , 3 $\beta$ , 19 $\alpha$ , 24-tetrahydroxy-23-norurs-12-en-28-oic acid (Fig.11), isolated from the root of *S. chinensis*, exhibited significant cytotoxic activity against B16 and BGC-

823 cells<sup>29</sup>. Symplocoside C showed cytotoxic activity against HCT-8 cells and BGC-823 cells, and symplocoside F was found to be cytotoxic against HCT-8 cells<sup>39</sup>.

Fig.10a: 2 $\alpha$ , 3 $\beta$ , 19 $\alpha$ , 23-tetrahydroxyurs-12-en-28-oic acid

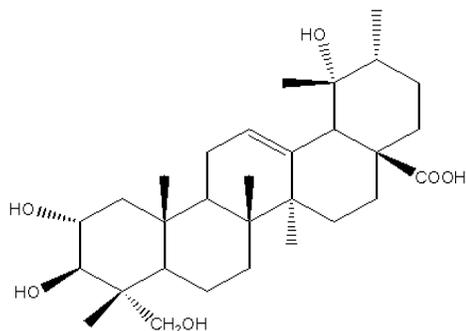


Fig.10b: 3-oxo-19 $\alpha$ , 23, 24-trihydroxyurs-12-en-28-oic acid

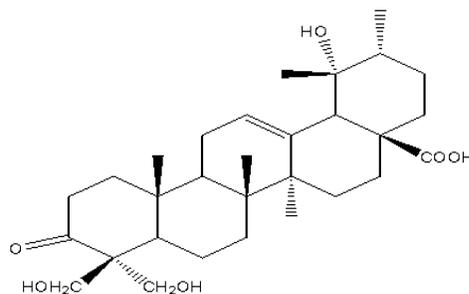


Fig 10c: 2 $\alpha$ , 3 $\alpha$ , 19 $\alpha$ , 23-tetrahydroxyurs-12-en-28-oic acid

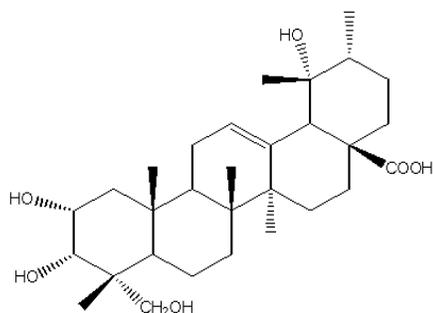


Fig 10d: 24-Hydroxytormentonic acid

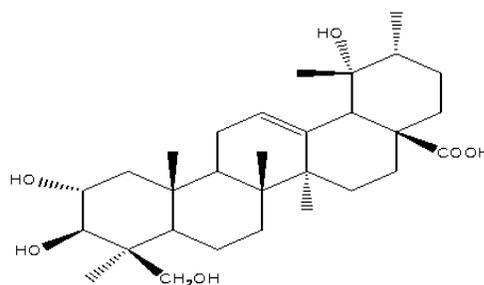
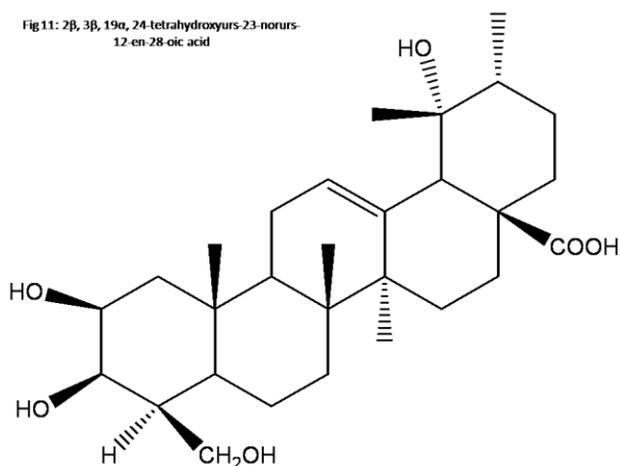


Fig 11: 2 $\beta$ , 3 $\beta$ , 19 $\alpha$ , 24-tetrahydroxyurs-23-norurs-12-en-28-oic acid



## Cytotoxicity

A new triterpenoid isolated from the roots of *S.*

*chinensis* have strong antitumor activities<sup>29</sup>. Triterpenoid saponins from the roots have symplocosides G-K which exhibited significant cytotoxic activities against some tumor cell line<sup>40</sup>. A new triterpene with strong cytotoxic activities was isolated along with three known triterpenes from the ethyl alcohol soluble fraction<sup>29</sup>.

## Antioxidant activity

The relationship between antioxidant capacity and total phenolic content of the fruit of *S. paniculata* was estimated in water and fat soluble fraction. It was found that the fruit has potential rich resources of natural antioxidants, and could be developed into functional foods or drugs for the prevention and treatment of diseases caused by oxidative stress.

The methanolic extract of *S. paniculata* was primarily assessed for its antioxidant activity against 1, 1-diphenyl-2-picrylhydrazyl (DPPH). Reducing power assay was assessed in the fat and water soluble fractions of *S. paniculata*<sup>41</sup>.

### Anti-poisonous activity

The phenolic glycoside derivatives showed inhibitory activity against snake-venom phosphodiesterase-I and human nucleotide pyrophosphatase phosphodiesterase I. The methanol extract of leaves and stem of *S. paniculata* showed *in vitro* PTP1B inhibitory activity. This extract was subjected to chemical analysis and afforded three ursane-type triterpenes, ursolic acid, corosolic acid, and 2 $\alpha$ , 3 $\alpha$ , 19 $\alpha$ , 23-tetrahydroxyurs-12-en-28-oic acid (Fig.10) which inhibited PTP1B. Kinetic studies suggest that ursolic acid is a competitive inhibitor whereas corosolic acid is a mixed-type inhibitor of PTP1B<sup>17</sup>.

### Anti-diabetic activity

Protein tyrosine phosphatase (PTPs), which dephosphorylate the tyrosine residues of proteins, play an important role in intra-cellular signaling and metabolism. Although several PTPs such as PTP $\alpha$ , leukocyte antigen-related tyrosine phosphatase and SH<sub>2</sub>-domain-containing phosphotyrosine phosphatase have been implicated in the regulation of insulin signaling, there is substantial evidence supporting PTP1B as the critical PTP controlling the insulin signaling pathway<sup>16,42</sup>.

Corosolic acid, a component of *S. paniculata* improves insulin pathway. The action of Insulin is mediated by tyrosine phosphorylation and initiated by the binding of insulin to the insulin receptor. It may act as an insulin sensitizer, enhancing insulin receptor B phosphorylation indirectly by inhibiting certain non receptor protein tyrosine phosphatases<sup>43</sup>. Corosolic acid may also enhance GLUT4 glucose transporter processing of glucose uptake into muscle cells<sup>44</sup>. Another study reported that corosolic acid inhibited gluconeogenesis by

increasing the production of the gluconeogenic intermediate fructose-2, 6-bisphosphate in isolated hepatocytes. Corosolic acid may promote glycolysis<sup>45, 46</sup>. Treatment with corosolic acid lowered plasma insulin levels and reduced the blood glucose levels in KK-Ay mice, after a single oral dose was reported<sup>47</sup>. Another experiment showed similar inhibitory action against increasing blood glucose levels and also increasing the concentration of corosolic acid may lead to enhanced glucose uptake activity<sup>48,49</sup>. Corosolic acid induced muscle GLUT4 translocation from low-density microsomal membrane to plasma membrane in genetically-induced type-2 diabetic mice<sup>44, 46</sup>.

### Antimicrobial activity

Ethanol extract of leaves showed activity against *Entamoeba histolytica* strain STA *Ascaridia galli*<sup>18, 34</sup>. *S. paniculata* plant has been used in bacterial infections<sup>25</sup>. The ethanol extract of stem bark as well the compounds isolated from the fractional distillation showed anti-bacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Escherichia coli*<sup>25</sup>. The compounds 3 and 5 isolated from stem bark showed a good antimicrobial agent and could be an alternate to the antibiotics in the treatment of infections caused by these microorganisms since most of them have developed resistance against the known antibiotics<sup>50</sup>. The extract of *S. paniculata* proved to have a potent antimicrobial activity<sup>25</sup>. Ethanol extract of leaves showed anti-bacterial activity against *Entamoeba histolytica* and *Ascaridia galli*<sup>51</sup>. Corosolic acid, a component of *S. paniculata* showed a synergistic activity with tobramycin against *Pseudomonas aeruginosa*<sup>52</sup>.

### Action on lipid metabolism

Corosolic acid was reported to have antihypertensive and lipid lowering. A study on rats showed that a reduced serum free fatty acid levels by corosolic and in turn controls the blood pressure<sup>53</sup>. There is an *in vitro* evidence for corosolic acid inhibiting protein tyrosine phosphatase

1B. This phosphatase play an important role in the control of obesity<sup>16</sup>. It is a pancreatic lipase inhibitor; it is a key enzyme in the absorption of lipids<sup>54</sup>. Also a study in mice revealed that the corosolic acid acted as a peroxisome proliferator activated receptor alpha agonist, regulating lipid metabolism and increasing fatty acid beta-oxidation in the liver<sup>55</sup>.

### Anti-inflammatory activity

The paste of the bark of *S.paniculata* used in the treatment of inflammation in traditional medicine but no scientific evidences available yet. The plant contains various triterpenoids exhibited potent anti-inflammatory activities<sup>56,57</sup>. Crude extract and isolated compounds from stem bark of *S. paniculata* showed a dose-dependent inhibition of swelling caused by carrageenan induced inflammation in rats<sup>25</sup>. Corosolic acid acted against the classical pathway of the complement system is documented<sup>58</sup>.

### Conclusion

The genus *Symplocos* is widespread all over the world, and many species of this genus have been used as traditional medicines for various ailments. These plants are well known for their traditional uses in leprosy, gynecological disorders, ulcers, leucorrhoea, malaria, nephritis, snake bite, menorrhagia, etc. The earlier reports on chemical investigation and pharmacological evaluation showed that the members of genus *Symplocos* contain a number of bioactive novel compounds of different nature like terpenoids, flavonoids, lignans, phenols, steroids, alkaloids, iridoids, etc. Among them, terpenoids (Symplocosides A-C, ursolic acid, corosolic acid, etc), flavonoids, lignans, phenols, alkaloids are potent bioactives. Despite many researches on the plants of this genus, a number of plants are yet chemically and pharmacologically unknown. Hence, a detailed study is required to understand the structure-activity relationship of these constituents. As the literature showed, many plants extracts have cytotoxic, diabetic, anti-HIV activities; hence, the particular

constituents responsible for the activities may be isolated for further process. In addition, some plant extracts were only screened for their preliminary *in vitro* activities, so the advanced clinical trial of them deserves to be investigated further. Herein, we described the possible applications in clinical research, but further investigations on phytochemical discovery and subsequent screening are needed for opening new opportunities to develop pharmaceuticals based on *Symplocos* constituents.

The properties of *S. paniculata* are same as of *S. recemosa*, but of the two species *S. paniculata* is better therapeutically (Ayurveda). In Ayurvedic literature, *Akshi bhashaja* (medicine for eye) term is used as synonym for lodhra. So far no research data is available on the role of *S. paniculata* in eye diseases. This area needs to be explored.

Lodhra should be used either in powder or decoction form. Alcoholic or aqueous extracts of lodhra kept for some time gets deteriorated and becomes physiologically inert. In all the diseases, in which this drug was tried under the auspices of the Indigenous Drugs Committee-the result was poor or negative as the drug was administered in liquid extract form. Hence, shelf-life studies are more important to evaluate its biological activity in all forms. Further study is needed to find out the various metabolic disorders that can be treated using isolated chemical constituents with demonstrated activities.

Pharmacognostical standards are available for other species of *Symplocos* but published data does not exist currently for *S. paniculata*. The microstructures will be recognized as a tool to measure the phylogenetic relationship to resolve the taxonomic controversies. The part of pharmacognostic review and phytochemical analysis will help to establish the botanical identity of this plant that could be made use of those who deal with the species and also in the quality assurance of this plant species. Some of the pharmacological and therapeutic activities are scientifically reported for this plant. These

investigations needs to be further studied for their meaningful extension in clinical usage. This review article will stimulate further research in the field of phytochemistry, pharmacology and also in the clinical application of phytochemical constituents of *Symplocos paniculata*.

### Conflict of interest statement

Author declares that there is no conflict of interest.

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