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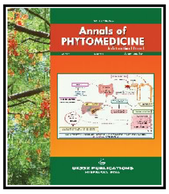

Review Article : Open Access

Systematic review on phytochemical profile and pharmacology of a mangrove shrub, *Scyphiphora hydrophyllacea* C.F. Gaertn.

K. Rama Devi*, G. Shravani, S. Pavani**, S. Nikhitha** and S.V.V.N.S.M. Lakshmi**◆**
**Department of Pharmaceutics, Raghu College of Pharmacy, Visakhapatnam-531162, Andhra Pradesh, India*
***Department of Pharmacognosy, Vishnu Institute of Pharmaceutical Education & Research, Narsapur-520313, Medak Dist, Telangana, India*

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Abstract

Chengham (Scyphiphora hydrophyllacea C.F. Gaertn., Rubiaceae) is a mangrove shrub commonly found in landward mangrove zones, having potential biological activities. Different parts of *S. hydrophyllacea* have components with biological and pharmaceutical properties. Comprehensive information regarding this mangrove plant was collected from various electronic databases such as PubMed, PubMed Central, SciFinder, Google Scholar, J-gate, Library Search, Science Direct, Elsevier, Semantic Scholar, ResearchGate. The isolated compounds and the extracts of the shrub were studied for pharmacological properties such as antitumor, antioxidant, and antidiabetic properties. This plant contains 11 types of secondary metabolites like iridoids, iridoid glucosides, noriridoids, triterpenes, steroids, coumarins, lignans, coumarino lignoids, flavonoids, fatty acid esters and a few miscellaneous compounds. The plant's morphological characteristics and phytochemical and pharmacological actions were highlighted in this article, which can be used as a resource for pharmaceutical research.

1. Introduction

For thousands of years, plants have had a very significant role in maintaining human health and improving the quality of human life and have served humans as precious components of medicines, beverages, cosmetics, and drugs (Ramakrishna *et al.,* 2023). Traditional medicinal methods are becoming an essential component of complementary medicine since they are readily available locally, may be easily used in simple medicinal preparations, and are less expensive than standard medicinal plants (Mehrotra, 2021). The phytoconstituents found in the plants are the primary determinant of all these treatments. These ideas compelled the discovery of modern medicines in the early 19th century, when the specific chemicals found in plants were shown to have therapeutic value. The evaluation of novel drugs that includes exploitation of phytochemicals has altogether opened new doors for widespread research and further assists in smoother transition from traditional medicine to contemporary medicine in India (Sandip *et al.,* 2021).

Indian mangroves consist of 46 true mangrove species belonging to 14 families and 22 genera, which include 42 species and 4 natural hybrids. In other words, India is home to around 57% of the world's mangrove species (Ragavan *et al.*, 2016). *S. hydrophyllacea* is one of the shrub evergreen mangrove plants belonging to Scyphiphora genus in the family Rubiaceae. It is a monotypic genus that spans southern India, Ceylon, Indochina, Hainan, the Philippines, the Malay Archipelago, tropical Australia, New Caledonia, and further north, the Solomon Islands, and Palau (Chen *et al.*, 2020). In India, it grows along the estuarine zones of the Coastal Andhra Pradesh (Venkanna and Rao, 1990). Round, glossy leaves, fringed stipules, tiny white flowers, and eight-ribbed drupe like fruits are some of its defining features. Noticeably, it is covered with a resinous material on its terminal nodes and shoots. This species is frequently found in pockets of dispersed, isolated shrubs throughout the high intertidal zones of the midestuarine reaches, where it is recognized as a minor component of the mangrove environment (Zhang *et al.*, 2019). Larger pieces of *S. hydrophyllcea* wood are used to make household items such as spoons, while smaller pieces are used to make fence posts and firewood (Basyuni *et al.*, 2021). The ethnomedicines obtained from the medicinal plants are thought to be safer, and they have been shown to be effective in treating a variety of ailments (Maroti *et al.*, 2022). The ethnobotanical use that has been reported was the use of an extract of the leaves for stomachache (Basyuni *et al.*, 2021; Lalitha *et al.*, 2019). Polyprenols and dolichols were found in higher content in the yellow leaves of this plant (Basyuni *et al.*, 2021). In conventional medical systems, about 90% of prescriptions were based on medications made from plants (Santhosha and Ramesh, 2022). Local ethnics utilize this plant as a source of malarial medicine in Indonesia (Nasir *et al.,* 2021). The plant yields good fiber. Local people use the species for fuel purposes along with other mangroves (Venkanna and Rao, 1990).

2. Materials and Methods

A comprehensive literature search was done on the plant *S. hydrophyllacea* to collect all significant information about its morphology, chloroplast genome, secondary metabolites and pharmacological activities. PubMed, PubMed Central, SciFinder, Google Scholar, J-gate, Library Search, Science Direct, Elsevier, Semantic Scholar, ResearchGate were searched from 1990 to 2023.

Corresponding author: Dr. SVVNSM Lakshmi
Professor, Vishnu Institute of Pharmaceutical Education & Research, Narsapur-502313, Telangana, India
E-mail: lakshmi.svvnsm@viper.ac.in
Tel.: +91-8099940666

Email: ukaaz@yahoo.com; Website: www.ukaazpublications.com

The details were taken from the gathered information. The plant was verified using The Plant List (www.theplantlist.org). Chemical structures were drawn using ChemDraw 10.0 software.

3. Morphology

The shrub has a short trunk, 10-15 cm in diameter, branching from the base. Branchlets are thick and bulging at the nodes. Young branches frequently have a reddish color and have internodes that are 2-5 cm long. Leaves are 5-8 × 2.5-3.5 cm, coriaceous, lustrous, obovate-oblanceolate, whole, rounded at apex, cuneate at base, midrib prominent, veinlets inconspicuous with gummy young leaves. Stipules are small, wide, and membranous, and the petiole is 1.5 cm long. Roots are devoid of pneumatophores.

Axillary inflorescence with dense compound dichasial cymes that are shortly pedunculate.

Flowers are small and purplish white. They are bisexual, tetramerous, epigynous, ebracteate, ebracteolate, subsessile, 1-1.5 cm. The calyx is joined, and is a cylindrical tube, 3 mm long, neck dilated with simple unicellular hairs. The corolla has four lobes that are oval, recurved, and twisted in the bud. Stamens are epipetalous, positioned at corolla tube throat, filaments short, anthers 2.5 × 0.5 mm, basifixed, longitudinally dehiscent. Pollen grains are prolate-spheroidal, tricolporate, and psilate in nature. Ovary disc is annual, lobed, inferior, 0.5 cm long, bicarpellary, syncarpous, bilocular, with two ovules in each lobule on axile placentation; style is slender 4 mm long, filiform, and exerted from the corolla tube; stigma bifid, linear, recurved, and obtuse at the apex.

Fruit is drupaceous, subcylindrical, 1-1.5 × 0.5-0.6 cm, yellowish green when young, dark brown when ripe, crowned by persistent calyx, 8-10 grooved and winged, with 2 crustaceous, connate 4-5 ribbed pyrenes (Venkanna *et al*., 1990).

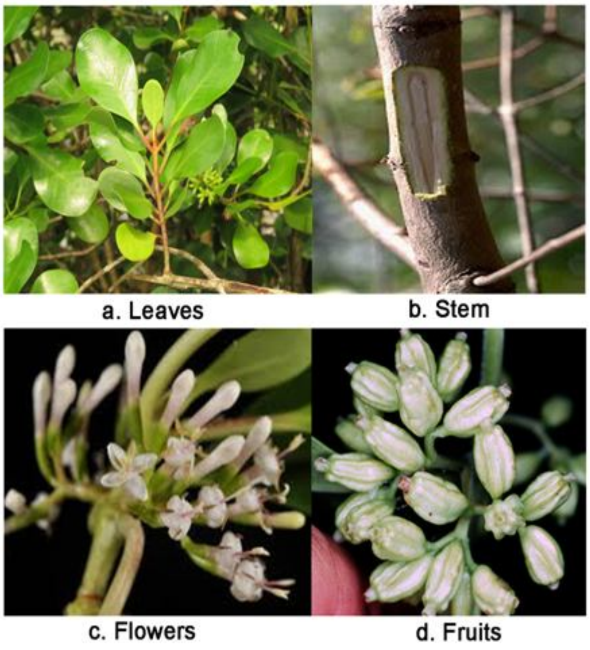

a. Leaves
b. Stem
c. Flowers
d. Fruits

Figure 1: Morphology of *S. hydrophyllacea*.

4. Chloroplast genome

The *S. hydrophyllaceae* chloroplast genome was found to be a circular molecule with a total size of 155,132 bp and a quadripartite structure. With 132 genes total, the entire chloroplast genome has a guanine-cyosine (GC) content of 37.60%. Of these, numbers88 and 36, are transfer RNA and protein-coding genes respectively. Four ribosomal RNA genes are also present. The chloroplast genome of *S. hydrophyllacea* had 52 microsatellites in total. Microsatellite marker identification revealed that the simplest sequence repeats in chloroplast genomes are A/T mononucleotides. These chloroplast genome analyses identified matK, rps16, and atpF as variable areas (Zhang *et al*., 2019).

5. Phytochemistry

From the three decades, extensive research is going on the plant S. *hydrophyllacea* for its active constituents. The phytochemical profile was given in Figure 2. The plant has a variety of compounds like iridoids shown in Figure 3, iridoid glucosides in Figure 4, noriridoids in Figure 5, triterpenes in Figure 6, steroids in Figure 7, flavonoids in Figure 8, coumarins in Figure 9, lignans in Figure 10, coumarino lignoids in Figure 11, fatty acid esters in Figure 12 and few miscellaneous compounds were shown in Figure 13. The structures were elucidated by spectral and chemical means like nuclear magnetic resonance (NMR), mass, infrared (IR), biosynthetic studies, degradation studies, supported by high-resolution mass spectrometry (HRMS) and optical rotation data. These were isolated and identified from various parts of the plants like bark, whole plant, leaves, stems, and aerial parts. Compounds isolated from the plant are broadly studied for different pharmacological activities and few of them were considered as therapeutically useful compounds. A total of 72 compounds were isolated from the plant. The details regarding phytochemistry were given in Table 1.

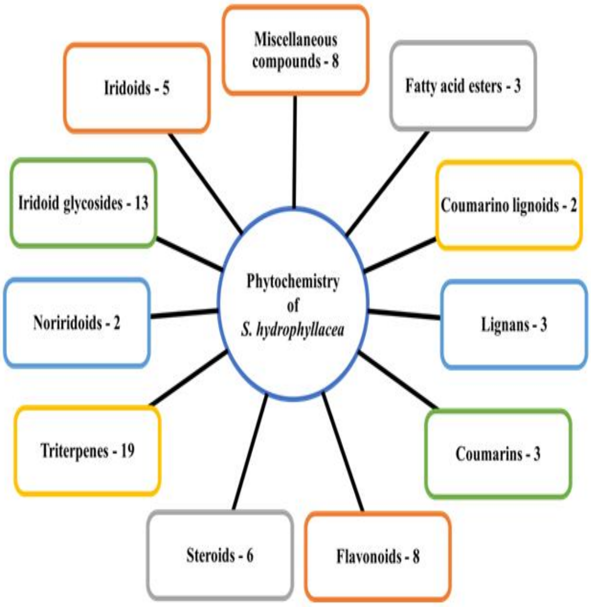


Figure 2: Phytochemistry of *S. hydrophyllacea*.

Table 1: List of chemical compounds of *S. hydrophyllacea*

Sl. No.	Compounds	Parts used	Type of extract	References
	Iridoids			
1	Scyphiphin A1	Aerial parts	Ethanol	Zeng *et al.*, 2007
2	Scyphiphin A2	Aerial parts	Ethanol	Zeng *et al.*, 2007
3	Scyphiphin B1	Aerial parts	Ethanol	Zeng *et al.*, 2007
4	Scyphiphin B2	Aerial parts	Ethanol	Zeng *et al.*, 2007
5	Scyphiphin C	Aerial parts	Ethanol	Feng *et al.*, 2010
	Iridoid glycosides			
6	Scyphiphorin A	Stem bark	Ethanol	Tao *et al.*, 2007
7	Scyphiphorin B	Stem bark	Ethanol	Tao *et al.*, 2007
8	Scyphiphorin C	Stem bark	Ethanol	Hong *et al.*, 2009
9	Scyphiphorin D	Stem bark	Ethanol	Hong *et al.*, 2009
10	10-O-acetylgeniposidic acid	Stem bark	Ethanol	Tao *et al.*, 2009
11	7-Deoxy-8-epiloganic acid	Stem bark	Ethanol	Tao *et al.*, 2009
12	Mussaenoside	Stem bark	Ethanol	Tao *et al.*, 2009
13	7-Deoxygardoside	Stem bark	Ethanol	Tao *et al.*, 2009
14	10-Deoxygeniposidic acid	Stem bark	Ethanol	Tao *et al.*, 2009
15	Shanzhiside methyl ester	Aerial parts	Ethanol	Feng *et al.*, 2010
16	Scyphiphin D	Aerial parts	Ethanol	Zeng *et al.*, 2010
17	Geniposidic acid	Stem bark	Ethanol	Tao *et al.*, 2007
		Aerial parts	Ethanol	Zeng *et al.*, 2010
18	Scyphiphoroid	Stem bark	Aqueous fraction of juice	Paulin *et al.*, 2020
	Noriridoids			
19	Hydrophylin A	Aerial parts	Ethanol	Zeng *et al.*, 2008
20	Hydrophylin B	Aerial parts	Ethanol	Zeng *et al.*, 2008
	Triterpenes			
21	Oleanolic acid	Leaves	Hexane and chloroform	Samarakoon *et al.*, 2018
		Stem bark	Ethanol	Tao *et al.*, 2007
		Aerial parts	Ethanol	Dai *et al.*, 2006
22	Ursolic acid	Leaves	Hexane and chloroform	Samarakoon *et al.*, 2018
		Aerial parts	Ethanol	Dai *et al.*, 2006
		N/A	N/A	Tao *et al.*, 2007
23	Eichlerianic acid	Leaves	Hexane and chloroform	Samarakoon *et al.*, 2018
24	Hopenone-1	Leaves	Hexane	Samarakoon *et al.*, 2016
25	Betulone	Whole plant	Ethanol	Zeng *et al.*, 2007
26	α-Amyrin	Whole plant	Ethanol	Zeng *et al.*, 2007
27	β-Amyrin	Whole plant	Ethanol	Zeng *et al.*, 2007
28	Pomonic acid	Stems and leaves	Ethanol	Yu, 2019
29	Euscaphic acid	Stems and leaves	Ethanol	Yu, 2019
30	Dammaradienyl acetate	Stems and leaves	Ethanol	Yu, 2019
31	Erythrodiol	Stems and leaves	Ethanol	Yu, 2019

32	Lup-20(29)-en-3-yl acetate	Stems and leaves	Ethanol	Yu, 2019
33	30 Oxolupeol	Stems and leaves	Ethanol	Yu, 2019
34	Maslinic acid	Stems and leaves	Ethanol	Yu, 2019
35	23-hydroxyursolic acid	Stems and leaves	Ethanol	Yu, 2019
36	β-amyrone	Stems and leaves	Ethanol	Yu, *2019*
37	Betulin	N/A	N/A	Tao *et al.*, 2007
38	Betulinic acid	N/A	N/A	Tao *et al.*, 2007
39	Friedelin	N/A	N/A	Tao *et al.*, 2009
	Steroids			
40	Beta sitosterol	Whole plant	Ethanol	Zeng *et al.*, 2007
41	Stigmasterol	Whole plant	Ethanol	Zeng *et al.*, 2007
42	Stigmasterol 3-O-β-D-glucoside	Stem bark	Ethanol	Tao *et al.*, 2007
43	Daucosterol	Aerial parts	Ethanol	Dai *et al.*, 2006
44	Cholesterol	N/A	N/A	Tao *et al.*, 2007
45	Stigmast-4-en-6β-ol-3-one	N/A	N/A	Tao *et al.*, 2007
	N/A	Petroleum ether	Tao *et al.*, 2009	
	Flavonoids			
46	Acacetin	Stems and leaves	Ethanol	Yu, 2019
47	Chrysoeriol	Stems and leaves	Ethanol	Yu, 2019
48	Jaceosidin	Stems and leaves	Ethanol	Yu, 2019
49	Kumatakenin	Stems and leaves	Ethanol	Yu, 2019
50	Isosakuranetin	Stems and leaves	Ethanol	Yu, 2019
51	Taxifolin	Stems and leaves	Ethanol	Yu, 2019
52	5,7,42 -Trihydroxy-32 -methoxy flavone	Aerial parts	Ethanol	Dai *et al.*, 2006
53	5,7-Dihydroxy-3,32,42-trimethoxy flavone	Aerial parts	Ethanol	Dai *et al.*, 2006
	Coumarins		Ethanol	Dai *et al.*, 2006
54	Scopoletin	Aerial parts	Ethanol	Dai *et al.*, 2006
		N/A	N/A	Tao *et al.*, 2007
55	Isoscopoletin	N/A	N/A	Tao *et al.*, 2009
56	Fraxetin	N/A	N/A	Tao *et al.*, 2009
	Lignans			
57	Lyoniresinol	Stems and leaves	Ethanol	Yu, 2019
58	Medioresinol	Stems and leaves	Ethanol	Yu, 2019
59	Balanophonin	Stems and leaves	Ethanol	Yu, 2019
	coumarino lignoid			
60	Cleomiscosin A	N/A	N/A	Tao *et al.*, 2007
61	Cleomiscosin B	N/A	N/A	Tao *et al.*, 2007
	Fatty acid esters			
62	Hexadecanoic acid methyl ester	N/A	Petroleum ether	Tao *et al.*, 2009
63	9-Octadecenoic acid methyl ester	N/A	Petroleum ether	Tao *et al.*, 2009
64	9,12-Octadienoic acid methyl ester	N/A	Petroleum ether	Tao *et al.*, 2009

	Sesquiterpene			
65	Cryptomeridiol	N/A	N/A	Tao *et al.*, 2007
	Misslaneous compounds			
66	4-(4-hydroxy-3-methoxybenzyl) butan-2-one	Stem bark	Ethanol	Tao *et al.*, 2007
67	3,4,5-Trimethoxyphenol-B-D-glucopyranoside	Whole plant	Ethanol	Zeng *et al.*, 2007
68	3,3,4'-Trimethoxy-ellagic acid	N/A	N/A	Tao *et al.*, 2007
69	Syringic acid	N/A	N/A	Tao *et al.*, 2009
70	1,2-Benzene-dicarboxylic acid (2-ethylhexyl) ester	N/A	Petroleum ether	Tao *et al.*, 2009
71	Casuarinondiol	N/A	N/A	Tao *et al.*, 2009
72	Guaiacylglycerol-â -ferulic acid ether	N/A	N/A	Tao *et al.*, 2009

N/A: Not available

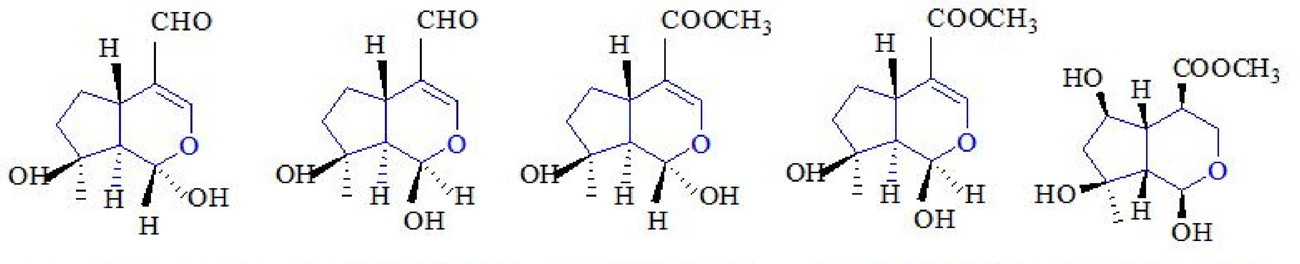
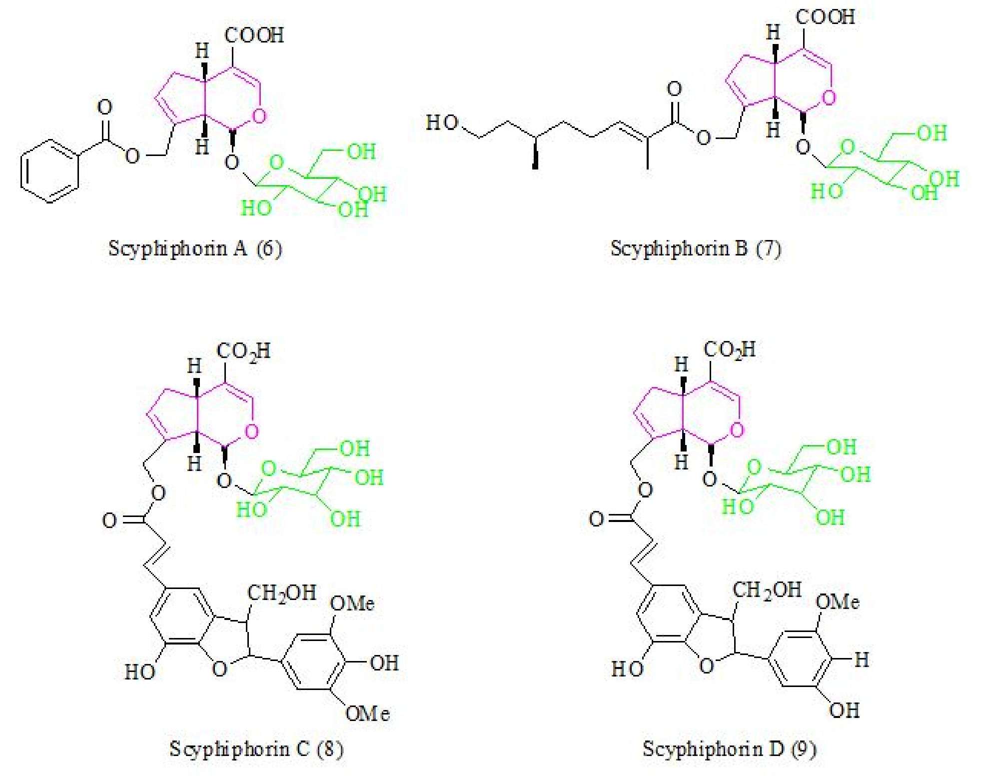

Scyphiphin A1 (1) Scyphiphin A2 (2) Scyphiphin B1 (3) Scyphiphin B2 (4) Scyphiphin C (5)

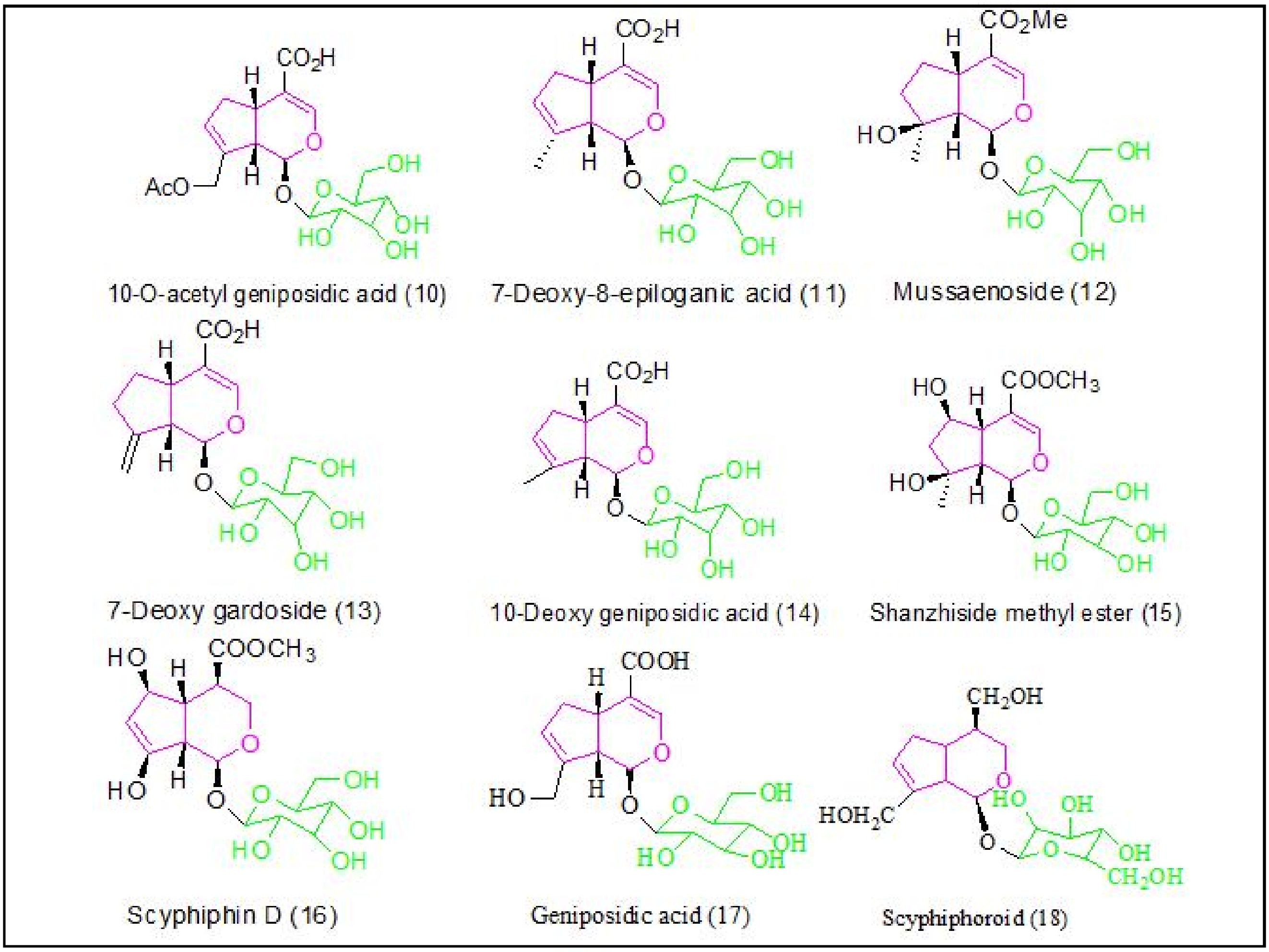
Figure 3: Chemical structures of iridoids (1-5) isolated from the plant *S. hydrophyllacea*.


Scyphiphorin A (6)

Scyphiphorin B (7)

Scyphiphorin C (8)

Scyphiphorin D (9)



10-O-acetyl geniposidic acid (10)

7-Deoxy-8-epiloganic acid (11)

Mussaenoside (12)

7-Deoxy gardoside (13)

10-Deoxy geniposidic acid (14)

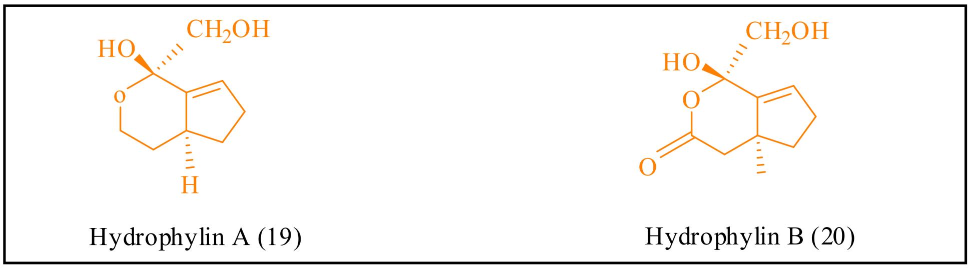
Shanzhiside methyl ester (15)

Scyphiphin D (16)

Geniposidic acid (17)

Scyphiphoroid (18)

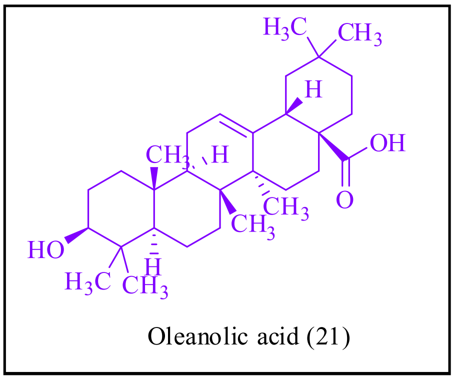
Figure 4: Chemical structures of iridoid glycosides (5-18) isolated from the plant *S. hydrophyllacea.*



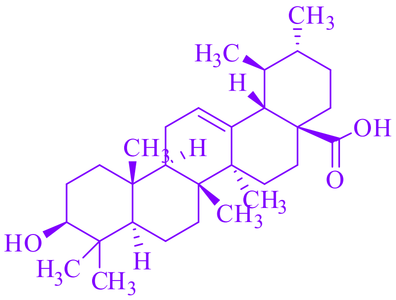
Hydrophylin A (19)

Hydrophylin B (20)

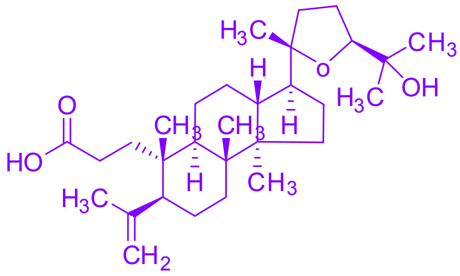
Figure 5: Chemical structures of noriridoids (19-20) isolated from the plant *S. hydrophyllacea.*



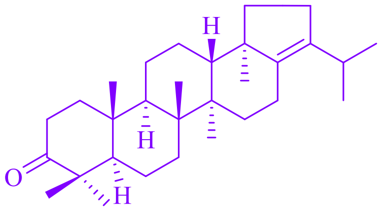
Oleanolic acid (21)



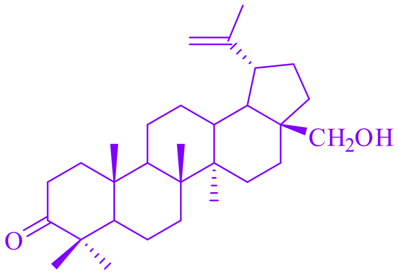
Ursolic acid (22)



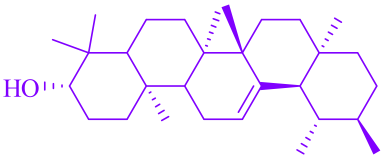
Eichlerianic acid (23)



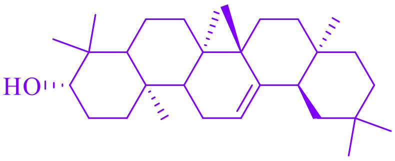
Hopenone I (24)



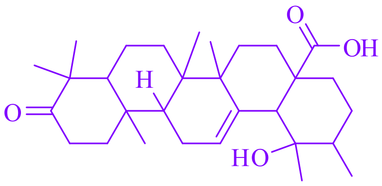
Betulone (25)



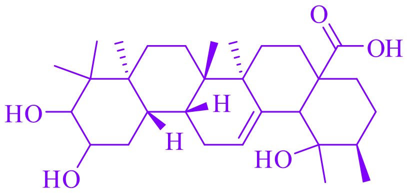
α-Amyrin (26)



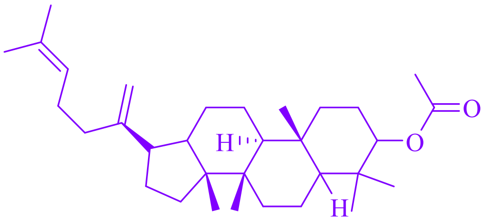
β-Amyrin (27)



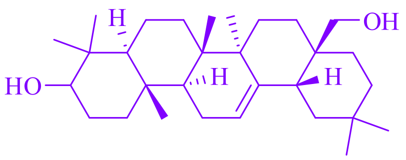
Pomonic acid (28)



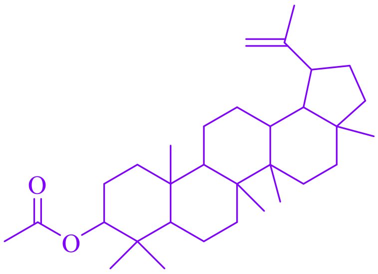
Euscaphic acid (29)



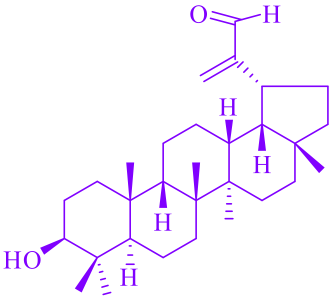
Dammaradienyl acetate (30)



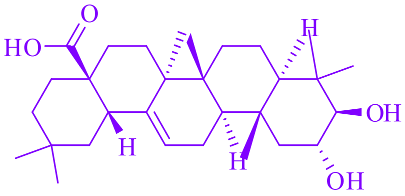
Erythrodiol (31)



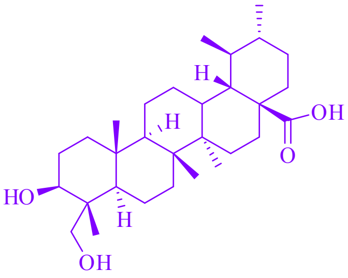
Lup-20(29)-en 3-yl acetate (32)



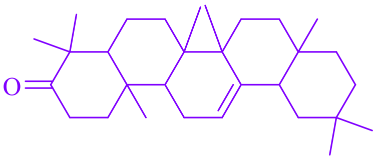
30-Oxolupeol (33)



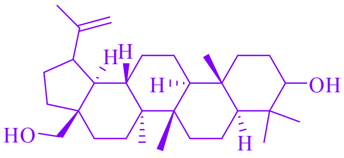
Maslinic acid (34)



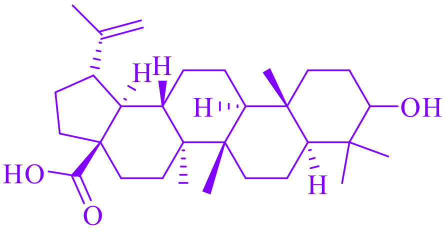
23-Hydroxyursolic acid (35)



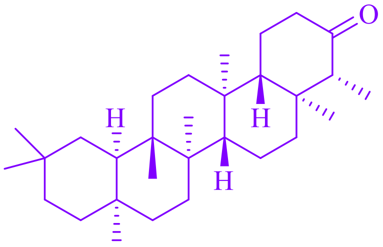
β-Amyrone (36)



Betulin (37)

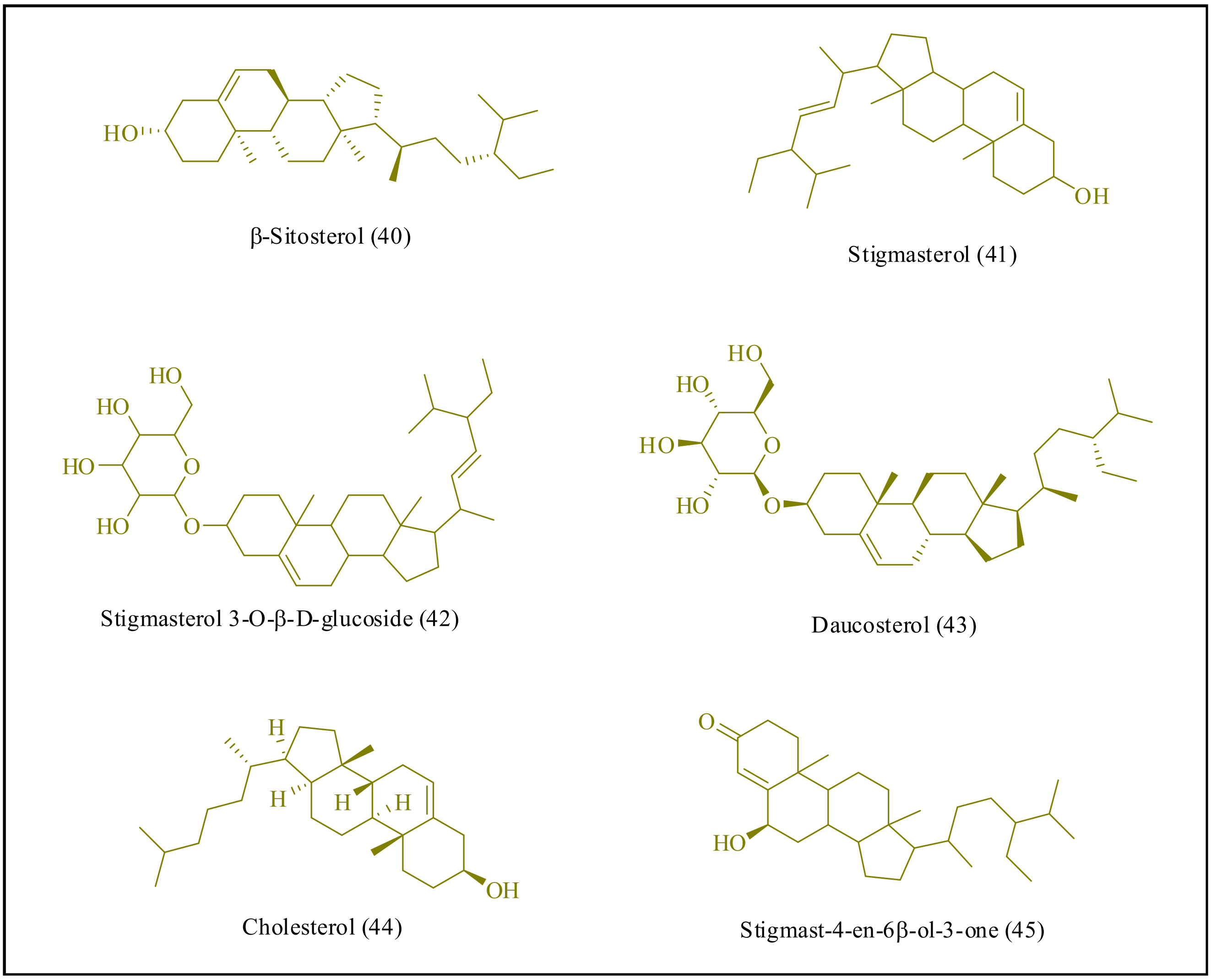


Betulinic acid (38)



Friedelin (39)

Figure 6: Chemical structures of triterpenes (21-39) isolated from the plant *S. hydrophyllacea*.



β-Sitosterol (40)

Stigmasterol (41)

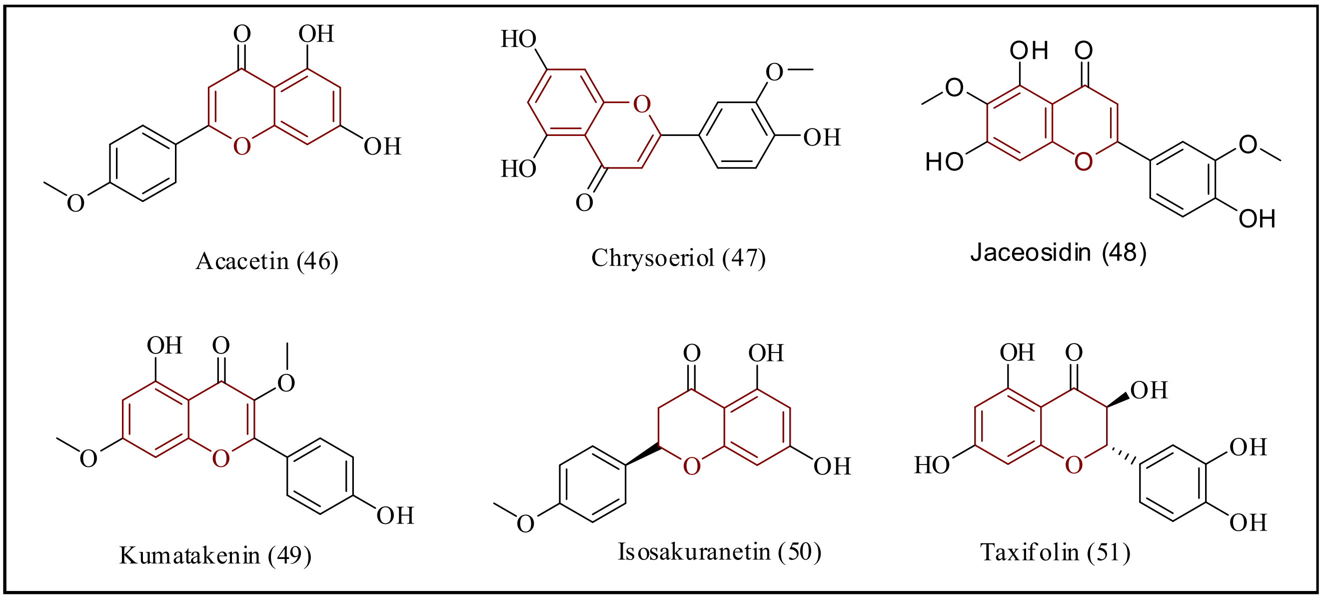
Stigmasterol 3-O-β-D-glucoside (42)

Daucosterol (43)

Cholesterol (44)

Stigmast-4-en-6β-ol-3-one (45)

Figure 7: Chemical structures of steroids (40-45) isolated from the plant *S. hydrophyllacea.*



Acacetin (46)

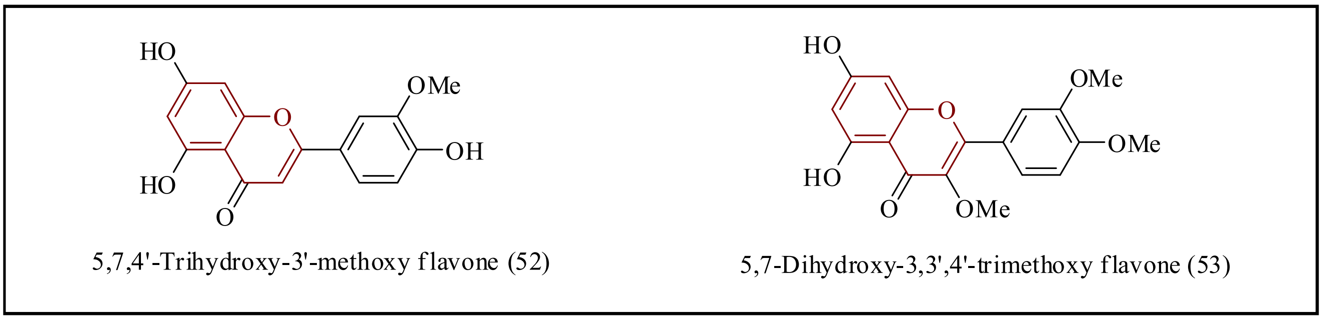
Chrysoeriol (47)

Jaceosidin (48)

Kumatakenin (49)

Isosakuranetin (50)

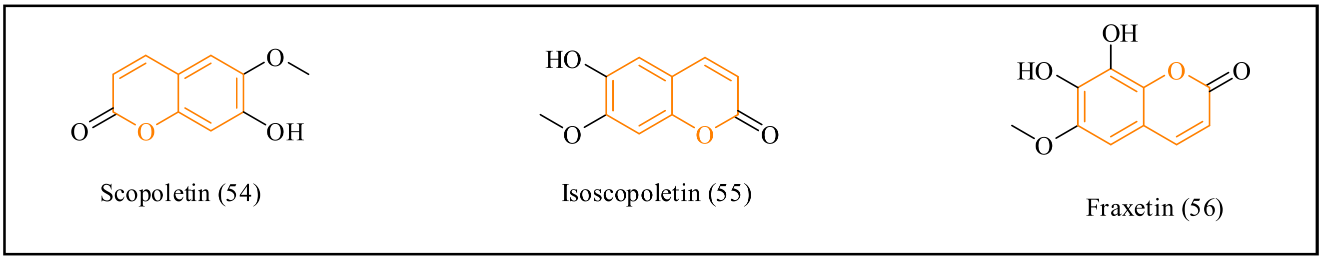
Taxifolin (51)



5,7,4'-Trihydroxy-3'-methoxy flavone (52)

5,7-Dihydroxy-3,3',4'-trimethoxy flavone (53)

Figure 8: Chemical structures of flavonoids (46-53) isolated from the plant *S. hydrophyllacea.*

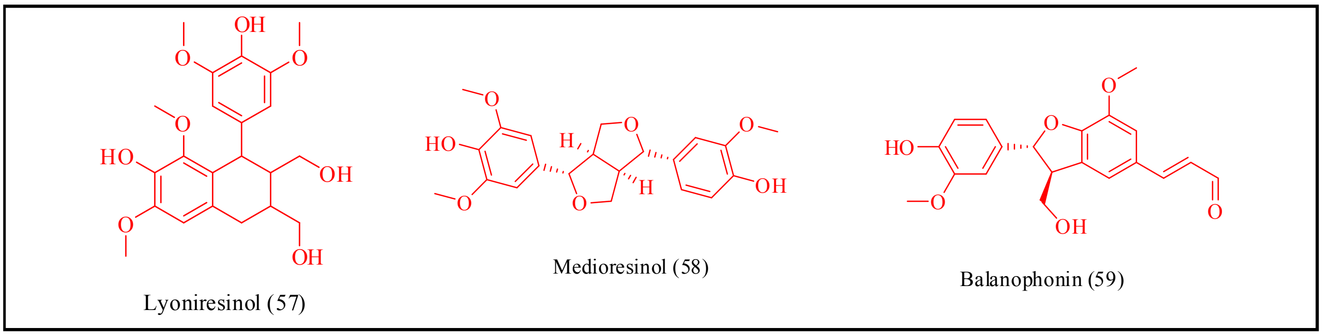


Scopoletin (54)

Isoscopoletin (55)

Fraxetin (56)

Figure 9: Chemical structures of coumarins (54-56) isolated from the plant *S. hydrophyllacea.*

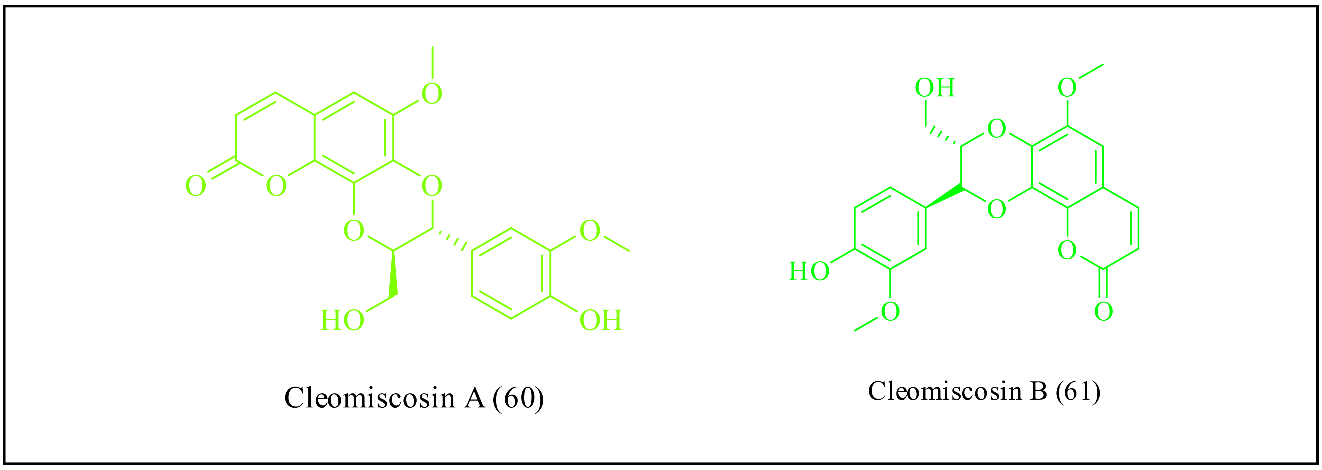


Lyoniresinol (57)

Medioresinol (58)

Balanophonin (59)

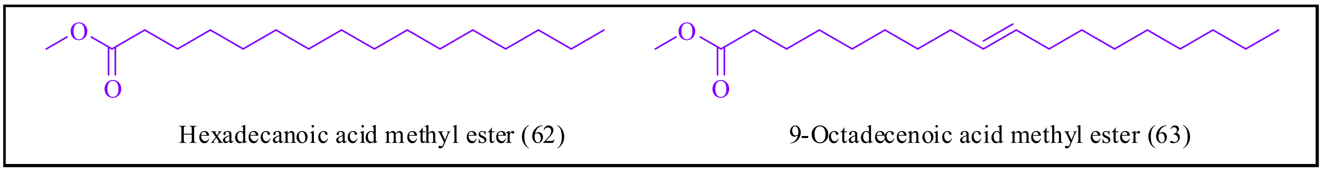
Figure 10: Chemical structures of lignans (57-59) isolated from the plant *S. hydrophyllacea.*



Cleomiscosin A (60)

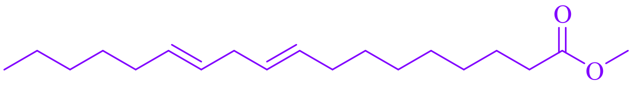
Cleomiscosin B (61)

Figure 11: Chemical structures of coumarino lignoids (60-61) isolated from the plant *S. hydrophyllacea.*



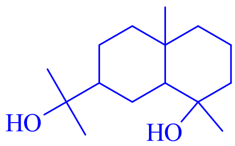
Hexadecanoic acid methyl ester (62)

9-Octadecenoic acid methyl ester (63)

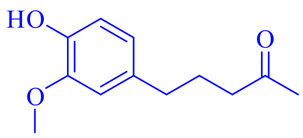


9,12-Octadecadienoic acid methyl ester (64)

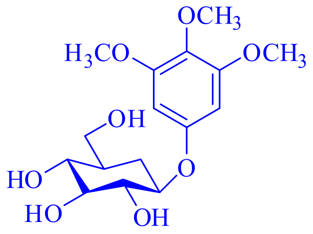
Figure 12: Chemical structures of fatty acid esters (62-64) isolated from the plant *S. hydrophyllacea.*



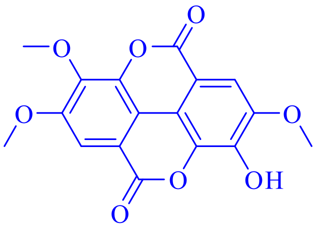
Cryptomeridiol (65)



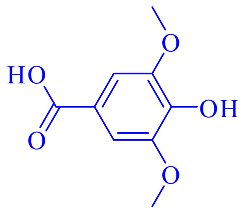
4-(4-hydroxy-3-methoxybenzyl)
butan-2-one (66)



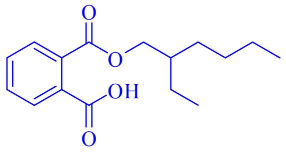
3,4,5-Trimethoxyphenol
β-D-glucopyranoside (67)



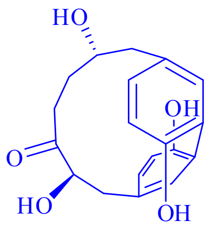
3,3,4'-Trimethoxy-ellagic acid (68)



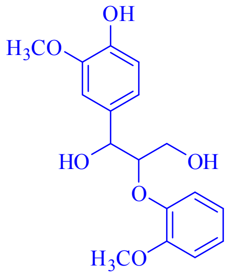
Syringic acid (69)



1,2-Benzene-dicarboxylic acid
(2-ethylhexyl) ester (70)



Casuarinondiol (71)



Guaiacylglycerol
β-ferulic acid ether (72)

Figure 13: Chemical structures of miscellaneous compounds (65-72) isolated from the plant *S. hydrophyllacea.*

6. Pharmacology

6.1 Cytotoxic activity

Two novel epimeric pairs of the iridoids 1, 2, 3 and 4 were isolated from *S. hydrophyllacea* by using MTT technique, both epimeric pairs of compounds were tested for cytotoxic activity against the human hepatoma SMMC-7721 cell line. Epimeric pair 3 and 4 demonstrated moderate cytotoxicity with the IC_{50} value of 59.1µg/ml (Zeng *et al.,* 2007).

Two novel compounds 19 and 20 were isolated from ethanol extract of the aerial portions of *S. hydrophyllacea*. The cytotoxic effect of both the compounds were investigated on the human hepatoma SMMC-7721 cell line by MTT method. Three days of incubation with different doses of substances were conducted on cancer cells at 37°C. The IC_{50} values of the two compounds were found to be more than 100 µgmL^{-1} (Zeng *et al.,* 2008).

Dried pulverized leaves of *S. hydrophyllacea* were extracted with hexane and chloroform. Three compounds, 21, 22 and 23 were isolated.

The cytotoxic effects of the compounds on oestrogen receptor positive breast (MCF-7) and non-small cell lung (NCIH- 292) cancer cells were assessed using the MTT test. At 24, 48, and 72 h after incubation, compounds 22 [IC_{50} - 8.47 µg/ml (24 h, MCF-7), 7.78 µg/ml (24 h, NCI-H292)] and 23 [IC_{50} - 8.86 µg/ml (24 h, MCF-7), 10.15 µg/ml (24 h, NCI-H292)] exhibited potent cytotoxic effects on MCF-7 and NCI-H292 cancer cells (Samarakoon *et al.,* 2018).

From hexane extract of leaves of *S. hydrophyllacea,* compound 24 was isolated and it was evaluated for their potential to inhibit cell proliferation using MTT assay on MCF-7, HepG2, and AN3CA cancer cell lines after 24 and 48 h of incubation. Compound 24 shows some encouraging anti-proliferative effects in all cancer cells in time and dose dependent manner (Samarakoon *et al.,* 2016).

Six compounds 25, 26, 27, 40, 41 and 67 were isolated from ethanol extract of mangrove. Their structures were elucidated. The MTT assay was used to measure cytotoxic activity. Compound 53 had an IC_{50} value of 12.5 µg/ml and inhibited SMMC-7721 cell lines (Zeng *et al.,* 2007).

The leaves and stem barks of 15 mangrove plants were extracted with hexane, chloroform, ethyl acetate and methanol. The resultant extracts were evaluated for cytotoxic activity against MCF-7 and HepG2 cells using the Sulforhodamine B (SRB) assay. The chloroform extract of the stem bark from *S. hydrophyllacea* was specifically cytotoxic to HepG2 cells (Samarakoon *et al.,* 2016).

Samarakoon *et al.* have tested anti-hepatocarcinogenic by *in vitro* method. The dried leaves of *S. hydrophyllacea* were extracted successively into hexane, chloroform, ethyl acetate, and methanol. Then, using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) and sulforhodamine B tests, the extracts were examined for cytotoxicity on HepG2 cells. The total phenolic and flavonoid contents were computed for each of the four extracts. In HepG2 cells, the extract's pro-apoptotic qualities were investigated, and gas chromatography-mass spectrometry (GC-MS) analysis was used to determine which bioactive components were present. The cytotoxic effects of the hexane and chloroform extracts were dose and time dependent. Under a fluorescence microscope, morphological alterations associated with apoptosis were seen, and cells treated with hexane and chloroform extract showed notably elevated levels of caspase 3 and 9. A very modest fragmentation of DNA was seen only in reaction to the chloroform extract. The expression of p53 and Bax mRNA was significantly elevated by low dosages of hexane and chloroform extracts. GC-MS profiles showed that the hexane and chloroform extracts, respectively, contained 24 and 4 significant components. These contained a few well-known anticancer components, including lupeol. They concluded that these hexane and chloroform extracts may be used to identify potential anticarcinogens (Samarakoon *et al.* 2017).

6.2 Antioxidant activity

Antioxidant activity was tested by *in vitro* method. The dried leaves of *S. hydrophyllacea* were extracted successively into hexane, chloroform, ethyl acetate, and methanol. The leaves were then tested for antioxidant activity using DPPH and ABTS assays. The most potent antioxidant activity was found in the methanol extract (Samarakoon *et al.,* 2017).

6.3 α-glucosidase inhibitory activity

The potential of the stem bark of *S. hydrophyllacea* to inhibit α-glucosidase was tested by the authors. The lyophilized expressed juice and fractions of *S. hydrophyllacea* were tested for α-glucosidase inhibition. IC_{50} of 8.63 2.16 g/mL was found for lyophilized expressed juice and IC_{50} of 2.40 0.29 g/ml was found for n-butanol fraction, the most active fraction. They have isolated compound 18 from n-butanol fraction and its structure was clarified using bioassay-guided extraction (Paulin *et al.,* 2020).

Table 2: Pharmacological activities of the plant *S. hydrophyllacea*

Name of the activity	Part used	Type of extract/ compound number	Model and animal used	Reference
Cytotoxic activity	Aerial	1,2,3 and 4	Human hepatoma SMMC-7721 cell lines by MTT assay	Zeng *et al.,* 2007
	Aerial	19,20	Human hepatoma SMMC-7721 cell line by MTT assay	Zeng *et al.,* 2008
	Leaves	21,22 and 23	Estrogen receptor positive (MCF-7) and non-small lung cancer (NCI-H-292) cells	Samarakoon *et al.,* 2018
	Leaves Whole plant	24, 25,26,27,40,41 and 67	MCF-7, AN3CA and HepG2 cell lines SMMC-7721 cell lines	Samarakoon *et al.,* 2016 Zeng *et al.,* 2007
	Leaves & Stem bark	Hexane, chloroform, ethyl acetate and methanol extract	MCF-7 & HepG2 cells using the sulforhodamine B (SRB) assay	Samarakoon *et al.,* 2016
	Leaves	Hexane, chloroform, ethyl acetate and methanol extract	HepG2 cells by 3-(4,5-dimethylthiazol -2-yl)-2,5-diphenyltetrazolium bromide) and sulforhodamine B assays	Samarakoon *et al.,* 2017
Antioxidant activity	Leaves	Hexane, chloroform, ethyl acetate and methanol extract	DPPH & ABTS assays	Samarakoon *et al.,* 2017
α-glucosidase inhibitory activity	Stem bark	Lyophilized expressed juice, n-butanol fraction and 18	p-nitrophenyl-α-D-glucopyranoside method	Paulin *et al.,* 2020

7. Discussion

The Plant List website was used to validate the plant name. According to this website, *S. hydrophyllacea* is a monotypic genus found in various countries. ChemDraw 10.0 software was used to draw chemical structures.

In this article we have given comprehensive information about phytochemistry and pharmacological uses of the plant along with its morphological profile. Traditionally, the plant was used in local and traditional medicine to treat stomachache and malaria (Basyuni *et al*., 2021; Nasir *et al.,* 2021).

More than 70 compounds were isolated from the plant. It has a variety of secondary metabolites like iridoids, iridoid glucosides, noriridoids, triterpenes, steroids, coumarins, lignans, coumarino lignoids, flavonoids, fatty acid esters and a few miscellaneous compounds. Spectral and chemical methods such as NMR, IR, HRMS and degradation studies have been used to clarify the structures. Total 10 types of secondary metabolites were present in the plant. More research has been conducted on photochemistry of secondary metabolites rather than pharmacological activities of isolated compounds and in extract form.

Three different therapeutic activities have been shown by the plant. They were cytotoxic, antioxidant and α-glucosidase inhibitory activity. All these 3 activities were tested by *in vitro* methods. Only a few authors have tested cytotoxic activity of the isolated compounds and other activities were tested for the different extracts of the plant.

The molecular processes were not well identified. To improve the applications of monomer compounds for human health, further study on the biological activity of different kinds of monomer compounds is necessary at cellular level. Additionally, well-developed procedures should be set up to guarantee the plant's efficacy, safety, and consistency.

8. Conclusion

S. hydrophyllacea is one of the shrub evergreen mangrove plants belonging to Scyphiphora genus in the family Rubiaceae. In India, it grows along the estuarine zones of the Coastal Andhra Pradesh. The ethnobotanical use that has been reported was the use of an extract of the leaves for stomachache and in malaria. The plant yields good fiber. Local people use the species for fuel purposes along with other mangroves. Studies on *S. hydrophyllacea* have important theoretical and economic results, and to support the modernization of traditional medicine, they should be conducted more methodically and completely based on previous findings. Around 72 compounds were isolated from this plant, but preclinical studies were done only to some extent. There is also need to discover the mechanisms of action of the bioactive compounds of this herb that result in its biological activities or effects. Furthermore, potential side effects need to be investigated. Thus, more work is still to be done to develop the plant compounds into leads for potential novel drug substances. Human safety and effectiveness of the plant have not been fully assessed, and clinical trials are necessary to validate preclinical results.

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Conflict of Interest

The authors declare no conflicts of interest relevant to this article.

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