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REVIEW

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Phytochemicals and potential health effects of *Sambucus williamsii* Hance (*Jiegumu*)

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Abstract

Sambucus williamsii Hance (*Jiegumu*) is traditionally used in Chinese medicine to treat bone and joint diseases. The major phytochemicals in *S. williamsii* are lignans, terpenoids, and phenolic acids, together with trace amounts of essential oils, minerals, amino acids, and natural pigments. In this review, a database search for studies published from 1990 to November 2015 was conducted using PubMed, the China Academic Journals Full-Text Database, and Google Scholar with the keywords "*Sambucus williamsii* Hance", "*Sambucus williamsii*", "*Sambucus williamsii* + clinic", "*Sambucus williamsii* + biology", "*Sambucus williamsii* + chemicals", and "*Jiegumu*", which covered chemical studies, cell culture studies, animal experiments, and clinical studies. This article reviewed the compounds isolated from *S. williamsii* that may reduce the risk of cancer, and exert antifungal, antioxidant, anti-inflammatory, bone fracture healing, and anti-osteoporotic effects.

Background

Sambucus williamsii Hance (*Jiegumu*) is traditionally used in Chinese medicine to treat bone fractures, rheumatoid arthritis, gout, Kaschin–Beck disease, inflammation-related gastrointestinal disorders, kidney diseases, and wounds [1]. Recent studies [2–12] identified the phytochemicals in *S. williamsii* that exhibit various biological activities, including antifungal effects [2, 3], effects on the proliferation and differentiation of osteoblastic cells [4, 5], fracture healing effects [6], antioxidant, antiglycemic, and hypolipidemic activities [7], anti-inflammatory, gastroprotective, and antinociceptive properties [8, 9], and antiviral [10], antidiabetic [11], antimalarial [12], and antitumor [10] activities. This review describes these phytochemicals and their potential health benefits.

Search strategy

A database search for studies published from 1990 to November 2015 was conducted using PubMed, the China Academic Journals Full-Text Database, and Google Scholar with the keywords "*Sambucus williamsii* Hance", "*Sambucus williamsii*", "*Sambucus williamsii* + clinic", "*Sambucus williamsii* + biology", "*Sambucus williamsii* + chemicals", and "Jiegumu", which covered chemical studies, cell culture studies, animal experiments, and clinical studies. The latest paper was published in October 2015, and the full literature search is outlined in Fig. 1. Using the key terms described above, 1087 publications were found without limiting language, type, or content. All the hits were de-duplicated, and after restricting to English and Chinese languages, research articles, books, or theses, and titles or abstracts containing "*Sambucus williamsii* Hance" or "Jiegumu", 606 papers were identified. Of these, 258 publications with full text were further extracted on the basis that they described chemical studies, in vitro activities, in vivo experiments, and clinical studies (omitting quantitative experiments, extraction and preparation methods, pharmacodynamic studies, and resource investigations). Finally, 102 papers were included in this review.

Botanical characteristics

The genus *Sambucus* was originally placed in the family *Caprifoliaceae*, but subsequently reclassified to *Adoxaceae* according to genetic evidence and morphological

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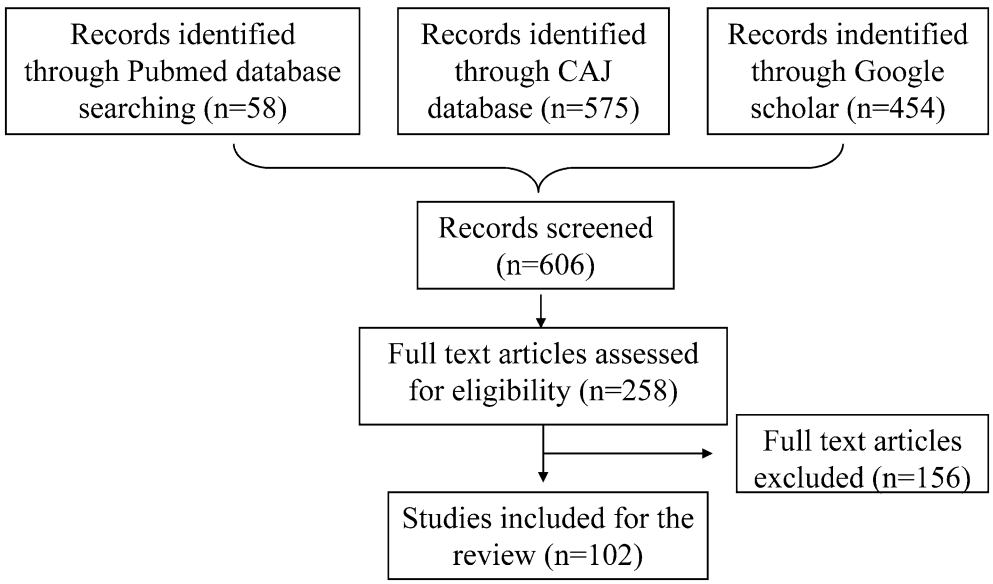

Fig. 1 Flowchart of the search strategy used in this review

comparisons, based on nucleotide sequences of the internally transcribed spacer region of nuclear ribosomal DNA, preliminary morphology, and a combination of the two data sets [13]. The family was reported to comprise at least 115 species and a large number of subspecific taxa [14, 15]. However, a recent revision by Bolli [16] recognized only nine species, with the remainder being synonymized or reduced to subspecific ranks. In China, there are five naturally occurring species within the *Sambucus Linn.* genus: *S. williamsii* and its varieties *var. williamsii* and *var. miquelii* (*Nakai*), *Sambucus adnata Wall.* (*Xuemancao*), *Sambucus sibirica Nakai* (*Xiboliya Jiegumu*) and *Sambucus chinensis Lindl.* (*Jiegucao*); and one introduced variety, *Sambucus nigra Linn.* (*Xiyang Jiegumu*) [17].

Sambucus williamsii is a shrub or small tree growing to a height of 5–6 m (Fig. 2a) that is widely distributed in northeastern China. The aging branches become reddish-brown and exhibit narrowly elliptic lenticels on their surface (Fig. 2b). The leaves are imparipinnate with 2- or 3-jugate leaflets, which are ovate–orbicular or narrowly elliptic at 5–15 × 1.2–7 cm, and irregularly serrate margins (Fig. 2c). The stems terminate in a cymose panicle of 5–11 × 4–14 cm in diameter, with numerous white or yellowish flowers (Fig. 2d). The fruit is a small glossy red berry of 3–5 mm in diameter (Fig. 2e). *Sambucus williamsii* flowers from April to May, and the seeds ripen from September to October. The plant is mostly located along mountain slopes, scrub, stream sides, and roadsides at altitudes of 540–1600 m, and has high environmental adaptability [1, 17].

Medicinal properties

The stem of *S. williamsii* has been used in Chinese medicinal formulae, in combination with other herbs, to treat bone fractures [18, 19]. Medicinal effects include relieving swelling and pain [19–21], promoting blood circulation [20, 21], and acting as an anti-inflammatory effect [21]. The other parts of *S. williamsii* such as the stem bark, root bark, fruit oil, and leaves have been investigated with various biological screening models [2–6, 22–46]. The root bark of *S. williamsii* exerted fracture healing effects [31, 34] similar to those of the stem while the other parts exhibited different effects, such as antifungal [22, 28], anti-inflammatory [33], anticancer [38], and antiaging [37] activities.

An extract of the stem prevented reductions in bone mass and bone strength induced by estrogen deficiency in ovariectomized (OVX) rats and mice [25–27], increased proliferation and differentiation of UMR-106 cells [4, 5, 30, 46], and induced differentiation of pluripotent stem cells into neurons [47]. A stem extract of *S. williamsii* exerted beneficial effects on the microarchitecture of trabecular bone and inhibitory effects on urinary calcium excretion in OVX mice by upregulating the ratio of osteoprotegerin to receptor activator of nuclear factor-κB ligand expression in bone obtained from OVX mice [26]. The stem extract exerted free radical-scavenging properties [23], reversed damage to the function of INS-1E β cells induced by alloxan, and increased insulin excretion [24], while the stem bark extract showed antifungal activities by damaging the fungal plasma membrane [2, 3, 22, 48]. The root bark extract exerted healing

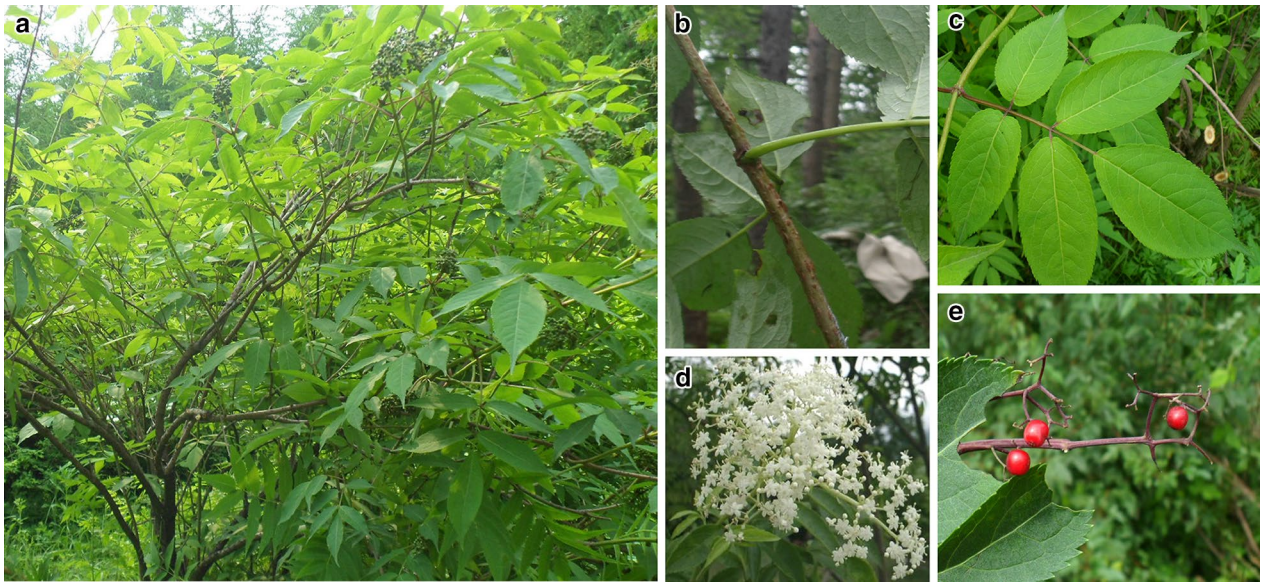

Fig. 2 *S. williamsii* Hance (*Jiegumu*) is characterized by elliptic lenticels on branches, imparipinnate leaves with irregularly serrate margins, white or yellowish flowers, and small glossy red berries. **a** *S. williamsii* Hance; **b** branch; **c** leaf; **d** flower; **e**: berry

effects on rabbit bone fractures [6, 31, 34], inhibitory effects on xylene-induced mouse ear edema and carrageenan-induced rat paw edema, and analgesic properties in rats and mice [33]. A mechanistic study showed that an ethanol extract of the root bark promoted MC3T3-E1 cell proliferation and differentiation through the bone morphogenetic protein 2/Smad/p38/c-Jun N-terminal kinase/runt-related transcription factor 2 signaling pathway [35]. The fruit oil exhibited immune-boosting [36], anticancer [38], and memory-improving [39] effects in mice, and antihyperlipidemic [37, 40] and antiaging [37] effects in rats. Furthermore, the leaves extract exhibited antibacterial [44] and anti-inflammatory [45] effects. The details of the bioactivities and chemical components in various parts of *S. williamsii* are listed in Additional file 1 [2–7, 20–34, 36–67].

Chemical composition and potential health effects

To date, publications have described chemical research on many parts of *S. williamsii*, including the stem, root bark, leaves, and berries. The chemicals discovered in these components currently include 59 lignans [2–4, 6, 22, 27, 28, 46, 49, 68], 26 terpenoids represented by 16 iridoids, two sesquiterpenoids, and eight triterpenoids [4, 6, 29, 30, 49–58], 13 phenolic acids [4, 5, 56, 58], seven aliphatic compounds [4, 7, 30, 50, 57], 50 essential oils [59, 60], and 23 other compounds [4, 6, 45, 50–52, 56, 58]. Furthermore, several minerals [61], amino acids [61], and natural pigments [62] were identified in the fruit of *S. williamsii*.

Lignans

Chemical

The lignans in *S. williamsii* include furofurans (**1**–**7**) [2, 4, 6, 28], dibenzyltyrolactones (**8**) [6], tetrahydrofurans (**9**–**15**) [4, 68], and arylnaphthalenes (**16**–**20**) [28, 63], representing the classical types of lignans, formed by oxidative coupling through a link between the β-carbons of the side chains of two phenylpropanoids (8–8′ link) [69] (Fig. 3). Benzodioxanes (**21**) [6], eupomatenoid benzofurans (**22**–**34**) [4, 6, 28, 46], and 8-*O*-4′ lignans (**35**–**43**) [6, 27, 28, 49, 63] are considered to be subtypes of neolignans, with carbon linkages between C8–*O*–C3′/C7–*O*–C4′, C8–C3′/C7–*O*–C4′, and C8–*O*–C4′, respectively (Fig. 4). Compounds **44**–**59** [4, 6, 28, 46] are oligomeric lignans composed of more than two C6–C3 units (Fig. 5). These lignans represent the most abundant compounds isolated from *S. williamsii*.

Health effects of lignans

These biphenolic compounds have similar structures to estrogens. They are the major source of phytoestrogens in the diets of Western populations and are primarily found in fiber-rich foods such as seeds, grains, vegetables, and fruits [70].

In the human gut, plant lignans are converted by intestinal bacteria into two enterolignans, enterolactone (ENL) and enterodiol (END), that exhibit biological activities and are absorbed into the bloodstream [71, 72]. Lignans also exhibit antiosteoporotic and antifungal effects [3] and can reduce the risk of cancer [73].

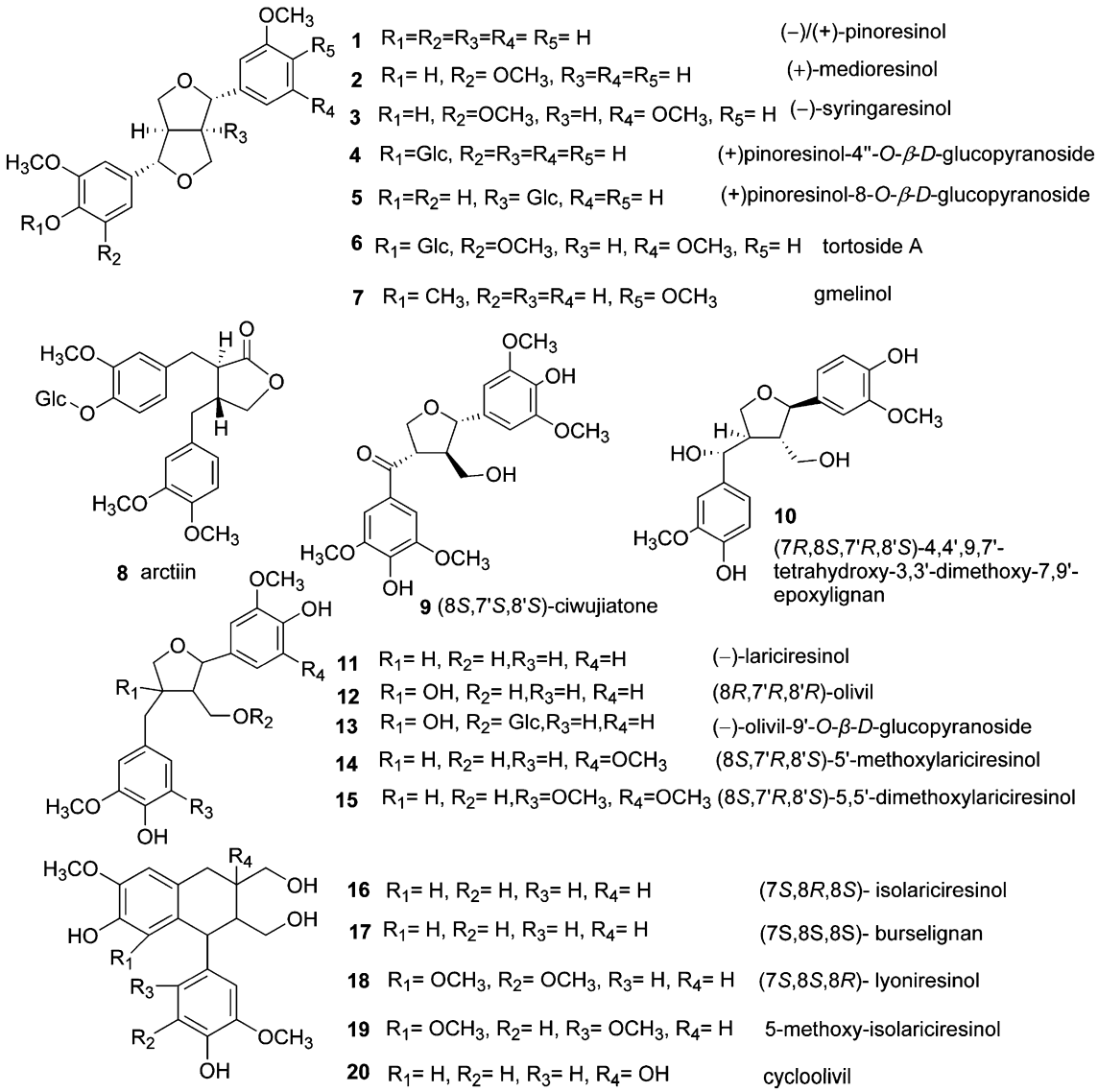

Fig. 3 Chemical structures of lignans in *S. williamsii* with representative structures: classical types of lignans with an 8–8′ link

Osteoprotective effects

The potential therapeutic effects of *S. williamsii* on postmenopausal osteoporosis in animal models and their underlying mechanisms of action [25–27] have been investigated. The active compounds with potential osteoprotective effects were identified by biological assay-guided fractionation [27, 46, 74]. Specifically, an ethanol extract of the stem of *S. williamsii* exhibited protective effects on trabecular bone mass and mechanical strength of cortical bone in OVX rats fed a normal diet and mice fed a phytoestrogen-free AIN-93M diet [25, 26]. Moreover, the chemicals including lignans, phenolic acids and triterpenoids in the ethanol extract of *S. williamsii* stem stimulated osteogenesis by promoting osteoblastic proliferation and differentiation [25, 27, 46, 68].

A combination of 50 and 95 % aqueous ethanolic fractions from a crude extract of *S. williamsii* stem purified on a reverse-phase macroporous resin column was the mixture exhibiting the most potent antiosteoporotic activity [27]. Further isolation of the *S. williamsii* active fraction by a series of chromatography steps and preparative high-performance liquid chromatography led to the separation and identification of 55 lignans [27, 28, 46, 49, 63].

In vitro experiments [75] revealed that one of these lignans, compound **38**, exhibited estrogen-like effects in osteoblast-like UMR-106 cells, MC3T3-E1 cells, and

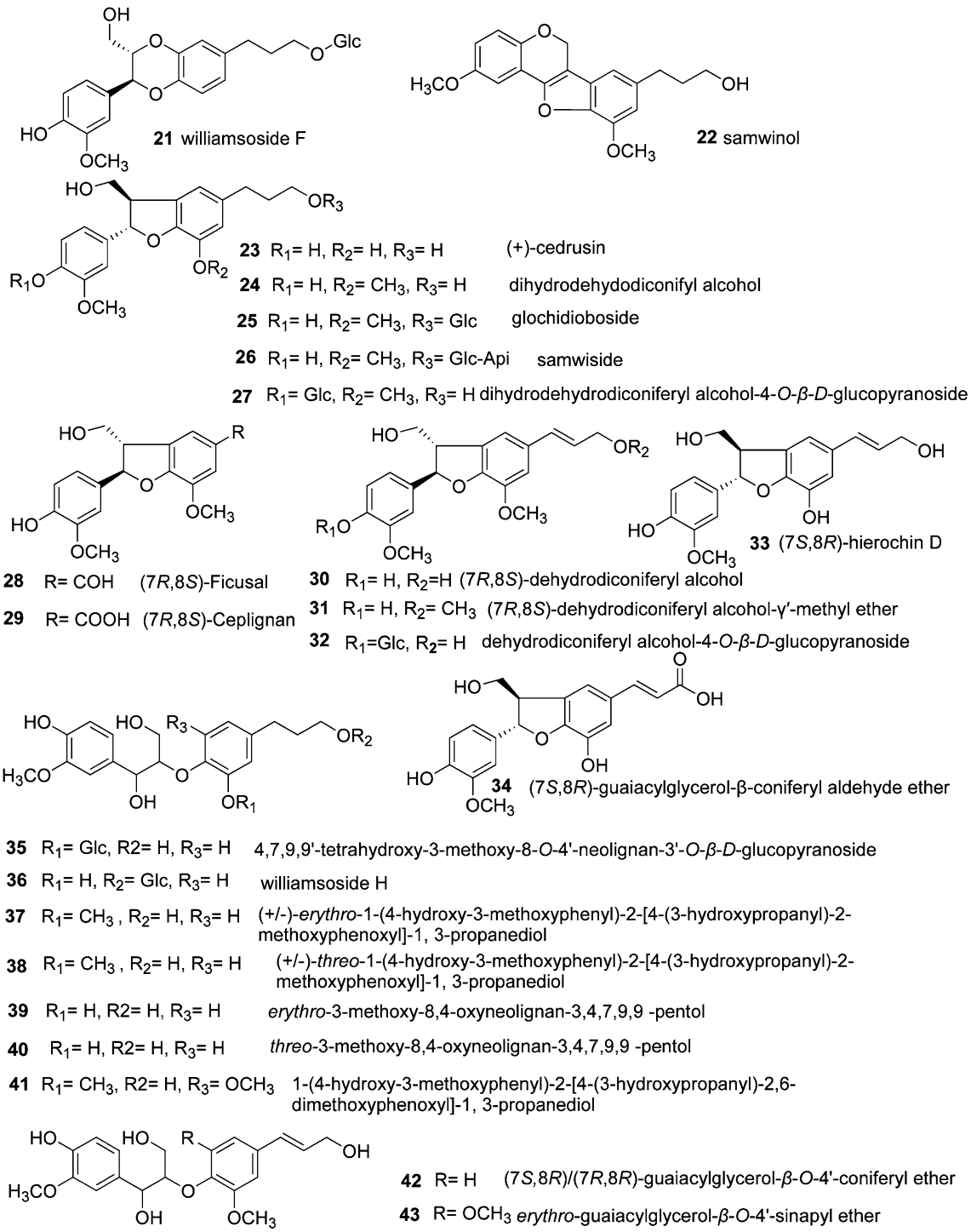

Fig. 4 Chemical structures of lignans in *S. williamsii* with representative structures: neolignans with carbon linkages between C8–*O*–C3′/C7–*O*–C4′, C8–C3′/C7–*O*–C4′, and C8–*O*–C4′

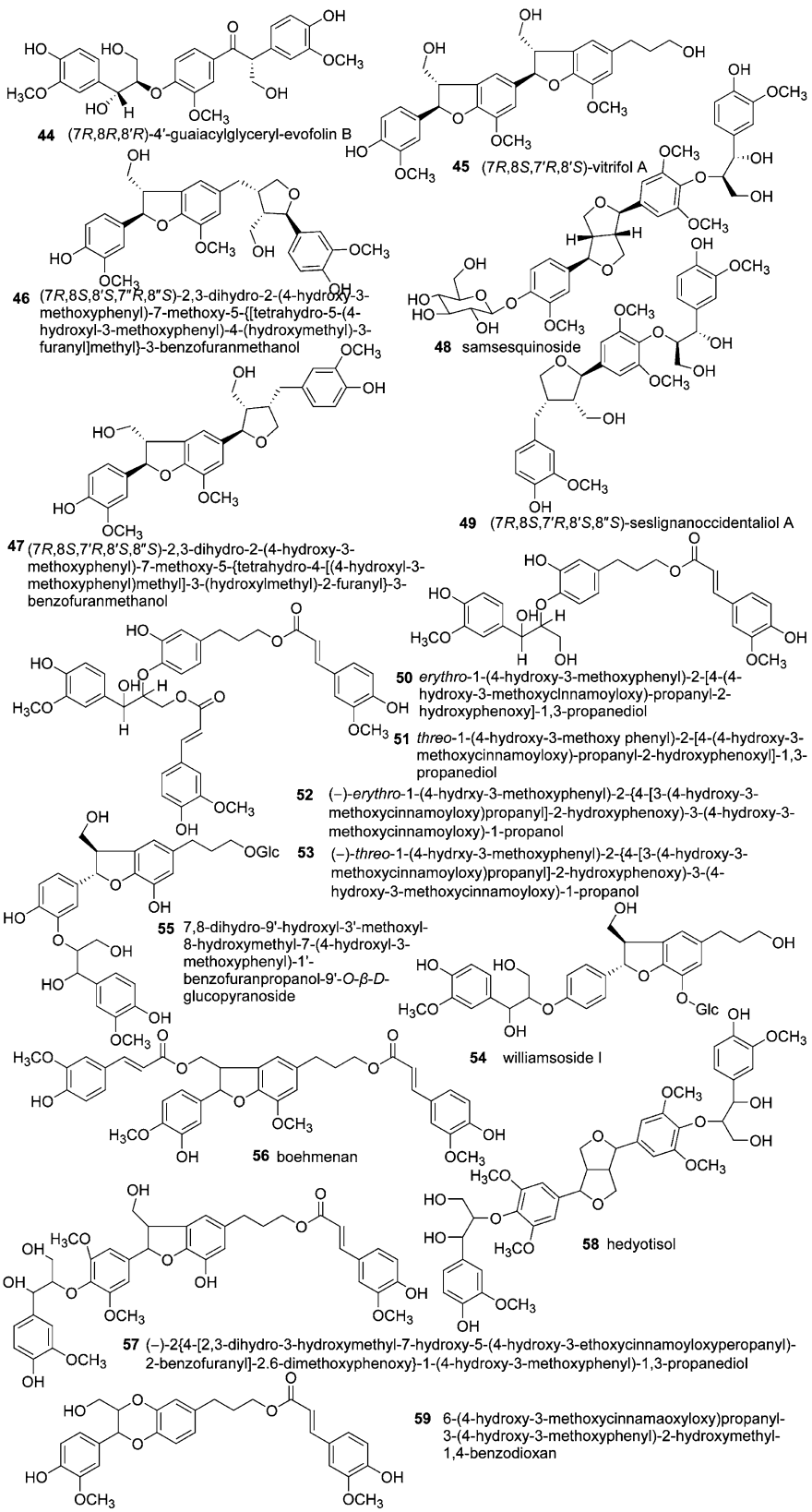

Fig. 5 Chemical structures of lignans in *S. williamsii* with representative structures: oligomeric lignans

bone mesenchymal stem cells. The results also showed that compound **38** exerted biological actions in osteoblast-like cells through ligand-independent, estrogen response element-independent, and mitogen-activated protein kinase-mediated rapid nongenomic estrogen receptor signaling pathways [75].

Antifungal activity

Pinoresinol (**1**), lariciresinol (**11**), (−)-olivil-9′-*O*-β-D-glucopyranoside (**13**), and glochidioboside (**25**) were all isolated from *S. williamsii*. They exhibited antifungal effects on human pathogenic strains through a membrane-disrupting action [2, 3, 22, 48]. (+)-Medioresinol (**2**), a furofuran-type lignan, isolated from the stem bark of *S. williamsii*, also exerted antifungal effects, but through the accumulation of reactive oxygen species in mitochondria [68].

Anticancer activity

Several studies [76, 77] showed that increased dietary lignan intake and/or increased levels of ENL and/or END might protect against or reduce the risk of breast, colon, and prostate cancers, and reduce hair loss. Lignans and their related metabolites were believed to be partly responsible for the growth inhibition of human prostate cancer cell lines [77]. ENL and END significantly inhibited the growth of prostate cancer PC-3 and LNCaP cells with 50 % inhibitive concentration at 57 and 100 μM respectively [77]. Treatment of human colon cancer SW480 cells with ENL and END, either alone or in combination, resulted in dose- and time-dependent decreases in cell number [78].

The administration of plant lignans, which were further metabolized to ENL and END, inhibited or delayed the onset of mammary cancer [71]. Although the mechanism of the anticarcinogenic action of ENL is not yet fully understood, there is intriguing evidence for ENL as a modulator of estrogen signaling [71]. Consumption of lignans such as lariciresinol (**11**) and pinoresinol (**1**) was associated with a significant reduction in breast cancer risk according to the clinical results of premenopausal women in Mexico [79].

Phenolic acids

Chemical characteristics

Thirteen phenolic compounds, vanillin (**60**), vanillic acid (**61**), acetovanillone (**62**), coniferyl aldehyde (**63**), ferulic acid (**64**), syringaldehyde (**65**), 4-hydroxybenzoic acid (**66**), 4-hydroxycinnamic acid (**67**), protocatechuic acid (**68**), indole-3-carboxylic acid (**69**), syringic acid-4-*O*-α-L-rhamnopyranoside (**70**), coniferyl alcohol (**71**), and methyl caffeate (**72**), were isolated from the stem and root bark of *S. williamsii* (Fig. 6) [5, 27, 28, 56, 58].

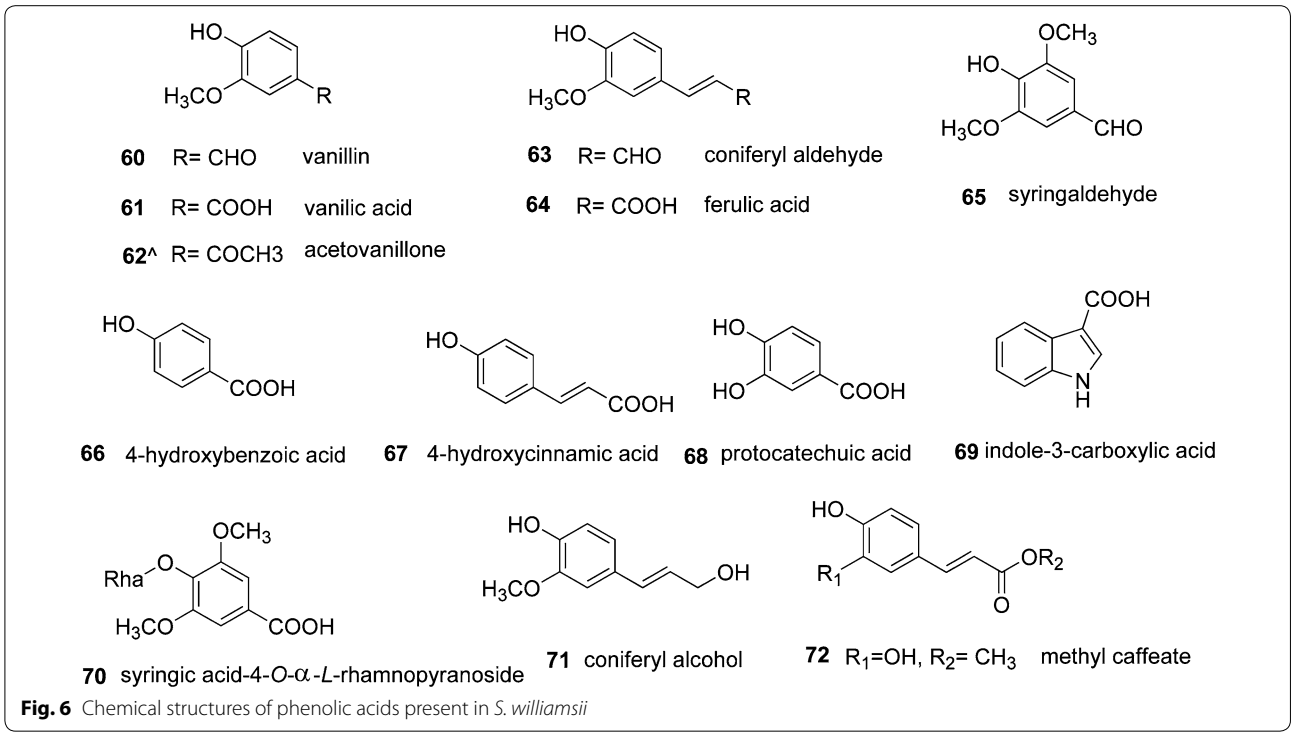

Fig. 6 Chemical structures of phenolic acids present in *S. williamsii*

Health benefits of phenolic acids

Vanillic acid (**61**) exerts estrogen-like actions in osteoblastic-like cells through a nongenomic estrogen receptor signaling pathway involving the mitogen-activated protein kinase pathway [80]. The compound also exhibits its antibacterial [81] and antimicrobial [82] activities and chemopreventive effects in experimentally induced carcinogenesis [83]. The protective effects of vanillic acid on myocardial infarction were studied in isoproterenol-induced cardiotoxic rats [84]. The free radical-scavenging, antioxidant, and anti-inflammatory activities of vanillic acid reduced isoproterenol-induced oxidative stress, downregulated myocardial interleukin-1β, interleukin-6, and tumor necrosis factor-α gene expression, and inhibited inflammation, thereby preventing cell death and protecting the myocardium [84].

Ferulic acid (**64**) possesses high antioxidant capacity and exhibits a longer residence time in rats than vitamin C [85]. Ferulic acid exhibits a wide range of therapeutic effects against many chronic conditions, including inflammation, cancer, apoptosis, diabetes, cardiovascular diseases, and neurodegenerative diseases [86]. It may also assist in plant host defense against pathogens and pests [87].

Protocatechuic acid (**68**) is an effective agent in reducing the carcinogenic actions of diethyl nitrosamine in the liver [88], 4-nitroquinoline-L-oxide in the oral cavity [89], azoxymethane in the colon [90], *N*-methyl-*N*-nitrosourea in the glandular stomach tissue [91], and *N*-butyl-*N*-(4-hydroxybutyl) nitrosamine in the bladder [92]. Protocatechuic acid also exhibits protective effects against the oxidative damage induced by tert-butyl hydroperoxide in rat primary hepatocytes by quenching free radicals [93]. Syringaldehyde (**65**) has six times higher antioxidant activity than protocatechuic acid [94]. Furthermore, syringaldehyde exerts antifungal activity against *Candida guilliermondii* [95], and exhibits antioncogenic activity through its inhibitory actions on murine pulmonary and hepatic microsomes [96]. Syringaldehyde shows stimulatory effects on both proliferation and alkaline phosphatase activity in UMR-106 cells [5]. 4-Hydroxybenzoic acid (**67**) exerts a hypoglycemic effect and increases serum insulin levels and liver glycogen contents in normal rats after oral administration at 5 mg/kg [97].

Terpenoids

Chemical characteristics

Sixteen iridoids [6, 49, 51, 52, 54, 56], two sesquiterpenoids [4, 30, 58], and eight triterpenoids [4, 29, 50, 57] were identified in *S. williamsii* (Fig. 7). The iridoids are characterized by the presence of a partially hydrogenated *cis*-fused cyclopenta [c] pyran system, arising from intramolecular acetylation of a 1,5-cyclopenta dialdehyde moiety, and they are usually stabilized by acetylation or esterification. Iridoids can be subdivided into four groups: iridoid glycosides, simple iridoids or non-glycosidic iridoids, secoiridoids, and bisiridoids [98]. Compounds **73**–**77** were isolated as iridoid glycosides possessing a 9-carbon skeleton with glycosides linked to C1–OH. Compounds **78**–**88** belong to the secoiridoid subclass indicated by a bond-break between C7 and C8. Compounds **89** and **90** are the two sesquiterpenoids that have been isolated from *S. williamsii*. The eight triterpenoids are compounds **91**–**98** and represent three subclasses: urane (**91**, **92**), lupine (**93**–**95**), and oleanane (**96**–**98**).

Health benefits of terpenoids

Triterpenoids from plants possess a wide spectrum of pharmacological activities such as anti-inflammatory, antiulcer, antihyperlipidemic, antitumor, and hepatoprotective actions [99, 100]. α-Amyrin (**91**) possesses antimicrobial, anti-inflammatory, gastroprotective, and antinociceptive properties [8, 9], while betulinic acid (**94**) exhibits anti-inflammatory [101], antiviral [10], antidiabetic [11], antimalarial [12], and antitumor [10] activities.

Aliphatic compounds

Chemical characteristics

Seven aliphatic compounds, triacontanoic acid (**99**), tianshic acid (**100**), hexadecanoic acid (**101**), (9*E*)-8,11,12-trihydroxyoctadecenoic acid methyl ester (**102**), linoleic acid (**103**), lupeol-3-palmitate (**104**), and 1-octacosanol (**105**), were isolated and identified from the stem of *S. williamsii* (Fig. 8) [4, 7, 30, 50, 57].

Health benefits of aliphatic compounds

Linoleic acid (**103**) extracted from *S. williamsii* seed oil with a yield of 65.81 % possesses antioxidant, antiglycemic, and hypolipidemic activities [7]. It exerts free radical-scavenging activity at 61.9 mg/mL, inhibits the activity of α-glucosidase at 1.5–25 mg/mL, and significantly improves serum lipid levels in hyperlipidemic mice [7].

Lupeol-3-palmitate (**104**) significantly reduced prostaglandin E2 production in A23187-stimulated macrophages [102]. The anti-inflammatory effect of a lupeol-rich extract was similar to that exhibited by the selective cyclooxygenase inhibitor indomethacin [102, 103].

Saturated aliphatic compounds are known to have harmful effects on human health, but only trace amounts of

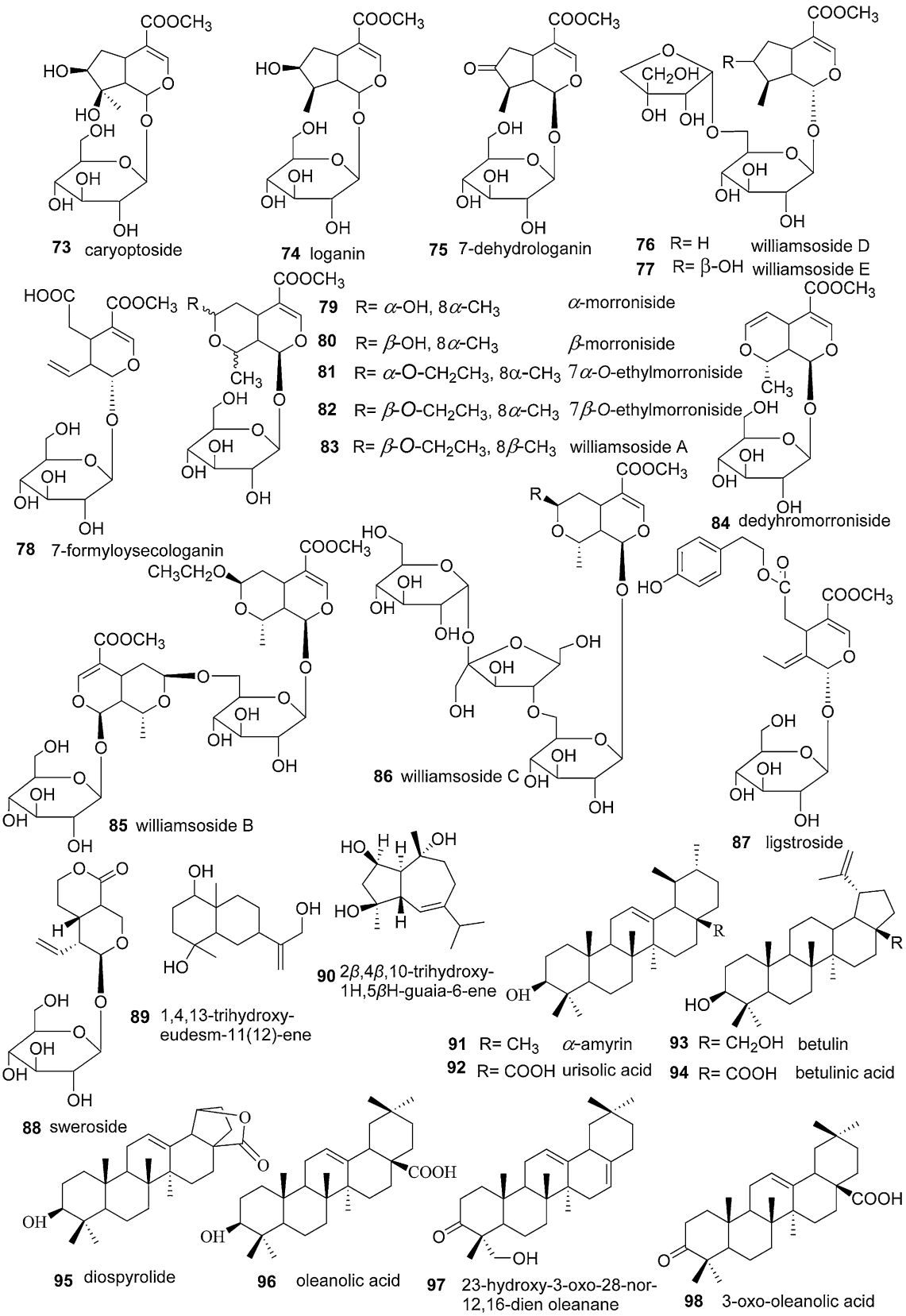

Fig. 7 Chemical structures of terpenoids present in *S. williamsii*

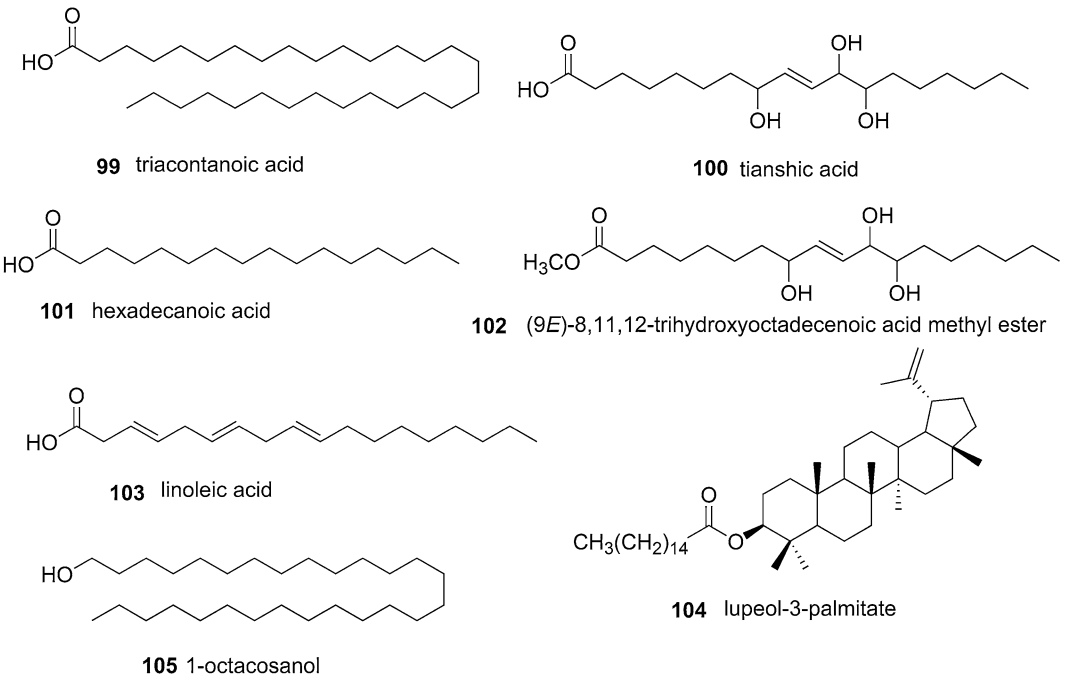

Fig. 8 Chemical structures of aliphatic compounds present in *S. williamsii*

saturated aliphatic compounds have been identified in *S. williamsii*. Hexadecanoic acid (**101**) found in *S. williamsii* induces oxidative stress and apoptosis of insulin-secreting cells [104, 105] and causes cardiac cells to undergo apoptosis [106]. It also causes insulin resistance in the brain by impairing the ability of insulin to activate intracellular signaling pathways [107], and accelerates obesity with diets containing high amounts of hexadecanoic acid [107].

Other compounds

Fifty essential oils in *S. williamsii* were extracted by steam distillation and identified by gas chromatography-mass spectrometry, as listed in Table 1. Among them, *cis*-3-hexenyl-3-methylbutanoate and salicylic acid methyl ester were the major components [60].

Several isoflavonoids, anthraquinones, steroids, alcohols, ketones, phenylpropanoids, acids, coumarins, and nitrogen-containing compounds were isolated from the stem and root bark of *S. williamsii* (Fig. 9). These compounds included puerarin (**106**), emodin (**107**), quercetin (**108**), kaempferol (**109**), 3-methoxy-4-(2-glycerol)-phenylpropanol (**110**), coniferyl alcohol 9-*O*-β-D-glucopyranoside (**111**), samwirin (**112**), samwiphenol (**113**), 8*R*-evofolin (**114**), 3-methoxy-4-(2-glycerol)-phenylpropanol (**115**), rosenonolactone (**116**), phaseic acid (**117**), umbelliferone (**118**), 3,4-dimethoxy-*N*-β-D-glucosyl pyrrole (**119**), 3-methoxyl-1*H*-pyrrole (**120**), *N*-methyl-β-alanine anhydride (**121**), β-sitosterol (**122**), β-sitosterol-β-D-glucoside (**123**), stigmasterol (**124**), 5-(1′-hydroxyethyl)-methyl nicotinate (**125**), 3-(hydroxyl-acetyl)indole (**126**), 4′-hydroxy-*N*-(4-hydroxy-3-methoxybenzoyl)-3′,5′-dimethoxy-benzamide (**127**), and (1*S*,3*S*)-1-methyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (**128**) [4, 6, 29, 45, 50, 51, 56, 58]. Du et al. [61] systemically studied the berries of *S. williamsii* and identified 17 amino acids and 14 microelements (Table 2), which may account for the fruit's nutritional properties.

Conclusions

This article reviewed the phytochemicals identified from *S. williamsii*, together with their biological activities and potential health benefits. Although several biological activities were ascribed to *S. williamsii*, the most important beneficial effects identified to date, based on

Table 1 The structures and molecular formula of essential oils in *S. williamsii*

No.	Compound	Molecular formula	Relative amount (%)
1	Hexanal	$C_6H_{12}O$	0.05
2	α-Terpineol	$C_{10}H_{18}O$	0.06
3	4-Terpineol	$C_{10}H_{18}O$	0.08
4	α-Pinene	$C_{10}H_{16}$	0.09
5	Camphor	$C_{10}H_{16}O$	0.11
6	δ-Elemene	$C_{15}H_{24}$	0.11
7	Heneicosane	$C_{21}H_{44}$	0.21
8	2-Pentadecanone	$C_{15}H_{30}O$	0.24
9	3-Methyl-pentanoic acid methyl ester	$C_7H_{14}O_2$	0.26
10	6,10-Dimethyl-5,9-undecadien-2-one	$C_{13}H_{22}O3$	0.38
11	Diallyl disulphide	$C_6H_{12}S_2$	0.41
12	Eicosane	$C_{20}H_{42}$	0.42
13	3-Vinyl-1,2-dithio cyclohe-5-ene	$C_7H_{10}S_2$	0.44
14	Thymol	$C_{10}H_{14}O$	0.48
15	β-Ionone	$C_{13}H_{20}O$	0.48
16	Hexadecane	$C_{16}H_{34}$	0.64
17	Epi-bicyclosequiphellandrene	$C_{15}H_{24}$	0.69
18	Ethyl salicylate	$C_9H_{10}O_3$	0.69
19	2,4,10,14-Tetramethyl pentadecane	$C_{20}H_{42}$	0.76
20	Hexanoic acid 2-hexenyl ester	$C_{12}H_{22}O_2$	0.83
21	Heptadecane	$C_{17}H_{36}$	0.85
22	Hyacinthin	C_8H_8O	0.87
23	Dihydro-β-agarofuran	$C_{15}H_{26}O$	0.89
24	3-Methyl-pentanoic acid	$C_6H_{12}O_2$	1.10
25	1,2-Dithiolane,1,1-dioxide	$C_3H_6O_2S_2$	1.26
26	Decanal	$C_8H_{16}O$	1.30
27	1-Heptan-3-ol	$C_7H_{14}O$	1.33
28	Ethyl caproate	$C_8H_{16}O_2$	1.34
29	Isoamyl isovalerate	$C_{10}H_{20}O_2$	1.52
30	Heptanal	$C_7H_{14}O$	1.53
31	Benzaldehyde	C_7H_6O	1.85
32	Cyclotetradecane	$C_{14}H_{28}$	1.95
33	Hexanoic acid hexyl ester	$C_{12}H_{24}O_2$	1.96
34	L-Linalool	$C_{10}H_{18}O$	2.04
35	Isovaleric acid	$C_5H_{10}O_2$	2.08
36	3-Methyl-1-butanol	$C_5H_{12}O$	2.11
37	Octanal	$C_7H_{14}O$	2.11
38	*cis*-3-Hexenol	$C_6H_{12}O$	2.19
39	trans-2-Hexenyl isovalerate	$C_{11}H_{20}O_2$	2.23
40	Benzyl isovalerate	$C_{12}H_{16}O_2$	3.04
41	4-Methoxy-6-(2-propenyl)-1,3-benzodioxole	$C_{18}H_{18}O_3$	3.10
42	2-Phenylethyl-3-methylbutanoate	$C_{13}H_{18}O_2$	3.11
43	*cis*-3-Hexenyl caproate	$C_{12}H_{22}O_2$	3.24
44	3-Methyl-butanoic acid ethyl ester	$C_7H_{14}O_2$	3.68
45	2-Heptanone	$C_7H_{14}O$	3.86
46	Hexyl isovalerate	$C_{11}H_{22}O_2$	4.02
47	1-Methoxy-4-(1-propenyl)benzene	$C_{10}H_{12}O$	6.29
48	1-Methoxy-4-(2-propenyl)benzene	$C_{10}H_{12}O$	6.79
49	*cis*-3-Hexenyl-3-methylbutanoate	$C_{11}H_{20}O_2$	14.03
50	Salicylic acid methyl ester	$C_8H_8O_3$	22.89

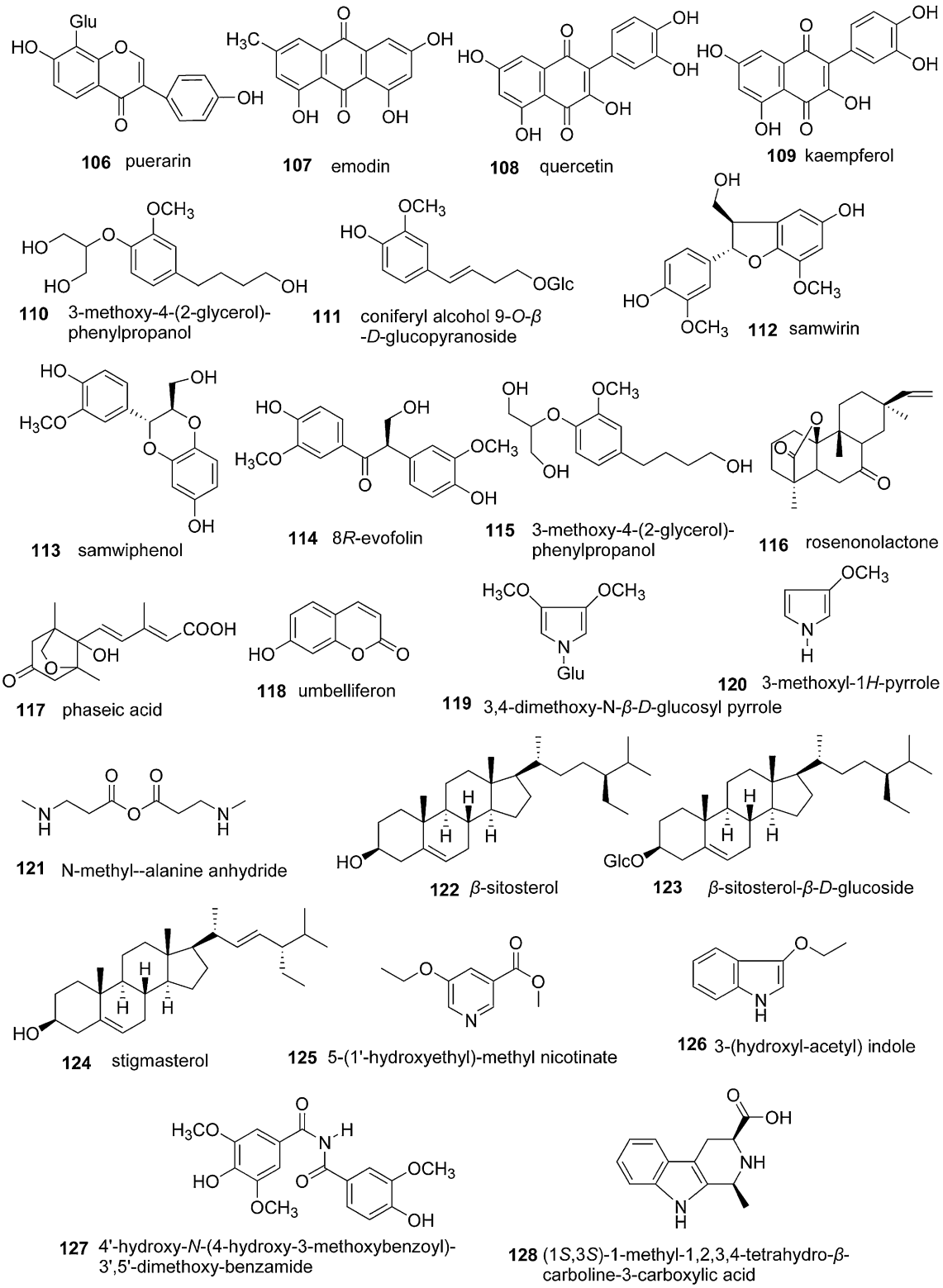

Fig. 9 Chemical structures of other compounds also present in *S. williamsii*

Table 2 The components of amino acids and microelements in *S. williamsii*

Amino acid	Content (mg/100 mL)
Aspartic acid	8.295
Threonine	2.253
Serine	3.145
Glutamic acid	9.759
Glycine	2.876
Alanine	3.152
Cysteine	0.420
Valine	2.615
Methionine	0.451
Isoleucine	2.158
Leucine	3.588
Tyrosine	1.784
Phenylalanine	2.216
Lysine	3.301
Histidine	1.279
Arginine	2.917
Proline	3.946
Microelements	**Content (μg/g)**
K	752
Ca	52.9
Zn	1.53
Fe	5.71
Cr	0.09
Cu	0.99
Mn	0.48
Ni	0.04
P	145
Sr	0.39
Ti	0.35
V	0.01
Al	10.4
Ba	0.46

the biological evidence outlined in this review, are those in the areas of osteoporosis, bone fractures, and other bone-related diseases.

Additional file

Additional file 1. The bioactivities and components of different usage parts of *S. williamsii*.

Abbreviations

END: enterodiol; ENL: enterolactone; OVX: ovariectomized; *S. williamsii*: *Sambucus williamsii* Hance.

Authors' contributions

HHX and YZ searched the literature, organized materials and wrote the manuscript. RC revised the structure and polished the language. MSW and XSY designed the study and revised the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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