Steroidal Saponins from the Genus *Smilax* and Their Biological Activities

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**Abstract** The *Smilax* species, widely distributed in tropical region of the world and the warm areas of East Asia and North America, are extensively used as folk medicine to treat inflammatory disorders. Chemical investigation on *Smilax* species showed they are rich sources of steroidal saponins with diversified structure types, including spirostane, isospirostane, furostane, pregnane, and cholestane. This review mainly summarizes the steroidal saponins (1–104) reported from the genus *Smilax* between 1967 and 2016, and their biological activities. The relationship between structures of steroidal saponins and related biological activities were briefly discussed.

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1 Introduction

The genus Smilax (Liliaceae family) comprises about 300 species of climbing shrubs. Plants of the genus are widely distributed in tropical region of the world, and also found in warm areas of East Asia and North America [1]. The juvenile leaves of S. riparia are used as vegetable product. The rhizomes of S. glabra are used in Southeast of China as food supplementary for health. Noteworthily, the rhizomes of Smilax species are most famous for their medical use. The rhizomes of S. china and S. glabra, called “Jin Gang Teng” and “Tu Fu Lin” in Pharmacopoeia of People’s Republic of China respectively, are clinically used to treat chronic pelvic inflammatory disease, rheumatic arthritis and so on [2]. The rhizomes of S. riparia, S. nipponica, S. bockii, S. microphylla, and S. discotis were recorded in the Chinese Herbal Medicines to treat joint pain, edema, and rheumatoid arthritis [3].

Previous studies on chemical constituents of Smilax species have disclosed the presence of steroidal saponins, flavonoids, phenylpropanoids, and stilbenoids [4]. Astilbin, a main flavonoid among Smilax species [5], showed unique immunosuppressive activity, and proved to be the active material basis of Smilax species for the treatment of human immune diseases [6]. Steroidal saponins are characteristic bioactive components of the genus Smilax in terms of chemotaxonomic value and biological activities [7]. So far, 104 steroidal saponins have been reported from 20 different Smilax species. These steroidal saponins showed significant antifungal, cytotoxic, anti-inflammatory, as well as cAMP phosphodiesterase inhibitory activities.

In this review, steroidal saponins reported from the genus Smilax between 1967 and 2016 were listed, and the biological activities of steroidal saponins were also included.

2 Chemistry of Steroidal Saponins

Steroidal saponins from the genus Smilax could be divided into five groups on the basis of the sapogenin structures: spirostane (A), isospirostane (B), furostane (C), pregnane (D), and cholestane (E) (Fig. 1). They are mostly mono- or bisdesmosides. A carbohydrate chain is always attached to the C-3 position of sapogenin by an ether linkage. Additionally, C-26 position of furostane-type saponin is always etherified with a glucopyranosyl moiety. So far only one steroidal saponin from the genus Smilax, (25S)-26-0-β-D-
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Fig. 1 Structures of a a spirostane backbone, b an isospirostane backbone, c a furostane backbone, d a pregnane backbone, e a cholestan backbone, a glucopyranosyl moiety (Glc), a glucopyranosyl-5β-furostan-1β,3β,22x,26-tetraol-1-O-β-D-glucopyranoside (92), has a glucopyranosyl moiety linked to the C-1 position. The sugar residues consist of linear or branched saccharidic chains, made up most often of glucopyranosyl (Glc), rhamnopyranosyl (Rha), galactopyranosyl (Gal), fructofuranosyl (Fru), and arabinopyranosyl (Ara) moieties (Fig. 1).

2.1 Spirostane-Type Saponins 1–11

Spirostane-type saponins are monodesmosidic glycosides with six rings A–F in sapogenin. They are characterized by an axial oriented methyl or hydroxymethyl (C-27) on F ring. The sapogenin of spirostane glycosides 1–11 possess either a cis or a trans fusion between rings A and B, or a double bond between C-5 and C-6, leading to 5α (neotigogenin), 5β (sarsasapogenin), and Δ5 (narthogenin) subtypes (Fig. 2). Neotigogenin glycosides 1–5, and 10 have been isolated from *S. riparia* [8], *S. nipponica* [9], and *S. officinalis* [7]. Both neotigogenin glycosides 5, 10 and sarsasapogenin glycoside 6 were identified from the rhizomes of *S. officinalis* [7]. Sarsasapogenin glycosides 7–9 were isolated from the root of *S. aspera* subsp. *mauritanica* [10], and *S. ornata* Lem. [11]. Compound 11, with a hydroxyl substitution on C-27, was the only narthogenin glycoside reported from *Smilax* species so far.

2.2 Isospirostane-Type Saponins 12–47

Isospirostane-type saponins are also monodesmosidic glycosides characterized by an equatorial oriented methyl or hydroxymethyl (C-27) on F ring. The isospirostane-type saponins 12–47 could be classified into four subtypes on the basis of sapogenin structures, including diosgenin, laxogenin, tigogenin, and smilagenin (Fig. 3). The variations of these sapogenins mainly comprise dehydrogenation between C-5 and C-6, carboxylation at C-6, hydroxylation at C-17 or C-27, and cis/trans fusion between rings A and B. Diosgenin glycosides 12–30 were characterized by a double bond between C-5 and C-6. Diosgenin-3-O-α-L-rhamnopyranoside (12) was the first diosgenin glycoside reported from the epigeal part of *S. excelsa* in 1975 [12]. Dioscin (13) was widely distributed among the *Smilax* species, including *S. china* [8], *S. menispermoidea* [13], *S. lebrunii* [14], *S. nigrescens* [15], *S. stans* [16], *S. excels* [17], *S. microphylla* [18], and *S. bockii* [19]. Parisyunnanosides C–E (18–20), with hydroxyl substitutions at C-7 or C-12, were isolated from the stems of *S. riparia* [20]. The occurrences of parisyunnanoside in the genus *Smilax* indicated the close chemtaxonomic relationship between the genus *Smilax* and *Paris*. Three isonarthogenin glycosides 24, 25, and 28 were isolated from *S. scobinicaulis*, together with two tigogenin...
glycosides 38–39 [21]. Sieboldogenin (33), with an additional hydroxy substitution on C-27 in comparison with laxogenin, was identified from the ethyl acetate fraction of S. china [22]. Laxogenin glycosides 34–36 were found in S. sieboldii [23]. Parisvietaiside A (37), characterized by a double bond between C-7 and C-8, was obtained from the roots and rhizomes of S. riparia [24]. The smilagenin glycosides 42–47 with a cis fusion rings A and B were isolated from the roots of S. medica [25, 26]. Hydroxyl substitution on C-7 or C-12, and double bond between C-7 and C-8 are the rare cases within the steroidal saponins of the genus Smilax.

### 2.3 Furostane-Type Saponins 48–93

Furostane-type saponins, F ring opened spirostanol glycosides, are another important group of steroidal saponins within Smilax species. The hemiketal hydroxy attached to the C-22 position of furostanol glycosides were sometimes methylated or dehydrated. The methylated derivatives were generally considered to be artifacts. Furostanol glycosides with both 25R and 25S configurations were reported from the genus Smilax. Additionally, furostanol glycosides always have two sugar chains attached to the C-3 and C-26 positions of the aglycone moiety (Fig. 4). Methylprotopodioscin (48), protodioscin (59), and pseudoprotodioscin (60) were common constituents among the different Smilax species (Table 1). Compounds 50, isolated from the roots of S. bockii, increased the nerve growth factor (NGF)-induced neurite outgrowth in PC 12D cells by 49% in comparison with the blank control at the concentration of 60 µg/mL [19]. Compounds 53–55, identified from the rhizomes of S. excelsa, were the only three steroidal saponins with acylated sugars moieties within the genus Smilax [17]. Furostane glycosides 62 and 63, with an oxygenated C-15, were isolated from the tubers of S. china [27]. Interestingly, the spirostane or isospirostane glycosides with an oxygenated C-15 have never been reported from Smilax so far. Compounds 67–70 with carbonylation on C-6 were isolated from the roots and rhizomes of S. scobinicaulis, together with a spirostane glycoside 35, and three furostane glycosides 89–91 [28]. Compounds 76 and 77, isolated from the root of S. officinalis, are the diastereoisomers with opposite configuration at C-5 [29]. Smilaxosides A–C (84, 86, 87), and (25R)-Smilaxchinoside A (85) were obtained from the tubers of S. china [30]. Of them, compounds 84 and 85 are diastereoisomers with opposite configuration at C-25. Compounds 92 and 93, identified from S. aspera [31], were rare examples with hydroxyl substitution on C-1 within the genus Smilax.

### 2.4 Pregnane-Type Saponins 94–102 and Others 103–104

Pregane-type saponins are C_{21} steroidal saponins with a sugar moiety linked to the alcoholic hydroxyl group of the sapogenin, most frequently at C-3. Compounds 94–98 are not real pregnane-type saponins from the perspective of biosynthetic pathway. Possibly, they are biosynthetically formed through oxidative cleavage of the double bond between C-20 and C-22 in furostane structures. Compounds 94 and 98 were isolated from the rhizomes and roots of S. trinervula, together with compounds 11, 60, 85, 88, and 103 [32]. Pregane glycosides 99–102 were found in S. nigrescens [15], S. menispermoidea [33], S. bockii [19], S. microphylla [18], and S. riparia [20]. Compounds 103 and 104, isolated from S. trinervula and S. china respectively, are belonged to cholestane-type saponins, or

![Fig. 2 Structures of compounds 1–11](image-url)
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Fig. 3  Structures of compounds 12–47

|   |   |
|---|---|
| 12 | $R_1 = S_{10}$, $R_2 = R_3 = R_4 = R_5 = H$ |
| 13 | $R_1 = S_9$, $R_2 = R_3 = R_4 = R_5 = H$ |
| 14 | $R_1 = S_{11}$, $R_2 = R_3 = R_4 = R_5 = H$ |
| 15 | $R_1 = S_{12}$, $R_2 = R_3 = R_4 = R_5 = H$ |
| 16 | $R_1 = S_{13}$, $R_2 = R_3 = R_4 = R_5 = H$ |
| 17 | $R_1 = S_{14}$, $R_2 = R_3 = R_4 = R_5 = H$ |
| 18 | $R_1 = S_{13}$, $R_2 = \alpha$-OH, $R_3 = R_4 = R_5 = H$ |
| 19 | $R_1 = S_{15}$, $R_2 = \alpha$-OH, $R_3 = R_4 = R_5 = H$ |
| 20 | $R_1 = S_{15}$, $R_2 = \beta$-OH, $R_3 = R_4 = R_5 = H$ |
| 21 | $R_1 = S_{14}$, $R_2 = OH$, $R_3 = R_4 = R_5 = H$ |
| 22 | $R_1 = S_{15}$, $R_2 = OH$, $R_3 = R_4 = R_5 = H$ |
| 23 | $R_1 = S_9$, $R_2 = R_3 = H$, $R_4 = R_5 = OH$ |
| 24 | $R_1 = S_{16}$, $R_2 = R_3 = H$, $R_4 = R_5 = OH$ |
| 25 | $R_1 = S_5$, $R_2 = R_3 = H$, $R_4 = R_5 = OH$ |
| 26 | $R_1 = S_{11}$, $R_2 = R_3 = H$, $R_4 = R_5 = OH$ |
| 27 | $R_1 = S_{22}$, $R_2 = R_3 = H$, $R_4 = R_5 = OH$ |
| 28 | $R_1 = S_{16}$, $R_2 = R_3 = R_4 = H$, $R_5 = OH$ |
| 29 | $R_1 = S_9$, $R_2 = R_3 = R_4 = H$, $R_5 = OH$ |
| 30 | $R_1 = S_5$, $R_2 = R_3 = R_4 = H$, $R_5 = OH$ |
| 31 | $R_1 = S_5$, $R_2 = OH$ |
| 32 | $R_1 = S_{16}$, $R_2 = OH$ |
| 33 | $R_1 = H$, $R_2 = OH$ |
| 34 | $R_1 = S_{17}$, $R_2 = H$ |
| 35 | $R_1 = S_{16}$, $R_2 = H$ |
| 36 | $R_1 = S_5$, $R_2 = H$ |
| 37 | $R = S_{14}$ |
| 38 | $R_1 = S_5$, $R_2 = R_3 = R_4 = H$ |
| 39 | $R_1 = S_9$, $R_2 = OH$, $R_3 = R_4 = H$ |
| 40 | $R_1 = S_5$, $R_2 = R_3 = H$, $R_4 = OH$ |
| 41 | $R_1 = S_5$, $R_2 = H$, $R_3 = R_4 = OH$ |
| 42 | $R = S_{18}$ |
| 43 | $R = S_{19}$ |
| 44 | $R = S_{20}$ |
| 45 | $R = S_{21}$ |
| 46 | $R = S_8$ |
| 47 | $R = S_3$ |
Fig. 4 Structures of compounds 48–83
| No. | Name                                      | Plant          | Parts                          | Ref. |
|-----|-------------------------------------------|----------------|--------------------------------|------|
| 1   | Neotigogenin-3-O-[α-L-rhamnopyranosyl-(1 → 6)]-β-D-glucopyranoside | *S. riparia* | Rhizomes and roots            | [8]  |
| 2   | Neotigogenin-3-O-β-D-glucopyranosyl-(1 → 4)-O-[α-L-rhamnopyranosyl-(1 → 6)]-β-D-glucopyranoside | *S. riparia* | Rhizomes and roots            | [8]  |
| 3   | Neotigogenin-3-O-β-D-glucopyranoside      | *S. nipponica* | Subterranean                   | [9]  |
| 4   | Smilanippin A                             | *S. nipponica* | Subterranean                   | [9]  |
| 5   | Neotigogenin-3-O-β-D-glucopyranosyl-(1 → 4)-O-[α-L-arabinopyranosyl-(1 → 6)]-β-D-glucopyranoside | *S. officinalis* | Rhizomes                        | [7]  |
| 6   | Sarsasapogenin-3-O-β-D-glucopyranosyl-(1 → 4)-O-[α-L-arabinopyranosyl-(1 → 6)]-β-D-glucopyranoside | *S. officinalis* | Rhizomes                        | [7]  |
| 7   | (25S)-5β-Spirostane-3β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranoside | *S. aspera subsp. mauritanica* | Roots                          | [10] |
| 8   | Curillin G                                | *S. aspera subsp. mauritanica* | Roots                          | [10] |
| 9   | Parillin                                  | *S. aristolochifolia* | Rhizomes and roots            | [38] |
| 10  | (25S)-Spirostan-6β-D-glucopyranosyl-(1 → 4)-O-[α-L-arabinopyranosyl-(1 → 6)]-β-D-glucopyranoside | *S. officinalis* | Rhizomes                        | [7]  |
| 11  | Trinervuloside C                          | *S. trinervula* | Rhizomes and roots            | [32] |
| 12  | Diosgenin-3-O-[α-L-rhamnopyranoside      | *S. excels* | Epigeal part                   | [12] |
| 13  | Dioscin                                   | *S. china*    | Roots                          | [8]  |
|     |                                           | *S. menisperoides* | Rhizomes                     | [13] |
|     |                                           | *S. lebruni*  | Roots                          | [14] |
|     |                                           | *S. nigrescens* | Roots                          | [15] |
|     |                                           | *S. stans*    | Roots                          | [16] |
|     |                                           | *S. bockii*   | Roots                          | [19] |
|     |                                           | *S. excelsa*  | Rhizomes                        | [17] |
|     |                                           | *S. microphylla* | Tubers                         | [18] |
|     |                                           | *S. china*    | Tubers                         | [30] |
| 14  | Diosgenin-3-O-[α-L-rhamnopyranosyl-(1 → 4)]-β-D-glucopyranoside | *S. nigrescens* | Roots                          | [15] |
|     |                                           | *S. menisperoides* | Rhizomes                     | [39] |
|     |                                           | *S. menisperoides* | Rhizomes                     | [33] |
|     |                                           | *S. china*    | Tubers                         | [30] |
| 15  | Diosgenin-3-O-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside | *S. nigrescens* | Roots                          | [15] |
|     |                                           | *S. menisperoides* | Rhizomes                     | [33] |
|     |                                           | *S. microphylla* | Tubers                         | [18] |
|     |                                           | *S. china*    | Tubers                         | [30] |
| 16  | (25R)-Spirostan-5-en-3-O-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside | *S. menisperoides* | Rhizomes                        | [40] |
|     |                                           | *S. microphylla* | Tubers                         | [18] |
| 17  | Gracillin                                 | *S. microphylla* | Tubers                         | [18] |
| 18  | Parissyunnanoside C                       | *S. riparia*  | Rhizomes and roots            | [20] |
| 19  | Parissyunnanoside D                       | *S. riparia*  | Rhizomes and roots            | [20] |
| 20  | Parissyunnanoside E                       | *S. riparia*  | Rhizomes and roots            | [20] |
| 21  | Paris D                                   | *S. riparia*  | Rhizomes and roots            | [20] |
| 22  | Paris H                                   | *S. riparia*  | Rhizomes and roots            | [20] |
| 23  | (25R)-Spirostan-5-en-3β,17β,27-triol-3-O-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside | *S. menisperoides* | Rhizomes                        | [40] |
Table 1 continued

| No. | Name                          | Plant          | Parts                      | Ref. |
|-----|-------------------------------|----------------|----------------------------|------|
| 24  | (255)-Spirostan-5-en-3β,17α,27-triol-3-O-α-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranoside | S. lebrunii | Roots                      | [14] |
|     |                               | S. lebrunii    | Roots                      | [41] |
|     |                               | S. scobinicaulis | Rhizomes and roots       | [21] |
| 25  | (255)-Spirostan-5-en-3β,17α,27-triol-3-O-β-D-glucopyranosyl-(1 → 4)-{α-L-arabinopyranosyl-(1 → 6)}-β-D-glucopyranoside | S. lebrunii | Rhizomes                   | [33] |
|     |                               | S. lebrunii    | Rhizomes                   | [42] |
|     |                               | S. scobinicaulis | Rhizomes and roots       | [21] |
|     |                               | S. scobinicaulis | Rhizomes                   | [43] |
| 26  | (255)-Spirost-5-ene-3β,17α,27-triol-3-O-α-L-rhamnopyranosyl-(1 → 4)-β-D-glucopyranoside | S. menispermoides | Roots                     | [39] |
| 27  | (255)-Spirost-5-ene-3β,17α,27-triol-3-O-β-D-galactopyranoside | S. menispermoides | Rhizomes                   | [33] |
| 28  | (255)-Spirostan-5-en-3β,27-diol-3-O-α-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranoside | S. scobinicaulis | Rhizomes and roots       | [21] |
|     |                               | S. lebrunii    | Roots                      | [14] |
| 29  | Isonarthogenin3-O-α-L-rhamnopyranosyl-(1 → 2)-O-{α-L-rhamnopyranosyl-(1 → 4)}-β-D-glucopyranoside | S. china       | Tubers                     | [30] |
|     |                               | S. scobinicaulis | Rhizomes and roots       | [44] |
|     |                               | S. sieboldii   | Subterranean               | [45] |
|     |                               | S. sieboldii   | Rhizomes                   | [23] |
|     |                               | S. scobinicaulis | Rhizomes                   | [46] |
|     |                               | S. sieboldii   | Subterranean               | [45] |
|     |                               | S. scobinicaulis | Rhizomes and roots       | [28] |
|     |                               | S. china       | Rhizomes                   | [22] |
| 30  | Smilscobinoside A             | S. scobinicaulis | Rhizomes and roots       | [44] |
| 31  | Sieboldiin A                  | S. sieboldii   | Subterranean               | [45] |
| 32  | Sieboldiin B                  | S. sieboldii   | Rhizomes                   | [23] |
|     |                               | S. scobinicaulis | Rhizomes                   | [46] |
|     |                               | S. scobinicaulis | Rhizomes and roots       | [28] |
|     |                               | S. china       | Rhizomes                   | [22] |
| 33  | Sieboldogenin                 | S. lebrunii    | Roots                      | [14] |
|     |                               | S. lebrunii    | Roots                      | [41] |
| 34  | (25R)-5β-Spirostan-3β-ol-6-one-3-O-α-L-arabinopyranosyl-(1 → 4)}-β-D-glucopyranoside | S. lebrunii | Roots                      | [14] |
|     |                               | S. lebrunii    | Roots                      | [41] |
|     |                               | S. sieboldii   | Subterranean               | [45] |
|     |                               | S. lebrunii    | Rhizomes                   | [47] |
|     |                               | S. scobinicaulis | Rhizomes                   | [48] |
| 35  | Smilaxin A                    | S. sieboldii   | Subterranean               | [45] |
| 36  | Smilaxin B                    | S. lebrunii    | Rhizomes                   | [47] |
|     |                               | S. sieboldii   | Rhizomes                   | [23] |
|     |                               | S. scobinicaulis | Rhizomes                   | [48] |
|     |                               | S. scobinicaulis | Rhizomes                   | [23] |
| 37  | Parisvietnaside A             | S. riparia     | Rhizomes and roots        | [20] |
| 38  | Smilaxin C                    | S. sieboldii   | Subterranean               | [45] |
|     |                               | S. sieboldii   | Rhizomes                   | [23] |
|     |                               | S. scobinicaulis | Rhizomes and roots       | [21] |
|     |                               | S. scobinicaulis | Rhizomes and roots       | [21] |
| 39  | (25R)-5β-Spirostan-3β,6β-diol-3-O-β-D-glucopyranosyl-(1 → 4)-{α-L-arabinopyranosyl-(1 → 6)}-β-D-glucopyranoside | S. scobinicaulis | Rhizomes and roots       | [44] |
| 40  | Smilscobinoside B             | S. scobinicaulis | Rhizomes and roots       | [44] |
| 41  | (25R)-5β-Spirostan-3β,17α,27-triol-3-O-β-D-glucopyranosyl-(1 → 4)-{α-L-arabinopyranosyl-(1 → 6)}-β-D-glucopyranoside | S. scobinicaulis | Rhizomes                   | [43] |
|     |                               | S. scobinicaulis | Rhizomes                   | [44] |
| 42  | (25R)-5β-Spirostan-3β-ol-3-O-β-D-glucopyranosyl-(1 → 4)-{β-D-glucopyranosyl-(1 → 6)}-β-D-glucopyranoside | S. medica | Rhizomes                   | [25] |
| 43  | (25R)-5β-Spirostan-3β-ol-3-O-β-D-glucopyranosyl-(1 → 2)-{β-D-glucopyranosyl-(1 → 4)}-β-D-glucopyranoside | S. medica | Rhizomes                   | [25] |
| 44  | Disporoside A                 | S. medica      | Rhizomes                   | [25] |
| 45  | (25R)-5β-Spirostan-3β-ol-3-O-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside | S. medica | Rhizomes                   | [26] |
| No. | Name | Plant | Parts | Ref. |
|-----|------|-------|-------|------|
| 46  | (25R)-5β-Spirostan-3β-ol-3-O-β-D-glucopyranosyl-(1 → 2)\{β-D-glucopyranosyl-(1 → 2)\}[α-L-rhamnopyranosyl-(1 → 4)]-β-D-glucopyranoside | S. medica | Rhizomes | [26] |
| 47  | Smilagenin 3-O-β-D-glucopyranoside | S. medica | Rhizomes | [26] |
| **Furostane-type saponin** | | | | |
| 48  | Methylprotodioscin | S. china | Roots | [8] |
| &nbsp; | | S. menispermoides | Rhizomes | [13] |
| &nbsp; | | S. stans | Roots | [16] |
| &nbsp; | | S. bockii | Roots | [19] |
| &nbsp; | | S. microphylla | Tubers | [18] |
| &nbsp; | | S. china | Tubers | [30] |
| 49  | 26-O-β-D-Glucopyranosyl-(25R)-furostan-5-en-3β,26-diol-22-methoxy-3-O-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside | S. nigrescens | Roots | [49] |
| 50  | 26-O-β-D-Glucopyranosyl-22α-O-methyl-(25R)-furost-5-en-3β,26-diol-3-O-[α-L-rhamnopyranosyl-(1 → 4)]-β-D-glucopyranoside | S. bockii | Roots | [19] |
| 51  | Protodioscin | S. excelsa | Rhizomes | [17] |
| &nbsp; | | S. microphylla | Tubers | [18] |
| &nbsp; | | S. china | Tubers | [30] |
| 52  | Protodiosgenin-3-O-α-L-rhamnopyranosyl-(1 → 4)-α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranoside | S. krausiana | Rhizomes | [50] |
| 53  | 26-O-β-D-Glucopyranosyl-22α-hydroxy-(25R)-furost-5-en-3β,26-diol-3-O-[4-O-acetyl-α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside | S. excelsa | Rhizomes | [17] |
| 54  | 26-O-β-D-Glucopyranosyl-22α-hydroxy-(25R)-furost-5-en-3β,26-diol-3-O-[2-O-acetyl-α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside | S. excelsa | Rhizomes | [17] |
| 55  | 26-O-β-D-Glucopyranosyl-22α-hydroxy-(25R)-furost-5-en-3β,26-diol-3-O-[3-O-acetyl-α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside | S. excelsa | Rhizomes | [17] |
| 56  | 26-O-β-D-Glucopyranosyl-(25R)-furostan-5-en-3β,17α-diol-3-O-α-L-rhamnopyranosyl-(1 → 2)-α-L-rhamnopyranoside | S. scobinicus | Rhizomes | [51] |
| 57  | Protogracillin | S. riparia | Rhizomes and roots | [20] |
| 58  | Parisaponin I | S. riparia | Rhizomes and roots | [20] |
| 59  | Parisunnanoside A | S. riparia | Rhizomes and roots | [20] |
| 60  | Pseudoprotodioscin | S. trinervula | Rhizomes and roots | [32] |
| &nbsp; | | S. menispermoides | Rhizomes | [13] |
| &nbsp; | | S. stans | Roots | [16] |
| &nbsp; | | S. excelsa | Rhizomes | [17] |
| &nbsp; | | S. china | Tubers | [30] |
| &nbsp; | | S. nigrescens | Roots | [49] |
| 61  | 26-O-β-D-Glucopyranosyl-(25R)-furostan-5,20(22)-dien-3β,26-diol-3-O-α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranoside | S. nigrescens | Roots | [49] |
| 62  | 15-Hydroxyprotodioscin | S. china | Tubers | [27] |
| 63  | 15-Methoxyprotodioscin | S. china | Tubers | [27] |
| 64  | 23-Oxoprotodioscin | S. microphylla | Tubers | [18] |
| 65  | 26-O-β-D-Glucopyranosyl-(25S)-5-furosa-(22)-en-3β,26-diol-3-O-α-L-rhamnopyranosyl-(1 → 2)-O-[α-L-rhamnopyranosyl-(1 → 6)]-β-D-glucopyranoside | S. riparia | Roots | [52] |
| No. | Name                           | Plant         | Parts                        | Ref.   |
|-----|--------------------------------|---------------|------------------------------|--------|
| 66  | Pseudoprotocohine              | *S. riparia*  | Rhizomes and roots           | [20]   |
| 67  | 26-β-D-glucopyranosyl-(25R)-3β-furostan-3β,22,26-triol-6-one-3-O-β-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranoside | *S. sieboldii* | Rhizomes                    | [23]   |
| 68  | 26-β-D-glucopyranosyl-(25S)-5β-furostan-3β,22,26-triol-6-one-3-O-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranoside | *S. sieboldii* | Rhizomes and roots           | [29]   |
| 69  | 26-β-D-glucopyranosyl-(25R)-3β-furostan-3β,26-diol-22-methoxy-6-one-3-O-β-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranoside | *S. scobinicaulis* | Rhizomes and roots           | [28]   |
| 70  | 26-β-D-glucopyranosyl-(25R)-5β-furostan-3β,26-diol-22-methoxy-6-one-3-O-β-D-glucopyranoside | *S. scobinicaulis* | Rhizomes and roots           | [28]   |
| 71  | 26-β-D-glucopyranosyl-(25S)-5β-furostan-3β,26-diol-22α,26β-methoxy-3-O-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranoside | *S. officinalis* | Roots                        | [29]   |
| 72  | (25S)-26-β-D-glucopyranosyl-3β,5β,22x-furostan-3,22,26-triol-3-O-β-L-arhamnopyranosyl-(1 → 2)-O-β-D-glucopyranosyl-(1 → 2)-O-β-D-glucopyranoside | *S. aspera subsp. mauritanica* | Roots                        | [10]   |
| 73  | Asparagoside E                 | *S. aspera subsp. mauritanica* | Roots                      | [10]   |
| 74  | Asparoside A                   | *S. aspera subsp. mauritanica* | Roots                      | [10]   |
| 75  | Asparoside B                   | *S. aspera subsp. mauritanica* | Roots                      | [10]   |
| 76  | 26-β-D-glucopyranosyl-(25S)-5β-furostan-3β,22α,26β-methoxy-3-O-β-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranoside | *S. officinalis* | Roots                        | [29]   |
| 77  | 26-β-D-glucopyranosyl-(25S)-5α-furostan-3β,22α,26β-methoxy-3-O-β-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranoside | *S. officinalis* | Roots                        | [29]   |
| 78  | 26-β-D-glucopyranosyl-(25S)-5α-furostan-3β,6β,22α,26α-tetraol-3-O-β-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranoside | *S. officinalis* | Roots                        | [29]   |
| 79  | Sarsaparilloside B             | *S. ornate*   | Rhizomes and roots           | [11]   |
| 80  | Sarsaparilloside C             | *S. ornate*   | Rhizomes and roots           | [11]   |
| 81  | Sarsaparilloside               | *S. ornate*   | Rhizomes and roots           | [11]   |
| 82  | Δ(20,22)-Sarsaparilloside      | *S. ornate*   | Rhizomes and roots           | [11]   |
| 83  | Riparoside A                   | *S. riparia*  | Rhizomes and roots           | [53]   |
| 84  | Smilaxchinoside A              | *S. china*    | Tubers                      | [30]   |
| 85  | (25R)-Smilaxchinoside A        | *S. china*    | Tubers                      | [30]   |
| 86  | Smilaxchinoside B              | *S. riparia*  | Rhizomes and roots           | [32]   |
| 87  | Smilaxchinoside C              | *S. riparia*  | Rhizomes and roots           | [32]   |
| 88  | Dioscoreside E                 | *S. riparia*  | Rhizomes and roots           | [20]   |
| 89  | (25R)-5α-Furostan-3β,26-diol-20(22)-en-6-one-26-O-β-D-glucopyranoside | *S. scobinicaulis* | Rhizomes and roots           | [28]   |
| 90  | (23R,25R)-5α-Furostan-3β,23,26-triol-20(22)-en-6-one-26-O-β-D-glucopyranoside | *S. scobinicaulis* | Rhizomes and roots           | [28]   |
| 91  | 26-β-D-glucopyranosyl-(25R)-5α-furostan-3β,26-diol-20(22)-en-6-one-3-O-β-L-arabinopyranosyl-(1 → 6)-β-D-glucopyranoside | *S. scobinicaulis* | Rhizomes and roots           | [28]   |
| 92  | (25S)-5β-Furostan-1β,2β,3β,5β,22α,26-hexaol-26-O-β-D-glucopyranoside | *S. aspera*   | Rhizomes                     | [31]   |
| 93  | 26-β-D-glucopyranosyl-(25S)-5β-furostan-1β,2β,22α,26-tetraol-1-O-β-D-glucopyranoside | *S. aspera*   | Rhizomes                     | [31]   |

**Pregnate-type saponin**

| No. | Name                           | Plant         | Parts                        | Ref.   |
|-----|--------------------------------|---------------|------------------------------|--------|
| 94  | Trinervuloside A               | *S. trinervula* | Rhizomes and roots           | [32]   |
open chain saponins in another way of saying [34]. S. riparia saponins, from which compounds 18–22, 57–59, 66, 85, 87, 95–97, and 102 were identified, exhibited the synergistic effects with allopurinol in reducing serum uric acid levels and increasing the urine uric acid level in a hyperuricemic mouse model [20]. The attenuation of hyperuricemia-induced renal dysfunction was linked to the inhibition of serum and hepatic xanthine oxidase, the down-regulation of renal mURAT1 and GLUT9, and the up-regulation of mOAT1. Structures of steroidal saponins (94–104) are shown in Fig. 5.

3 Biological Activities of Steroidal Saponins

Steroidal saponins are considered to be responsible for pharmacological properties of Smilax species. Many pharmacological in vitro and in vivo studies revealed significant biological activities, including cAMP phosphodiesterase inhibitory, anti-fungal, cytotoxic, and anti-inflammatory activities.

3.1 cAMP Phosphodiesterase Inhibitory Activity

The cAMP phosphodiesterase is an enzyme that degrades the phosphodiester bond in the second messenger molecule cAMP. It regulates the localization, duration, and amplitude of cyclic nucleotide signaling within subcellular domains. Compounds 1, 2, 29 and 60, showed cAMP phosphodiesterase inhibitory activities with IC50 values of 102, 55, 93, and 47 µM, respectively, which were almost equal to that of positive control papaverine (IC50 = 30 µM) [8]. Laxogenin glycosides 34, 35, and isospirostanol glycoside 38 displayed cAMP phosphodiesterase inhibitory activities with IC50 values of 83, 34, and 32 µM, respectively. While compound 36, with an additional hydroxyl substitution on C-27 in comparison with compound 34, showed no obvious inhibitory activity. Furostane glycosides 67–68 were inactive [23].

3.2 Antifungal Activity

C27 steroidal glycosides are well known for their antifungal activities [35]. Sarsasapogenin glycosides 7, 8, and four furostane glycosides 72–75, were tested for their antifungal activity. Compound 8 showed antifungal activity against three human pathogenic species, Candida albicans, C. glabrata, and C. tropicalis, with minimal inhibitory concentration (MIC) values of 25, 25 and 50 µg/mL, respectively. While compounds 7 and 72–75 showed no obvious antifungal activity at concentration of 200 µg/mL [10]. Six smilagenin glycosides 42–47 and a furostane glycoside 71 were also evaluated for their antifungal activities against these three pathogenic species. Compounds 42–46 demonstrated moderate antifungal activity with MIC values between 12.5 and 50 µg/mL [25, 26]. With regard to

| No. | Name          | Plant         | Parts                          | Ref.   |
|-----|---------------|---------------|--------------------------------|--------|
| 95  | Riparoside B  | S. riparia    | Rhizomes and roots             | [20]   |
| 96  | Timosaponin J | S. riparia    | Rhizomes and roots             | [55]   |
| 97  | Timosaponin K | S. riparia    | Rhizomes and roots             | [20]   |
| 98  | Trinervulose B| S. trinervula | Rhizomes and roots             | [20]   |
| 99  | Pregna-5,16-diene-3β-ol-20-one-3-O-[2α-L-rhamnopyranosyl-(1→4)2]-β-D-glucopyranoside | S. nigrescens | Roots                          | [15]   |
| 100 | Pregna-5,16-diene-3β-ol-20-one-3-O-[2α-L-rhamnopyranosyl-(1→4)2]-β-D-glucopyranoside | S. bockii    | Roots                          | [19]   |
| 101 | Pregna-5,16-diene-3β-ol-20-one-3-O-[2α-L-rhamnopyranosyl-(1→4)2]-β-D-glucopyranoside | S. microphylla | Tubers                        | [18]   |
| 102 | Pallidifloside D | S. riparia | Rhizomes and roots             | [20]   |
| 103 | Anguviside XV  | S. trinervula | Rhizomes and roots             | [32]   |
| 104 | Smilaxchinoside D | S. china | Tubers                        | [30]   |
Fig. 5 Structures of compounds 84–104
structure–activity relationships between the saponin structures and antifungal activities, the following points were suggested: (1) the close F ring is essential for the antifungal activities. (2) The cis/trans fusion between rings A and B has no significant difference in terms of antifungal activities. (3) Steroidal saponins bearing a saccharidic chain with more than one sugar were better antifungal agents (Figs. 6, 7).

Fig. 6 Sugar residues of S₁–S₁₆
3.3 Cytotoxicity

Spirostane glycoside 9 and four furostane glycosides 79–82 were evaluated for their cytotoxicities against six human cancer cells (NFF, Hela, HT29, MCF7, MM96L, and K562). Compounds 79 and 80 selectively inhibited the proliferation of the HT29 colon cancer cell lines with IC\textsubscript{50} values of 4.8 and 5.0 \(\mu\text{g/mL}\), respectively; while
compounds 80 and 81 showed significant cytotoxicities against MCF7 cell lines with IC_{50} values of 9.5 and 3.4 µg/mL, respectively [11]. Compounds 24, 25, 28, 38, and 39, were evaluated for the cytotoxicities against three human cancer cell lines (A549, LAC and Hela). Only compound 38 possessed significant cytotoxicities with IC_{50} values of 3.70, 5.70 and 3.64 µM, respectively [21]. Another cytotoxic compound is isoprostane glycoside 32, which displayed potent cytotoxicities against the Hela and SMMC-7221 cancer cell lines with IC_{50} values of 9.73 ± 1.64 and 21.54 ± 1.64 µM, respectively [28]. The above results indicated that the hydroxyl substitutions on C-6 or C-17 of isoprostane glycosides decrease the cytotoxicities. Furfurostane glycoside 69 showed cytotoxicities against the Hela and SMMC-7221 cancer cell lines with IC_{50} values of 18.79 ± 1.12 and 28.57 ± 1.57 µM, respectively; while the demethylated analogue 67 and the dehydrated analogues 89–91 showed no obvious cytotoxicities. Additionally, the sapogenin 70 was less cytotoxicities than that of corresponding glycoside 69 [28]. Compounds 11, 60, 85, 88, 94, 98 and 103, were tested for their cytotoxicities against SH-SYSY, SGC-7901, HCT-116 and Lovo cell lines. Only compound 98 showed significant cytotoxicities against SGC-7901 and HCT-116 cell lines with IC_{50} values of 8.1 and 5.5 µM, respectively [32].

3.4 Anti-inflammatory Activity

The aqueous extracts of the tubers of S. china showed the similar anti-inflammatory effects in vivo to that of acetylsalicylic acid (200 mg/kg, i.g.) [36]. Sieboldogenin (33) showed significant lipoxygenase inhibition activity with IC_{50} value of 38 µM. It also exhibited significant inhibition on carrageenan-induced hind paw oedema at the doses of 10 and 50 mg/kg [22]. Compounds 13, 14, 16, 48, 84–87, and 104 inhibited the lipopolysaccharide (LPS) induced prostaglandin E_{2} (PGE_{2}) production in murine peritoneal macrophages by 81.5, 81.7, 76.5, 82.5, 76.1, 59.1, 78.5, 75.9, and 82.0%, respectively, at the concentration of 10 µM. These nine compounds also moderately inhibited the tumor necrosis factor α (TNF-α) production on LPS stimulated murine peritoneal macrophages [30].

4 Prospects

The plants of the genus Smilax are widely spread in China. Their medical use for the treatment of inflammation and rheumatism has a long history in folk China. Previous studies on chemical constituents of Smilax sp. yielded diversified steroidal saponin. However, the biological activities studies of these isolated steroidal saponins lag behind, especially in anti-inflammatory related activities.
