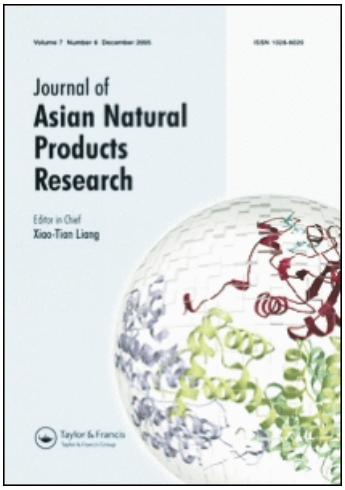


Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Chemical constituents and biological applications of the genus *Symplocos*

Ruchi Badoni[a]; Deepak K. Semwal[b]; Sudhir K. Kothiyal[a]; Usha Rawat[a]
[a] Department of Chemistry, H.N.B. Garhwal University, Srinagar, Uttarakhand, India [b] Department of Chemistry, Panjab University, Chandigarh, Punjab, India

Online publication date: 01 December 2010

To cite this Article Badoni, Ruchi , Semwal, Deepak K. , Kothiyal, Sudhir K. and Rawat, Usha(2010) 'Chemical constituents and biological applications of the genus *Symplocos*', Journal of Asian Natural Products Research, 12: 12, 1069 — 1080
To link to this Article: DOI: 10.1080/10286020.2010.532789
URL: http://dx.doi.org/10.1080/10286020.2010.532789

Journal of Asian Natural Products Research
Vol. 12, No. 12, December 2010, 1069–1080

Chemical constituents and biological applications of the genus *Symplocos*

Ruchi Badoni[a], Deepak K. Semwal[b]*, Sudhir K. Kothiyal[a] and Usha Rawat[a]

[a]*Department of Chemistry, H.N.B. Garhwal University, Srinagar 246174, Uttarakhand, India;*
[b]*Department of Chemistry, Panjab University, Sector-14, Chandigarh 160014, Punjab, India*

(*Received 9 May 2010; final version received 13 October 2010*)

The genus *Symplocos* has been reviewed for its chemical constituents and biological activities including traditional importance of some common species. The plants of this genus contain terpenoids, flavonoids, lignans, phenols, steroids, alkaloids, and iridoids. Terpenoids are the major constituents within the genus *Symplocos* and most of them exhibit antiproliferative effects. Some phenolic glycoside derivatives showed inhibitory activity against snake-venom phosphodiesterase I and human nucleotide pyrophosphatase phosphodiesterase I. The members of genus *Symplocos* are well known for their traditional uses in the treatment of various diseases like leprosy, gynecological disorders, ulcers, leucorrhea, menorrhagia, malaria, and tumefaction. The aim of the present paper is to review the comprehensive knowledge of the plants of this genus including the traditional uses, chemistry, and pharmacology.

Keywords: antitumor; snake venom; anti-HIV activity; triterpenoids; flavonoids

1. Introduction

Symplocaceae is a unigeneric family consisting of only one genus named *Symplocos*. The genus *Symplocos* consists of almost 300–500 species. These plants are distributed in tropical and subtropical Asia, Malaysia, and America [1]. A large number of plants of this genus have been traditionally used in the treatment of bacterial diseases [2], diarrhea, dysentery, eye disease, hemorrhagic gingivitis, menorrhagia, uterine disorders [3], bowel complaints, ulcers [4], malaria, tumefaction, enteritis, and snake bite [5]. Recently, the members of genus *Symplocos* have been gaining popularity due to their diverse biological activities, particularly for anti-HIV, antitumor, and phosphodiesterase inhibitory activities [6]. Previously, the work based on the chemistry and pharmacology of this genus has been reviewed [6,7]. In recent years, an extensive work in chemistry and pharmacology on the genus *Symplocos* has been recorded. Therefore, in the present review, the emphasis has been given to the recent progress in the chemical and biological investigations of the genus.

2. Objectives of the review

Symplocos is one of the most selected genera having potential medicinal values. The plants of this genus and their constituents have been found to be active against most dangerous lives threatening disorders such as AIDS and cancer. Therefore, the aim of this paper is to review the current advances in chemistry and pharmacology of the genus *Symplocos*. The

*Corresponding author. Email: dr_dks.1983@yahoo.co.in

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020.2010.532789
http://www.informaworld.com

structure–activity relationship has been given in many cases to understand the mechanism of any particular activity. Various traditional uses of some common species were also discussed. This database may provide the guidance for researchers and herbologists for further investigations in the field.

3. Traditional uses

The members of genus *Symplocos* are well known for their traditional medicinal values. These have been used as remedy for the treatment of various diseases including leprosy, gynecological disorders, ulcers, leucorrhea, menorrhagia, malaria, tumefaction, etc. *S. chinensis*, a toxic herb found in Guangxi Province, South China, has been used as a folk medicine for malaria, tumefaction, enteritis, nephritis, and snake bite [5]. *S. racemosa* was used to manage menstrual disorders; it provides firmness to spongy and bleeding gums; its decoction has also been used for the treatment of bowel complaints and ulcers [4]. In Ayurveda, the astringent bark of *S. racemosa* has been recommended as a potent medicine for the treatment of diarrhea, dysentery, eye diseases, gum bleeding as well as menorrhagia, and uterine disorders [8]. The bark is useful in the treatment of eye diseases, spongy gums, and bleeding. It has been used for the treatment of 'Kapha' disease of the blood, leprosy, dropsy, and liver complaints. It is widely used as an Ayurvedic remedy, mainly, for gynecological disorders and, is useful in the treatment of abortions and miscarriages and for ulcers of the vagina. Unani medicine uses it as an emmenagogue and aphrodisiac. It is a potent remedy for inflammation, cleaning of the uterus, leucorrhea, and menorrhagia [9]. The roots of *S. caudata* have been used as a remedy for icterus and arthritis in Chinese folk medicine, and the roots of this plant have been traditionally used to treat jaundice, dysentery, and profuse uterine bleeding by local citizens [10,11]. *S. cochinchnensis* is widely used in the treatment of various disorders like leprosy, tumors, diarrhea, dysentery, menorrhagia, inflammation, and uterine disorders [3]. *S. spicata* is the source of an Ayurvedic crude drug 'Lodhara' in Travancore, Cochin, South India [12], and on the basis of this property, the plant has been affirmed as an Indian folk medicine [13].

4. Chemical constituents of genus *Symplocos*

The plants of genus *Symplocos* contain a variety of constituents viz. terpenoids, flavonoids, lignans, phenols, steroids, alkaloids, iridoids, and many others. The plants and their chemical constituents are summarized in Table 1, whereas the chemical structures of various compounds are given in Figure 1.

5. Biological activities of genus *Symplocos*

5.1 *Antifibrinolytic activity*

Dhaon *et al.* [4] reported the antifibrinolytic activity from the ethanol extract of *S. racemosa* along with the isolation and characterization of two flavans, i.e. symposide and its glycoside, (–)-epiafzelechin.

5.2 *Bactericidal effects*

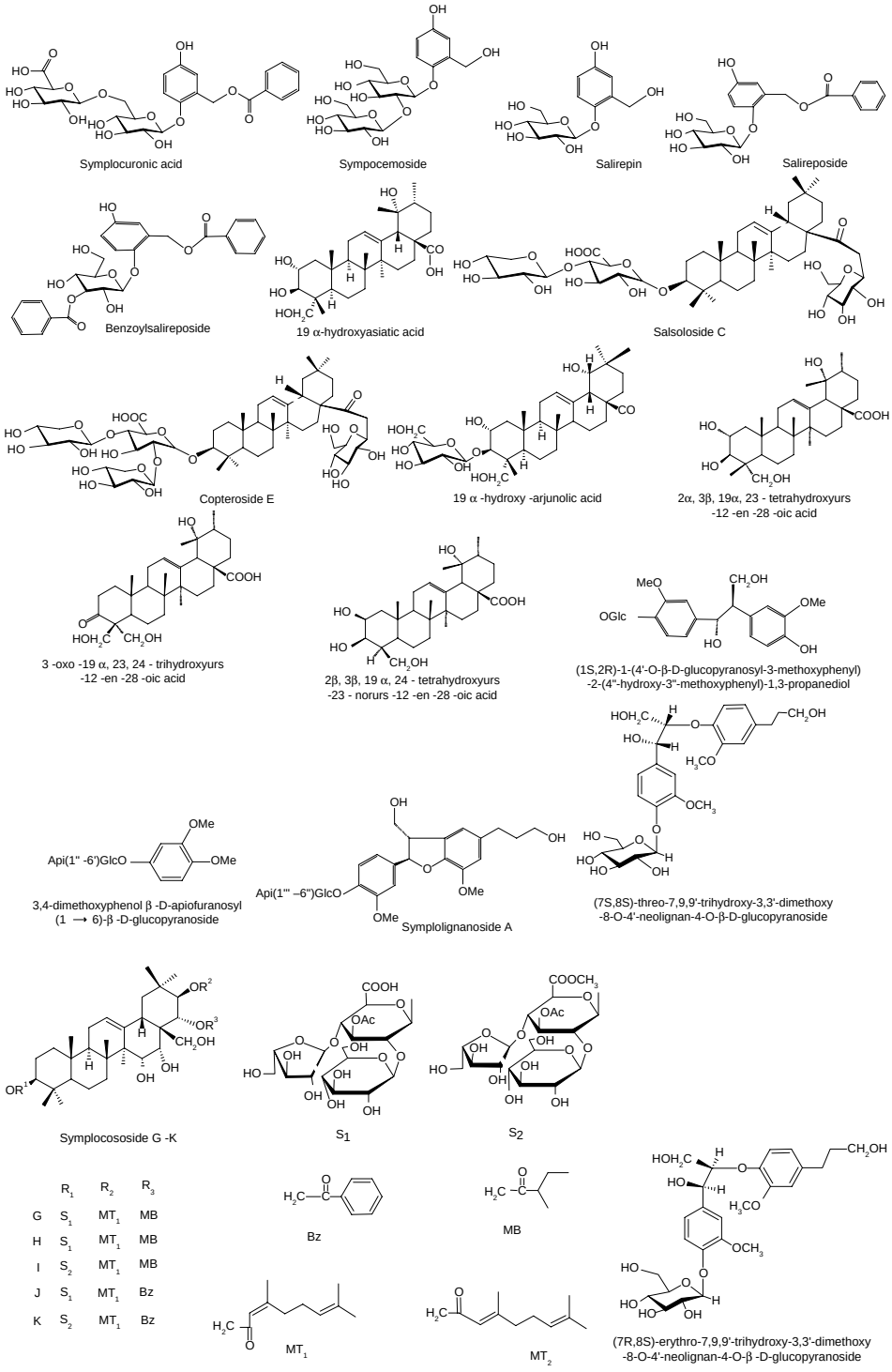
The methanol extracts of leaves, roots, and stem bark of *S. cochinensis* and their fractions obtained by partition (petroleum ether, CH_2Cl_2, and EtOAc) were screened for antimicrobial activity. The extracts and fractions showed a broad spectrum of antibacterial activity that was enhanced on fractionation [2]. The ethanol extract of *S. racemosa* bark showed antibacterial activities against *Propionibacterium acnes* and *Staphylococcus epidermidis* [14,15], and various other micro-organisms have also been inhibited by the extract [16].

Table 1. Chemical constituents of the genus *Symplocos*.

Plant's name	Constituents
S. caudata	(1*S*,2*R*)-1-(4′-*O*-β-D-glucopyranosyl-3′-methoxyphenyl)-2-(4″-hydroxy-3″-methoxy-phenyl)-1,3-propanediol, symplolignanoside A and 3,4-dimethoxyphenol β-D-apiofuranosyl (1 → 6)-β-D-glucopyranoside [49] (7*S*,8*S*)-*threo*-7,9,9′-trihydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-4-*O*-β-D-glucopyranoside, (7*R*,8*R*)-*threo*-7,9,9′-trihydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-4-*O*-β-D-glucopyranoside, (7*R*,8*S*)-*erythro*-7,9,9′-trihydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-4-*O*-β-D-glucopyranoside, (7*S*,8*R*)-*erythro*-7,9,9′-trihydroxy-3,3′-dimethoxy-8-*O*-4′-neolignan-4-*O*-β-D-glucopyranoside, 8*R*,8′*R*-matairesinol-4-*O*-β-D-xylopyranosyl-(1 → 2)-*O*-β-D-glucopyranoside, 1-*O*-(β-D-xylopyranosyl-(1 → 6)-*O*-β-D-glucopyranosyl)-2,6-dimethoxy-4-propenyl-phenol, matairesinoside and (*R*)-1-*O*-(β-D-glucopyranosyl)-2-(2-methoxy-4-(ω-hydroxypropyl)-phenoxyl)-propan-3-ol [50]
S. celastrinea	*N*-methyllaurelliptin, isoboldin, and 5-hydroxy-6-methoxynor-aporphine [51]
S. chinensis	Symplocososides A–F [7] Symplocososides G–K [52] Triterpenoids, 2β,3β,19α,24-tetrahydroxy-23-norurs-12-en-28-oic acid, 3-oxo-19α,23,24-trihydroxyurs-12-en-28-oic acid, 2α,3β,19α,23-tetrahydroxyurs-12-en-28-oic acid and 2α,3α,19α,23-tetrahydroxyurs-12-en-28-oic acid [5,53] Glucuronide triterpenoid saponins [54,55]
S. confusa	Dihydrochalcone glucoside: confusoside [56]
S. glauca	Verbenalin [57] 6-Dihydroverbenalin and verbenalin [58]
S. glomerata	Bidesmosidic 3-*O*-glucuronide oleanane triterpenoid saponins, salsoloside C and copteroside E, lignans, (−)-pinoresinol and (−)-pinoresinol-4′-*O*-β-D-glucopyranoside [29]
S. lancifolia	Ursolic acid, quercetin 3-*O*-β-D-glucopyranoside, quercetin 3-*O*-β-D-galactopyranoside, quercetin, kaempferol 3-*O*-β-D-glucopyranoside, kaempferol 3-*O*-α-L-rhamnoside, kaempferol 3-*O*-β-D-galactopyranoside, kaempferol, syringaresinol, 1,2-di-*O*-galloyl-β-D-glucopyranose, 4-hydroxy-3,5-dimethoxycinnamic acid and gallic acid [59] Phloridin [56]
S. lucida	Symplocosigenol [6] (−)-Pinoresinol β-D-glucoside [60]
S. microcalyx	Confusoside and trilobatin [61]

Table 1 – *continued*

Plant's name	Constituents
	Trilobatin [56]
S. paniculata	Ursolic acid, corosolic acid and 2α,3α,19α,23-tetrahydroxyurs-12-ene-28-oic acid [32] Flavonoids [62]
S. racemosa	Saponin glycosides, carbohydrate [25] 1-Ethyl brachiose-3′-acetate, ketochaulmoogric acid, nonaeicosanol, triacontyl palmitate, and methyl triacontanoate [39] Symplocuronic acid, sympocemoside, and salirepin [63] Harmine [64] Alkaloids [15] 28-Hydroxy-20α-urs-12,18(19)-dien-28-oic acid and 24-hydroxyolean-12-en-3-one [3] Phenolic glycoside benzoylsalireposide and salireposide [16] Dithiadiazetidin derivative, symploate [40] Symconosides A and B [65] Locoracemosides A–C [41] Symploracemoside and symplomoside [17] Symposide and (−)-epiafzelechin [4] 5,4′-Dihydroxy-7-methoxyflavan-3,4-diol 3-*O*-β-D-glucofuranoside and 5,7-dihydroxy-4′-methoxyflavan-3,4-diol 3-*O*-β-D-glucofuranoside [6] Oleanolic acid [66] Symplocomoside, symponoside, symplososide, and symploveroside [19]
S. spicata	3,28-*O*-bis-β-D-glucopyranosides of 19α-hydroxy-arjunolic acid and 19α-hydroxyasiatic acid [67] α-Spinasterol [27] Flavonol glycoside [68]
S. tinctoria	Sugars, polysaccharides and polyol [69]
S. uniflora	Flavanol glycoside (Symplocoside) 3′-*O*-methyl-(−)-epicatechin 7-*O*-β-glucoside [70]
S. vacciniifolia	Dihydrochalcone glucoside, vacciniifolin (2′,3,4,4′-tetrahydroxy-dihydrochalcone 4′-*O*-β-D-glucopyranoside), confusoside, trilobatin, and sieboldin [71]



	R_1	R_2	R_3
G	S_1	MT_1	MB
H	S_1	MT_1	MB
I	S_2	MT_1	MB
J	S_1	MT_1	Bz
K	S_2	MT_1	Bz

Figure 1. Structures of compounds isolated from the genus *Symplocos*.

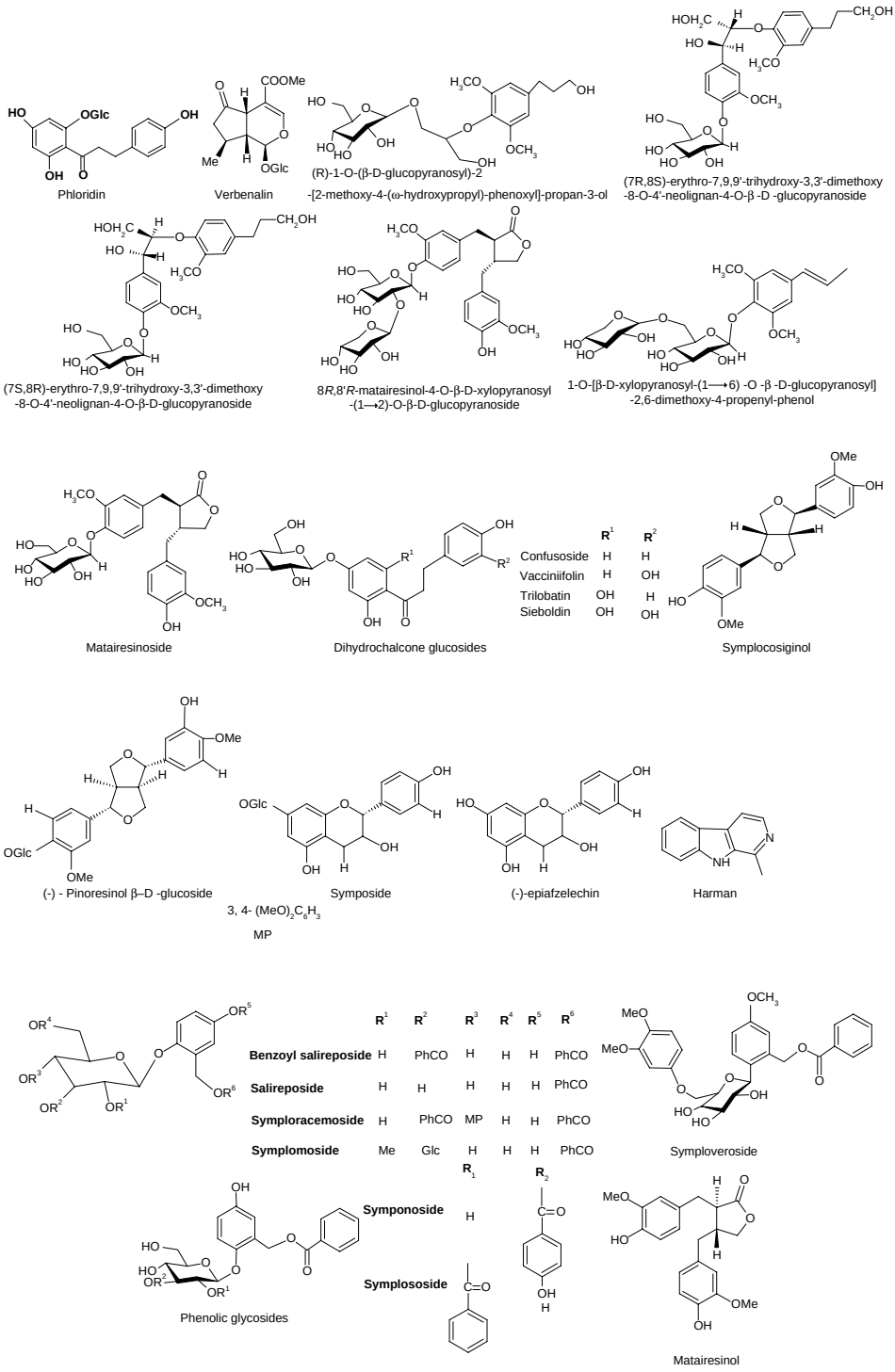


Figure 1. (*Continued*).

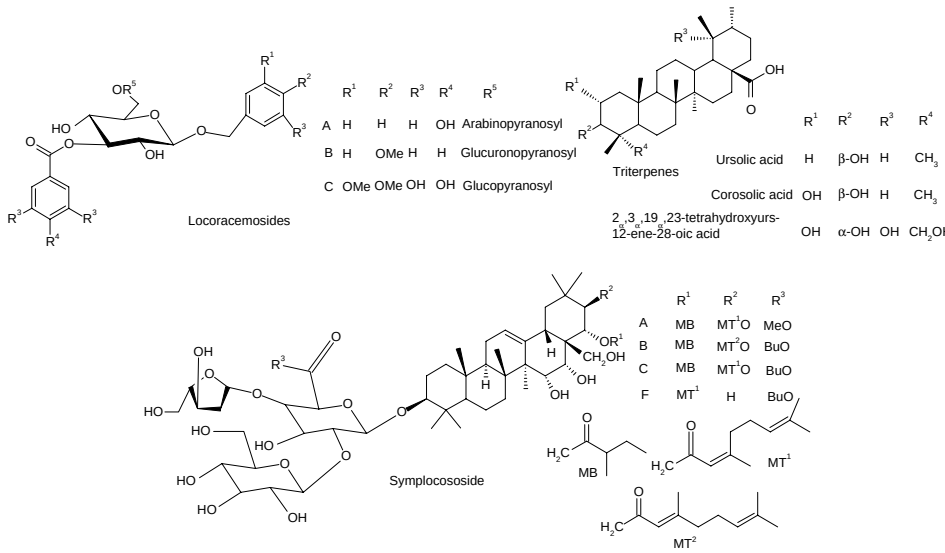


Figure 1. (*Continued*).

5.3 Phosphodiesterase inhibitory activity

Four phenolic glycosides, benzoyl salireposide, salireposide, symploracemoside, and symplomoside from *S. racemosa* were evaluated for their inhibitory activity against snake-venom phosphodiesterase I. Symploracemoside showed moderate inhibitory activity with an IC_{50} value of 590 μM, while symplomoside showed a weak activity with an IC_{50} value of 998 μM, as compared to the strong inhibitory potential of benzoyl salireposide (IC_{50}, 171 μM) and moderate inhibitory activity of salireposide (IC_{50}, 544 μM) [17,18]. Benzoyl salireposide and salireposide were also evaluated for their inhibitory activity against human nucleotide pyrophosphatase phosphodiesterase I. Benzoyl salireposide showed inhibitory activity with an IC_{50} value of 90 μM, whereas salireposide showed a weak activity with an IC_{50} value of 383 μM. These compounds are potential candidates for the therapy of arthritis [19]. Four glycosides, symplocomoside, symponoside, symplososide, and symploveroside isolated from *S. racemosa* displayed *in vitro* inhibitory activity against phosphodiesterase I with IC_{50} values of 122, 698, 722, and 909 μM, respectively [20].

5.4 Anti-HIV activities

The ethanolic extract from the stem bark of *S. setchuensis* showed significant HIV replication-inhibitory activity ($EC_{50} < 20$ mg/ml, $TI > 5$) in H9 lymphocyte cells. Subsequent bioassay-directed fraction of this extract identified matairesinol and harman as anti-HIV principles. The IC_{50} values of these two compounds were 21.9 and 111.5 μM, respectively. In terms of their EC_{50} values (2.0 and 10.7 μM, respectively), their TI values were 11.0 and 10.4, respectively [21].

5.5 Anticancerous activity

The extract of *S. chinensis* roots itself and an ursane triterpenoid, 2β,3β,19α,24-tetrahydroxy-23-norurs-12-en-28-oic acid, isolated from it exhibited significant cytotoxic activity against B16 and BGC-823 cells (IC_{50} values of 0.025 and 0.068 μM, respectively). The values of B16-BL6 (IC_{50}, 0.26 μM) and Ketr-3

(IC_{50}, 0.35 μM) also indicated relatively a weaker activity [5]. Six triterpenoid saponins, symplocososides A–F isolated from *S. chinensis*, were examined for antiproliferative activity against KB, HCT-8, A549, BGC-823, and HELF cells. Among them, symplocososide A exhibited activity against KB cells (IC_{50}, 1.72 mg/ml), HCT-8 cells (IC_{50}, 4.31 mg/ml), A549 cells (IC_{50}, 0.67 mg/ml), and HELF cells (IC_{50}, 4.62 mg/ml). Symplocososide C showed cytotoxic activity against HCT-8 cells (IC_{50}, 2.86 mg/ml) and BGC-823 cells (IC_{50}, 7.29 mg/ml), and symplocososide F was found to be cytotoxic against HCT-8 cells (IC_{50}, 4.04 mg/ml) [22]. The butanolic and ethyl acetate extracts of *S. racemosa* demonstrated a strong cytotoxic potential. Cell proliferation assay showed dose-dependent inhibition of cell growth. The butanolic extract was found to be cytotoxic against HL 60 (human leukemia cell line, IC_{50} 27,183 μg/ml), HeLa (human cervix cancer cell line, IC_{50} 22,861 μg/ml), whereas ethyl acetate extract was found to be less cytotoxic against HL 60 (IC_{50} 117,084 μg/ml) and HeLa (IC_{50}, 137,151 μg/ml) [23].

5.6 Central nervous system depressant activity

The aqueous extract of *S. racemosa* stem bark significantly reduced the spontaneous motor activity (central nervous system depressant activity) of the treated animals [24].

5.7 Anti-inflammatory activity

The ethanol extract of *S. racemosa* bark displayed significant anti-inflammatory activity [25]. α-Spinasterol isolated from *S. spicata* stem bark exhibited potent anti-inflammatory activity in carrageenin-induced acute paw edema in rats [26,27]. The methanol extract of *S. cochinchnensis* was studied for *in vitro* anti-inflammatory activity by human red blood cells (HRBC) membrane stabilization method and showed 67% protection of HRBC in hypotonic solution at a concentration of 1000 μg/ml [28].

5.8 Hemolytic activity

The mixture of nine bidesmosidic 3-*O*-glucuronide oleanane triterpenoid saponins isolated from *S. glomerata* stem bark showed hemolytic activity at a concentration of 370 μg/ml and caused 50% hemolysis of a 10% suspension of sheep erythrocytes [29].

5.9 Antioxidant activity

The methanol extract of *S. paniculata* was primarily assessed for potential to scavenge stable 1,1-diphenyl-2-picylhydrazyl (DPPH) free radicals. As a result, the extract was found to exhibit the DPPH free radical scavenging activity in the criteria of IC_{50} value of 23.0 μg/ml [30].

5.10 Antispasmodic activity

The effect of Neblon on the transit time of ingesta in the gut of albino rats indicated that *S. paniculata* reduced the transit time of ingesta through the gut significantly as observed by the pellet excretion and charcoal travel methods. With atropine sulfate, antispasmodic activity of the same degree was achieved by both the pellet inhibition and the charcoal travel methods [31].

5.11 Inhibitory activities against protein tyrosine phosphatase 1B (PTP1B)

Inhibition of protein tyrosine phosphatase 1B (PTP1B) has been proposed as a therapy for the treatment of type-2 diabetes and obesity. 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

2α,3α,19α,23-tetrahydroxyurs-12-en-28-oic acid which inhibited PTP1B with IC_{50} values of 3.8 ± 0.5, 7.2 ± 0.8, and 42.1 ± 1.5 μM, respectively [32].

5.12 Inhibitory activities against monoamine oxidases A and B

S. odoratissima was shown to have potent inhibitory activity against rat brain mitochondrial monoamine oxidases A and B [33].

5.13 Inhibitory activities against lipoxygenase and urease enzymes

Lipoxygenase constitutes a family of iron-containing enzymes that catalyze the dioxygenation of polysaturated fatty acids and lipids. In mammalian cells, these are key enzymes in the biosynthesis of a variety of bioregulatory compounds such as hydroxyeicosatetraenoic acids, leukotrienes, lipoxins, and hepoxylines [34]. It has been found that these lipoxygenase products play a role in a variety of disorders such as bronchial asthma, inflammation [35], and tumor angiogenesis [36], whereas urease is directly involved in the formation of infection stones and contributes to the pathogenesis of urolithiasis, pyelonephritis, ammonia and hepatic encephalopathy, hepatic coma, and urinary catheter encrustation [37,38]. Phytochemical investigation of *S. racemosa* resulted in the isolation of an ethyl-substituted glycoside, 1-ethyl brachiose-3′-acetate along with ketochaulmoogric acid, nonaeicosanol, tricontyl palmitate, and methyl triaconate. 1-Ethyl brachiose-3′-acetate and tricontyl palmitate displayed inhibitory potential against lipoxygenase and urease enzymes, respectively [39].

5.14 Inhibitory activity against α-glucosidase in a concentration-dependent fashion

The phytochemical investigation of the *n*-butanol-soluble fraction of *S. racemosa* resulted in the isolation of a dithiadiazetidin derivative, symploate which showed moderate inhibitory activity against α-glucosidase in a concentration-dependent fashion with an IC_{50} value of 691.1 ± 3.29 μM [40].

5.15 Inhibitory activity against α-chymotrypsin

Three benzylated glycosides, locoracemosides A, B, and C, isolated from *S. racemosa* stem bark displayed *in vitro* inhibitory activity against α-Chymotrypsin [41].

5.16 Antidiarrheal study

The extract of *S. racemosa* stem bark was shown to have potent induced diarrheal activity [24,42,43].

5.17 Hormonal disbalances in women

An aqueous extract of *S. racemosa* showed potential *in vivo* activity on serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels in immature female Sprague–Dawley rats under basal conditions. This plant has been used in Indian System of Medicine (ISM) for various female disorders. An aqueous extract on oral administration significantly stimulated the serum FSH level ($p < 0.016$) along with the rise in the serum LH level ($p < 0.001$). The histopathological studies revealed enhanced folliculogenesis, presence of mature follicles, and detached oocytes caused by increased FSH and LH levels. Furthermore, an increase in the ovary weight of treated animals was found due to observed FSH surge. These results are in concordance with the traditional use of the drug for female disorders [9,44].

5.18 Estrogenic activity of M2 tone

M2 tone contains extract of *Tinospora cordifolia*, *Saraca indica*, *S. racemosa*,

and *Asparagus racemosus* along with their ingredients. M2 tone in various doses inhibits normal uterine spontaneity. The most effective inhibiting dose was found to be 0.8 ml in a 20-ml bath [45,46].

5.19 Effect of Evecare in oligomenorrhea

The main ingredients of Evecare are *S. indica*, *S. racemosa*, *Aloe barbadensis*, *Cyperus rotundus*, and *T. cordifolia*. Twenty patients were treated with Evecare syrup at a dose of two tablespoonfuls twice daily for a period of 3 months, then followed up at regular 1-month intervals. Out of 20 patients, only four cases were conceived during the study period, which proved that Evecare was significant in curing infertility and scanty menstruation [47].

5.20 Acute metabolic and chronic toxicity study

The aqueous extract of stem bark *S. racemosa* was shown to have acute metabolic and chronic toxicity effects on food and water intake in Swiss Webster mice [48].

6. Future prospects and 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, leucorrhea, 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 (symplocososides A–C, ursolic acid, corosolic acid, etc.), flavonoids (symposide, epiafzelechin, etc.), lignans (matairesinol, etc.), phenols (benzoyl salireposide, salireposide, symploracemoside, etc.), alkaloids (Harman, etc.) 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.

Acknowledgement

The authors pay their sincere thanks to UGC New Delhi, India [Grant No. 33-282/2007(SR)], for financial assistance.

References

[1] R. Hegnauer, in *Chemotaxonomie der Pflanzen, Band VI*, edited by R. Hegnauer (Birkh Nuser Verlag, Basel, Stuttgart, 1973), p. 478.
[2] M.R. Khan, M. Kihara, and A.D. Omoloso, *Fitoterapia* **72**, 825 (2001).
[3] M. Ali, K.K. Bhutani, and T.N. Srivastava, *Phytochemistry* **29**, 3601 (1990).
[4] R. Dhaon, G.K. Jain, J.P.S. Sarin, and N.M. Khanna, *Indian J. Chem. B* **28**, 982 (1989).
[5] X.H. Li, D.D. Shen, N. Li, and S.S. Yu, *J. Asian Nat. Prod. Res.* **5**, 49 (2003).
[6] C.H. Huo, L.R. Shen, Y.Y. Zhao, and H. Liang, *Chem. Biodiver.* **4**, 1 (2007).
[7] M.J. Tang, J. Zhao, X.H. Li, and S.S. Yu, *China J. Chin. Mater. Med.* **29**, 390 (2004).

[8] G. Watt, *A Dictionary of the Economic Products of India* (Periodical Reports, Delhi, 1972), p. 398.
[9] K.K. Bhutani, N.J. Atul, and V. Kalia, *J. Ethnopharmacol.* **94**, 197 (2004).
[10] CCTHD, *Compendium of Chinese Traditional Herbal Drugs* (People's Health Press, Beijing, 1992), Vol. 2, p. 798.
[11] JCM, *A Dictionary of Traditional Chinese Medicines* (Jiangsu College of Medicine, Shanghai Science and Technology Press, Shanghai, 1977), p. 362.
[12] K.N. Aiyar, A.N. Namboodiri, and M. Kolammal, *Pharmacognosy of Ayurvedic drugs (Kerala)* (The Central Research Institute, University of Travancore, Trivandrum, 1975), p. 68.
[13] CSIR, *The Wealth of India, Raw Materials* (Council of Scientific and Industrial Research, New Delhi, 1976), Vol. 10, p. 89.
[14] G.S. Kumar, K.N. Jayaveera, C.K. Kumar, S.B.M. Vrushabendra, U.P. Sanjay, and K.D.V. Kishore, *Pharmacologyonline* **2**, 34 (2007).
[15] V.P. Devmurari, *Int. J. PharmTech. Res.* **2**, 1359 (2010).
[16] G.S. Kumar, U.P. Sanjay, S. Vrushabendra, B.M.R. Dhanapal, A.C.K. Kumar, and K.N. Jayveera, *Asian J. Chem.* **19**, 3537 (2007).
[17] V.U. Ahmad, M.A. Abbasi, H. Hussain, M.N. Akhtar, U. Farooq, N. Fatima, and M.I. Choudhary, *Phytochemistry* **63**, 217 (2003).
[18] V.U. Ahmad, M.A. Abbasi, M. Zubair, N. Fatima, U. Farooq, and M.I. Choudhary, *Helv. Chim. Acta* **87**, 67 (2004).
[19] M.I. Choudhary, N. Fatima, M.A. Abbasi, S. Jalil, V.U. Ahmad, and A. Rahman, *Bioorg. Med. Chem.* **12**, 5793 (2004).
[20] M.A. Abbasi, V.U. Ahmad, M. Zubair, N. Fatima, U. Farooq, S. Hussain, M.A. Lodhi, and M.I. Choudhary, *Planta Med.* **70**, 1189 (2004).
[21] J. Ishida, H.K. Wang, M. Oyama, M.L. Consentino, C.Q. Hu, and K.H. Lee, *J. Nat. Prod.* **64**, 958 (2001).
[22] M.J. Tang, D. Shen, Y.C. Hu, S. Gao, and S.S. Yu, *J. Nat. Prod.* **67**, 1969 (2004).
[23] R.P. Bhuvan, P.D. Jignesh, P.A. Bhavik, and G.L. Ashok, *Rom. J. Biol. Plant Biol.* **54**, 135 (2009).
[24] M.S. Shahrair, M.T.H. Khan, M.A. Gafur, and M.S.K. Chaudhari, *Hamdard Med.* **43**, 8 (2000).
[25] S. Kambhoja and M.K.R. Keshava, *Iran J. Pharm. Res.* **3**, 44 (2004).
[26] M.H. Frotan, S.B. Acharya, R. Froton, N.K.R. Pathak, and M. Biswas, *Indian J. Pharmacol.* **15**, 197 (1983).
[27] N.K.R. Pathak, M. Biswas, P. Neogi, M.H. Frotan, and S.B. Acharya, *J. Res. Ayurveda Siddha* **7**, 146 (1986).
[28] V. Rajendran and K.S. Lakshmi, *Bangladesh J. Pharmacol.* **3**, 121 (2008).
[29] P. Waffo-Teguo, L. Voutquenne, O. Thoison, V. Dumontet, V.H. Nguyen, and C. Lavaud, *Phytochemistry* **65**, 741 (2004).
[30] Y. Kim, H.Y. Min, E.J. Park, and S.K. Lee, *Nat. Prod. Sci.* **9**, 80 (2003).
[31] D.N. Srivastava and K.R. Bhatt, *Indian J. Indigen. Med.* **10**, 23 (1993).
[32] M.K. Na, S. Yang, L. He, H. Oh, B.S. Kim, W.K. Oh, B.Y. Kim, and J.H. Ahn, *Planta Med.* **72**, 261 (2006).
[33] H. Haraguchi, T. Sakai, and A. Yagi, *Nat. Med.* **57**, 196 (2003).
[34] W.E.M. Lands, *Adv. Drug. Res.* **14**, 147 (1985).
[35] D. Steinhilber, *Curr. Med. Chem.* **6**, 71 (1999).
[36] D. Nie and K.V. Honn, *Cell Mol. Life Sci.* **59**, 799 (2002).
[37] H.L.T. Mobley and R.P. Hausinger, *Microbiol. Mol. Biol. Rev.* **53**, 85 (1989).
[38] H.L.T. Mobley, M.D. Island, and R.P. Hausinger, *Microbiol. Mol. Biol. Rev.* **59**, 451 (1995).
[39] M.A. Abbasi, V.U. Ahmad, M. Zubair, S.A. Nawaz, M.A. Lodhi, U. Farooq, and M.I. Choudhary, *Nat. Prod. Res.* **19**, 509 (2005).
[40] M.A. Abbasi, V.U. Ahmad, M. Zubair, M.A. Rashid, S.N. Khan, U. Farooq, M.I. Choudhary, and K. Zeller, *Heterocycles* **65**, 1837 (2005).
[41] M.A. Rashid, V.U. Ahmad, M.A. Abbasi, Z. Ali, N. Rasool, M. Zubair, M.A. Lodhi, M.I. Choudhary, and I.A. Khan, *Phytochem. Lett.* **1**, 54 (2008).
[42] K.R. Kohli, S. Gharge, and S. Naik, *Indian J. Int. Med.* **3**, 199 (1993).
[43] K.P. Singh and G.N. Chaturvedi, *Nagarjun* **25**, 130 (1982).
[44] V. Singh, S.S. Abbas, and N. Singh, *Second World Congress on Biotechnological Development of Herbal Medicine*, February 20–22 (NRBI, Lucknow, 2003), p. 147.
[45] S.N. Joglekar, S.D. Nabar, and S.S. Hegde, *Indian Pract.* **37**, 847 (1984).
[46] S.N. Joglekar and S.S. Hegde, *Curr. Med. Pract.* **26**, 108 (1982).
[47] S. Venugopal, *Antiseptic* **95**, 329 (1998).

[48] M. Shahriar, M.S.K. Choudhuri, M. Alamgir, J.M.F. Rahman, and S. Rahman, *Hamdard Med.* **42**, 62 (1999).
[49] J.S. Jiang, Z.M. Feng, Y.H. Wang, and P.C. Zhang, *Chem. Pharm. Bull.* **53**, 110 (2005).
[50] C.H. Huo, H. Liang, Y.Y. Zhao, B. Wang, and Q.Y. Zhang, *Phytochemistry* **69**, 788 (2008).
[51] R. Tschesche, P. Welzel, R. Moll, and G. Legler, *Tetrahedron* **20**, 1435 (1964).
[52] G.M. Fu, Y.H. Wang, S. Gao, M.J. Tang, and S.S. Yu, *Planta Med.* **71**, 666 (2005).
[53] G. Fu, Y. Liu, S. Yu, X. Huang, Y. Hu, X. Chen, and F. Zhang, *J. Nat. Prod.* **69**, 1680 (2006).
[54] B. Li, Z. Abliz, M.J. Tang, G. Fu, and S.S. Yu, *J. Chromatogr. A* **1101**, 53 (2006).
[55] B. Li, Z. Abliz, G. Fu, M.J. Tang, and S.S. Yu, *Rapid Commun. Mass Spectrom.* **19**, 381 (2005).
[56] T. Tanaka, K. Kawamura, H. Kohda, and O. Tanaka, *Chem. Pharm. Bull.* **30**, 2421 (1982).
[57] T. Tanaka, K. Yamasaki, H. Kohda, O. Tanaka, and S.B. Mahato, *Planta Med* Suppl. 81 (1980).
[58] I. Junko, H. Merimasa, M. Takeshi, O. Masami, I. Kenichiro, and F. Tetsuro, *J. Chromatogr.* **515**, 503 (1990).
[59] L.C. Lin, W.J. Tsai, and C.J. Chou, *Chin. Pharm. J.* **48**, 441 (1996).
[60] I. Hiroyuki, T. Yoshio, and N. Hiroshi, *Yakugaku Zasshi* **93**, 44 (1973).
[61] H. Miura, Y. Kitamura, and M. Sugii, *Shoyakugaku Zasshi* **39**, 312 (1985).
[62] P.C. Dandiya, Y.M. Chopra, and S.P. Banerjee, *Indian J. Pharm.* **28**, 344 (1966).
[63] V.U. Ahmad, M.A. Rashid, M.A. Abbasi, N. Rasool, and M. Zubair, *J. Asian Nat. Prod. Res.* **9**, 209 (2007).
[64] G.S. Kumar, S.B.M. Vrushabendra, V.L. Ashoka Babu, S. Chandaman, R.T. Srinivasa, and K. Tarakaram, *Asian J. Chem.* **18**, 2851 (2006).
[65] V.U. Ahmad, M. Zubair, M.A. Abbasi, F. Kousar, F. Ullah, N. Fatima, and M.I. Choudhary, *Z. Naturforsch B* **60**, 1101 (2005).
[66] L.B. Desilva, U.L.L. Desilva, and M. Mahendran, *J. Nat. Sci. Council. Sri Lanka* **7**, 1 (1979).
[67] R. Hinguchi, T. Kawaski, M. Biswas, and V.B. Pandey, *Phytochemistry* **21**, 907 (1982).
[68] R.D. Tiwari and H.L. Tripathi, *Phytochemistry* **15**, 833 (1976).
[69] R.A. Hussain, Y.M. Lin, L.J. Poveda, E. Bordas, B.S. Chung, J.M. Pezzuto, D.D. Soejarto, and A.D. Kinghorn, *J. Ethnopharmacol.* **28**, 103 (1990).
[70] R. Tschesche, T.M. Braun, and W.V. Sassen, *Phytochemistry* **19**, 1825 (1980).
[71] T.J. Ling, L.D. Lin, W.U. Ping, W.H. Zhou, H.G. Ye, M.F. Liu, and X.Y. Wei, *Chin. Chem. Lett.* **15**, 1182 (2004).