REVIEW

Smilax glabra Roxb.: A Review of Its Traditional Usages, Phytochemical Constituents, Pharmacological Properties, and Clinical Applications

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Abstract: *Smilax glabra Roxb.* (SGB) is a medicinal plant widely distributed in 17 countries worldwide. It is the primary raw material of the world-famous and best-selling functional food and beneficial tea. SGB was first recorded in Ben Cao Jing Ji Zhu of the Southern and Northern Dynasties (420–589 AD) and was reported for nutritional and medicinal properties for thousands of years. This review searched PubMed, Web of Science, and other databases for relevant literature on SGB species until April 2022. It aims to provide more integrated thinking, detailed awareness, and better knowledge of SGB. More than 200 chemical components have been discovered, including flavonoids, phenolic, phenolic acids, stilbenes, organic acids, phenylpropanoids, and others. Previous studies have demonstrated that SGB and its active ingredients show a wide range of pharmacological effects, including anti-infective, anti-cancer, anti-inflammatory, antioxidant, cardiovascular protection, etc. However, many studies on the biological activity of this plant were mainly based on crude extracts and active ingredients, and there is a lack of clinical studies and toxicity studies to support the development of drug design, development, and therapy. In summary, this review will provide specific and valuable suggestions and guidelines for further research and application of this plant in the medicinal field.

Keywords: *Smilax glabra* Roxb, astilbin, traditional usages, phytochemical constituents, pharmacological properties, clinical applications

Introduction

Smilax glabra Roxb. (SGB) is the rhizome of the Liliaceae plant, named *Tu fuling* in Chinese. There are more than 300 species of the *Smilax* genus in the world, most of which grow on hillsides, barren hills, and semi-shady land near forests.[1] They are rich in resources and are widely distributed in 17 countries globally, including Asia, Europe, South America, etc. And it has been used as food and folk medicine in many countries for a long time.

SGB has been widely used worldwide due to its evident pharmacological activity for treating syphilitic, poisoned sores, pathological leucorrhea, eczema itching, carbuncle poisoning, and other diseases.[2–4] Modern research has shown that SGB mainly includes flavonoids,[5–8] phenolic and phenolic aids,[9,10] stilbene and organic acids,[11–13] phenylpropanoids,[13,14] and others.[14–16] Pharmacological studies have shown that the active ingredients in SGB have a variety of pharmacological effects, including anti-infective,[17–19] anti-cancer,[20–22] anti-inflammatory,[16,23,24] antioxidant,[25,26] and cardiovascular protection etc.[27–29] Simultaneously, SGB is the primary raw material of the world-famous and best-selling functional food, soup and beneficial tea. It has the functions of nourishing yin and detoxification due to heat and humidity. In addition, the rhizome of SGB is rich in starch and can also be used to make cakes or winemaking.[30–33]

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This product is cylindrical, flat or irregular, with nodular swelling, short branches, 5–22cm in length and 2–5cm in diameter. The surface is yellow-brown or gray-brown, uneven, with hard, fibrous root residues, round bud marks on the top of the branches, irregular cracks in the outer skin, and residual scales and leaves. The slices are elliptical or irregular, 1–5mm thick, with rough edges; the cut surface is white to light reddish brown, powdery, punctate vascular bundles.

This study conducted the latest and most comprehensive review of SGB, focusing on its traditional usages, phytochemical constituents, pharmacological properties, and clinical applications. It provides a basis for studying pharmacological and phytochemicals' biological activity. This review aims to ensure the medicinal safety of SGB and provide guidance for its application in the medicinal field.

Research Methodology

This review searched relevant literature about SGB species from PubMed, Sci-Finder, Google Scholar, Wiley, Web of Science, Springer, Elsevier, Plant List Database, Weipu, and China Knowledge Network. It includes medical books, Ph.D., and MSc published research before April 2022. Data inclusion criteria included (a) published scientific manuscripts; (b) studies on ethnopharmacology; (c) plant extracts in different solvents; (d) mechanisms of action of plant extracts and their plant components; (e) Computational, in vitro, and in vivo studies.

Traditional Usage and the Distribution of *Smilax glabra* Roxb

Traditional Uses of *Smilax glabra* Roxb

SGB was first recorded in *Ben Cao Jing Ji Zhu* of the Southern and Northern Dynasties (420–589 AD) and written by Tao Hongjing. In the Tang Dynasty (618–907 AD), *Ben Cao Shi Yi* records that SGB could be used as food. The *Ben Cao Tu Jing*, written by Su Song in the Song Dynasty (AD 960-AD 1279), first recorded that SGB was sweet, calm in nature, non-toxic, and had a record of its efficacy. The *Ben Cao Gang Mu*, written by Li Shizhen in the Ming Dynasty (AD 1368-AD 1644), recorded that SGB could cure "syphilitic skin lesion". Another herbal directory in the Ming Dynasty, *Dian Nan Ben Cao*, also recorded the efficacy of SGB and pointed out that it is the best medicine for treating syphilis. Until the Qing Dynasty (AD1636-AD1912), *Ben Cao Bei Yao*, written by Wang Ang, further described SGB. The effects were anti-infective, removing rheumatism, facilitating urination, stopping diarrhea, and treating muscles and bones. The modern 2020 edition of Chinese Pharmacopoeia described SGB as the dry rhizome of the Liliaceae family *Smilax glabra*, treating for syphilis, turbidity, and carbuncle, scrofula, scabies (Chinese Pharmacopoeia Commission, 2020).

The Distribution of *Smilax glabra* Roxb. Throughout the World

SGB is geographically distributed in China, Nepal, Pakistan, Mexico, Viet Nam, India, Cambodia, Thailand, Bangladesh, Belgium, Lao People's Democratic Republic, Brazil, Myanmar, Australia, Malaysia, Japan, and the United States of America. In Asian countries, SGB is commonly used in foods, teas, and herbs, while in the West, SGB is an ingredient in draft beer and other beverages due to its foaming properties. And according to the database of the Global Biodiversity Information Facility (https://www.gbif.org/) and consultation of Flora of countries, Asia, including China (Taiwan, Hong Kong, and Macao, etc), harbors the most significant proportion of SGB-producing sites. In Thailand, traditional practitioners have widely used it to treat cancer, AIDS, and other infectious diseases[17,34] (Figure 1).

Phytochemical Constituents of the *Smilax glabra* Roxb

More than 200 compounds, including flavonoids, phenolic and phenolic acids, stilbenes, organic acids, and phenylpropanoids, have been isolated and identified from SGB. Flavonoids, phenolics, and phenylpropanoids are the most widely studied and used biologically active ingredients and are considered essential active ingredients. For example, astilbin, neoastilbin, isoastilbin, and resveratrol may be used as markers for future quality control and quantitative plant verification. It shows the compounds isolated and identified from SGB (Table 1) and the main biologically active compounds.
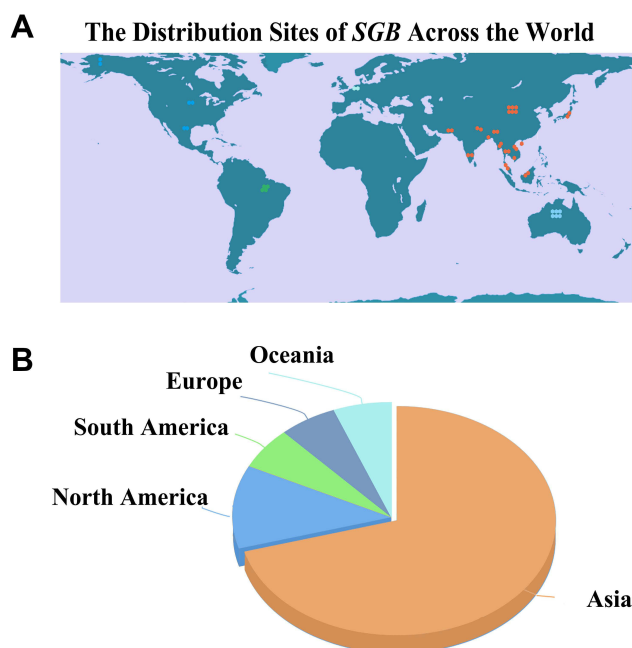
Figure 1 Geographical distribution of SGB throughout the world. (**A**) Planar map of the distribution of SGB. (**B**) Distribution in all continents of the world. (A total of 17 countries were searched).

Flavonoids and Flavonoid Glycosides

Flavonoids are pigments derived from 2-phenylchromone as the parent nucleus, including the isomers of flavonoids and their hydrogenated and reduced products. Flavonoids can be divided into different categories according to the type of parent nucleus, flavones, flavonols, dihydroflavones, dihydroflavonols, isoflavones, dihydroisoflavones, chalcones, flavones, anthocyanidins, biflavones, and others. Flavonoids in SGB are mainly dihydroflavonols, including taxifolin, astilbin, neoastilbin, isoastilbin, engeletin, isoengeletin, etc (Figure 2). Flavonols include quercetin and dihydro flavonoids include naringenin. Content range of (-)-epicatechin, 5-O-caffeoylshikimic acid, neoastilbin, astillbin, neoisoastilbin, isoastilbin and engeletin in 84 pieces of SGB medicinal samples were in the range of 1.381, 9.913, 3.673, 27.08, 1.181, 4.833, 2.754 mg/g, respectively. The representative component of astilbin content is about 1–2%, accounting for the largest proportion of total flavonoids. And it exhibits pharmacological activities such as antioxidant,[35–42] actions on the cardiovascular system,[43,44] antimicrobial,[45–49] immunosuppressive,[50–54] and anti-inflammatory.[38,55–59] In the Chinese Pharmacopoeia Commission (2020), astilbin is used for quality inspection of SGB, with a minimum content of 0.45%.[11,14,60–62]

Phenolic and Phenolic Acids

The phenolic acid compound is an aromatic carboxylic acid compound whose benzene ring is substituted by multiple phenolic hydroxyl groups. The structure has more phenolic hydroxyl groups substituted, so its structure is not stable Studies have shown that phenolic acid compounds in SGB include chromones, phenol glycosides, acetophenones, phenethyl alcohols, and caffeic acid esters. Among them, eurryphin, kelampayoside A, osmanthuside F, and syringic acid are the primary phenolic acids in SGB (Figure 3). These compounds have solid pharmacological effects as antioxidants, antibacterial, anti-inflammatory, hypolipidemic, etc.[9,10]

Stilbene

Stilbene compounds refer to the general term for a class of substances with a stilbene core or its polymers. This type of substance has a low content in the normal tissues of the plant kingdom. Mono- and phenolic hydroxytoluene compounds are mainly found in plant tissues in the parenchyma cells of the xylem. The stilbene compounds in SGB are mostly

Table 1 Chemical Constituents Isolated from SGB

No.	Compounds	Part	Reference
Flavonoids and flavonoid glycosides			
1	Taxifolin	Rhizomes	[5]
2	Naringenin	Rhizomes	[6]
3	Dihydrokaempferol	Rhizomes	[7]
4	Sakuranetin	Rhizomes	[7]
5	Isoastilbin	Rhizomes	[6]
6	Astilbin	Rhizomes roots	[14]
7	Neoisoastilbin	Rhizomes	[60]
8	Neoastilbin	Rhizomes	[7]
9	Engeletin	Rhizomes	[12]
10	Arthromerin B	Rhizomes	[7]
11	Sinensin	Rhizomes	[7]
12	(2R,3R)-taxifolin 3'-O-A-D-glucopyranoside	Rhizomes	[60]
13	(2S,3S)-glucodistylin	Rhizomes	[7]
14	Isoengeletin	Rhizomes	[14]
15	Quercetin-4'-O-β-D-pyr-anglucoside	Rhizomes	[61]
16	(-)-epicatechin	Rhizomes	[11]
17	(+)-catechin	Rhizomes	[7]
18	Cinchonain Ib	Rhizomes	[7]
19	Cinchonain Ia	Rhizomes	[7]
20	Apigenin	Rhizomes	[7]
21	Quercetin	Rhizomes	[7]
22	Luteolin	Rhizomes	[7]
23	Myricetin	Rhizomes	[7]
24	Kukulkanin B	Rhizomes	[7]
25	Smilachromanone	Rhizomes	[7]
26	4,4', 6-trihydroxyaurone	Rhizomes	[7]
27	Aureusidin	Rhizomes	[7]
28	7,6'-dihydroxy-3'-methox-yisoflavone	Roots	[7]
29	(2R, 3R) -taxifolin-3'-O-β-D-pyr angl-ucoside	Rhizomes	[60]
30	2(S)-5-hydroxy-6, 8-dimethoxyflavanone-7-O-beta-D-glucopyranosyl-(16)-O-beta-D-glucopyranoside	Rhizomes	[8]
31	5-hydroxy-3, 8-dimethoxyflavone-7-O-beta-D-glucopyranosyl-(16)-O-beta-D-glucopyranoside	Rhizomes	[8]
32	3, 7-dihydroxy-8-methoxyflavone-6-O-beta-D-glucopyranosyl-(16)-O-beta-D-glucopyranoside	Rhizomes	[8]
33	Dihy-droquercetin	Rhizomes	[8]
Phenolic and phenolic acids			
34	Smiglabrone A	Rhizomes	[7]
35	Smiglabrone B	Rhizomes	[7]
36	Smilachromanone	Rhizomes	[7]
37	Smiglastilbene	Rhizomes	[7]
38	Smiglactone	Rhizomes	[7]
39	Smiglabrol	Rhizomes	[7]
40	Vanillin	Rhizomes	[7]
41	p-hydroxy-benzaldehyde	Rhizomes	[7]
42	Acetovanillone	Rhizomes	[7]
43	(+)-scytalone	Rhizomes	[7]
44	Glucosyringic acid	Rhizomes	[7]
45	Protocatechuic acid	Rhizomes	[7]
46	3-methoxygallic acid	Rhizomes	[7]
47	Vanillic acid 1-O-β-D-glucopyranosyl ester	Rhizomes	[7]
48	Hydroxytyrosol	Rhizomes	[7]
49	Lasiodiplodin	Rhizomes	[9]
50	De-O-methyllasiodiplodin	Rhizomes	[9]
51	Resveratrol-3-O-β-D-gluco-pyranoside	Rhizomes	[10]
52	3,4,5-tri-methoxyphenyl-1-O-[β-D-apiofuranosyl-(1-6)]-β-D-glucopyranoside	Rhizomes	[10]
53	3,4,5-tri-methoxyphenyl-1-O-β-D-glucopyranoside	Rhizomes	[10]

(*Continued*)

Table 1 (Continued).

No.	Compounds	Part	Reference
54	3,4-di-hydroxyphenothyl-3-O-β-D-glucopyranoside	Rhizomes	[10]
55	2,4,6-trihydroxy acetophenone-2,4-di-O-β-D-glucopyranoside	Rhizomes	[10]
56	8,8'-bisdihydrosyringeninglucoside	Rhizomes	[10]
Stilbene and organic acids			
57	Resveratrol	Rhizomes	[11]
58	Trans-resveratrol	Rhizomes	[7]
59	Trans-piceid	Rhizomes	[7]
60	Piceatannol	Rhizomes	[7]
61	Syringic acid	Rhizomes	[7]
62	5-O-caffeoylshikimic acid	Rhizomes	[12]
63	2-methyl-succinic acid	Rhizomes	[7]
64	Shikimic acid	Rhizomes	[13]
65	Ferulic acid	Rhizomes	[13]
66	Palmitic acid	Rhizomes	[14]
67	Lignoceric acid	Rhizomes	[13]
68	Succinic acid	Rhizomes	[14]
Phenylpropanoids and lignans			
69	Trans-caffeic acid	Rhizomes	[7]
70	5-O-caffeoylshikimic acid	Rhizomes	[7]
71	3-O-p-coumaroylshikimic acid	Rhizomes	[7]
72	(2S)-1,2-O-di-trans-p-coumaroylglycerol	Rhizomes	[7]
73	Juncusyl ester B	Rhizomes	[7]
74	1-O-p-coumaroylglycerol	Rhizomes	[7]
75	(-)-secoisolariciresinol	Rhizomes	[7]
76	4-ketopinoresinol	Rhizomes	[7]
77	Smiglabranol	Rhizomes	[7]
78	(+)-lyoniresinol	Rhizomes	[7]
79	KompasinolA	Rhizomes	[7]
80	Aiphanol	Rhizomes	[7]
81	Smiglaside A	Rhizomes	[94]
82	Smiglaside B	Rhizomes	[94]
83	Smiglaside C	Rhizomes	[94]
84	Smiglaside D	Rhizomes	[94]
85	Smiglaside E	Rhizomes	[94]
86	Helonioside A	Rhizomes	[94]
87	(3,6-di-O-feruloyl)-b-D-fructofuranosyl-(3,6-di-O-acetyl)-a-D-glu-copyranoside	Rhizomes	[94]
88	Smiglanin	Rhizomes	[7]
89	Smiglabranol	Rhizomes	[15]
90	Syringaresinol	Rhizomes	[9]
91	1,4-bis(3,4,5-trimethoxyphenyl)-2,3-bis(hydroxymethyl)-1,4-butanediol	Rhizomes	[94]
92	Methylcaffeate	Rhizomes	[94]
93	3-O-β-D-glucopyranosyl-1-(40-hydroxy-30, 50-dimeth oxyphenyl)-1-propanone	Rhizomes	[96]
94	(+)-syringaresinol-4-O-β-D-glucopyranosyl-(1-6)-β-D-glucopyranoside	Rhizomes	[94]
Steroids and steroid glycosides			
95	β-sitosterol	Rhizomes	[14]
96	Daucosterol	Rhizomes	[14]
97	Stigmasterol	Rhizomes	[97]
98	Stigmasterol-3-O-β-D-gluco-pyranoside	Rhizomes	[97]
99	Diosgenin	Rhizomes	[99]
100	Smilagenin	Rhizomes	[98]
101	β-sitosterol palmitate	Rhizomes	[61]
Volatile oil			
102	Heptanoic acid, isopropyl ester	Rhizomes	[14]
103	Pentanoic acid, propyl ester	Rhizomes	[14]
104	Butanedioic acid, diethyl ester	Rhizomes	[14]

(*Continued*)

Table 1 (Continued).

No.	Compounds	Part	Reference
105	Caproic acid, methyl ester	Rhizomes	[14]
106	Hexanedioic acid, ethylmethyl ester	Rhizomes	[14]
107	Pentanoic acid 4-oxo-, butyl ester	Rhizomes	[14]
108	Nonanoic acid, ethyl ester	Rhizomes	[14]
109	Butane,1,1,1''-methylidynetris(oxy) tris	Rhizomes	[14]
110	Octane diacid, dimethyl ester	Rhizomes	[14]
111	Nonane diacid, dimethyl ester	Rhizomes	[14]
112	Heptane- diacid, dimethyl ester	Rhizomes	[14]
113	Nonanediacid, ethyl methyl ester	Rhizomes	[14]
114	Longipinanes	Rhizomes	[14]
115	3-methyldodecane	Rhizomes	[14]
116	Dodecanoic acid, methyl ester	Rhizomes	[14]
117	4-dodecanoic acid, methyl ester	Rhizomes	[14]
118	Butanedioic acid, dibutylester	Rhizomes	[14]
119	Pentanedioic acid, dibutyl ester	Rhizomes	[14]
120	Dodecanoic acid, ethyl ester	Rhizomes	[14]
121	Butanoic acid, octyl ester	Rhizomes	[14]
122	3-hydroxy-dodecanoic acid methyl ester	Rhizomes	[14]
123	Honandioic acid, diethyl ester	Rhizomes	[14]
124	Hexadecane	Rhizomes	[14]
125	Tetradecanoic acid, methyl ester	Rhizomes	[14]
126	Tetradecanoic acid, ethyl ester	Rhizomes	[14]
127	2,4-dimethyl-3-hexanone	Rhizomes	[14]
128	Pentadecanoic acid, methyl ester	Rhizomes	[14]
129	Decanedioic acid, diethyl ester	Rhizomes	[14]
130	5-hexadecenoic acid, ethyl ester	Rhizomes	[14]
131	Pentadecanoic acid, ethyl ester	Rhizomes	[14]
132	5,9-tetradecadienoic acid, methyl ester	Rhizomes	[14]
133	Hexadecanoic acid, methyl ester	Rhizomes	[14]
134	1,1-benzenedicarboxylic acid, butyl ester	Rhizomes	[14]
135	10-hexadecenoic acid, ethyl ester	Rhizomes	[14]
136	Hexadecenoic acid	Rhizomes	[14]
137	Heptadecanoic acid	Rhizomes	[14]
138	Hexadecanoic acid, ethyl ester	Rhizomes	[14]
139	Eicosane	Rhizomes	[14]
140	Heptadecanoic acid, methyl ester	Rhizomes	[14]
141	9,12-octadecadienoic acid,methyl ester	Rhizomes	[14]
142	7-octadecenoic acid, methyl ester	Rhizomes	[14]
143	16-octadecenoic acid, methyl ester	Rhizomes	[14]
144	Octadecanoic acid, methyl ester	Rhizomes	[14]
145	9,10-octadecadienoic acid, ethyl ester	Rhizomes	[14]
146	8-octadecenoic acid, ethyl ester	Rhizomes	[14]
147	9-octadecenoic acid, ethyl ester	Rhizomes	[14]
148	Octadecanoic acid 2-methyl methyl ester	Rhizomes	[14]
149	Octadecanoic acid, ethyl ester	Rhizomes	[14]
150	Nonane	Rhizomes	[15]
151	L-linalool	Rhizomes	[15]
152	1-terpineol	Rhizomes	[15]
153	L-borneol	Rhizomes	[15]
154	Terpinen-4-ol	Rhizomes	[15]
155	Alpha-Terpineol	Rhizomes	[15]
156	(-)-bormylacetate	Rhizomes	[15]
157	(E,E)-2,4-decadienal	Rhizomes	[15]
158	Dihydrop-Ionon	Rhizomes	[15]
159	a-cedrol	Rhizomes	[15]

(*Continued*)

Table 1 (Continued).

No.	Compounds	Part	Reference
160	B-eudesmol	Rhizomes	[15]
161	a-eudesmol	Rhizomes	[15]
162	Myristic acid	Rhizomes	[15]
163	Methyl palmitate	Rhizomes	[15]
164	8,11-octadecadienoic acid	Rhizomes	[15]
165	Methyl linolenate methyl ester	Rhizomes	[15]
166	Linoleic acid	Rhizomes	[15]
167	Stearic acid	Rhizomes	[15]
168	Docosane	Rhizomes	[15]
169	Tricosane	Rhizomes	[15]
170	Hexanal	Rhizomes	[16]
171	Phenylethylene	Rhizomes	[16]
172	7-methyl-7H-Dibenzo[b, g]carbazole	Rhizomes	[16]
173	Octanal	Rhizomes	[16]
174	D-Limonene	Rhizomes	[16]
175	g-Terpinene	Rhizomes	[16]
176	Nonanal	Rhizomes	[16]
177	(-)-4-Terpineo	Rhizomes	[16]
178	Decanal	Rhizomes	[16]
179	Tridecane	Rhizomes	[16]
180	Dodecanal	Rhizomes	[16]
181	11-Diacetoxydodecane	Rhizomes	[16]
182	Caryophyllenel	Rhizomes	[16]
183	Geranylacetone	Rhizomes	[16]
184	2,5-bis(1,1-dimethylethyl)-Phenol	Rhizomes	[16]
185	Nonahexacontanoic acid	Rhizomes	[16]
186	Hentriacontane	Rhizomes	[16]
187	7,9-dimethyl-Hexadecane	Rhizomes	[16]
188	2,2,5,5-tetramethylbiphenyl	Rhizomes	[16]
189	7-Methyl-octadecane7	Rhizomes	[16]
190	Pristane	Rhizomes	[16]
191	1-(hexadecyloxy)-Hexadecane	Rhizomes	[16]
192	2,6,10,14-tetramethyl-Octadecane	Rhizomes	[16]

resveratrol, and resveratrol-3-O-β-D-pyranoglucoside, which have anti-inflammatory,[63–67] antioxidant,[68–70] anti-cancer,[71] and other activities (Figure 4).[72–76]
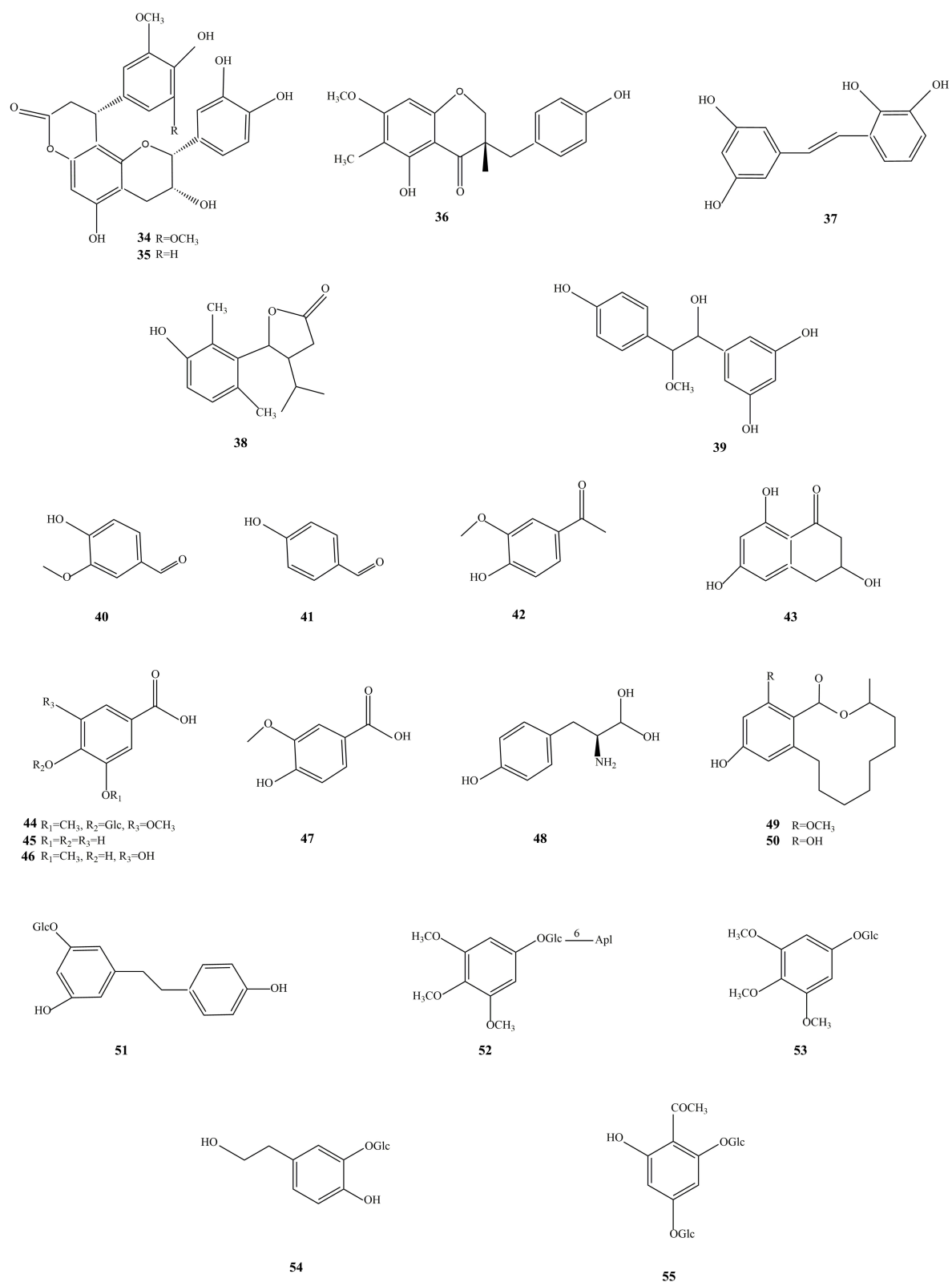
Organic Acids

Organic acids refer to organic compounds with acidity. Organic acids include natural organic acids and synthetic organic acids. Natural organic acids are mainly organic acids with a specific physiological activity extracted from plants in nature. In contrast, synthetic organic acids are organic acids obtained through chemical synthesis, enzymatic catalysis, and microbial fermentation. SGB contains natural organic acids, including succinic acid, palmitic acid, ferulic acid, shikimic acid, oleic acid, linoleic acid, 2-methyl succinic acid, oxalic acid, etc, which have to protect against cardio-vascular disease,[77–84] anti-cancer,[85–93] antibacterial, anti-inflammatory, hypoglycemic, antioxidant (Figure 4).[12,13]
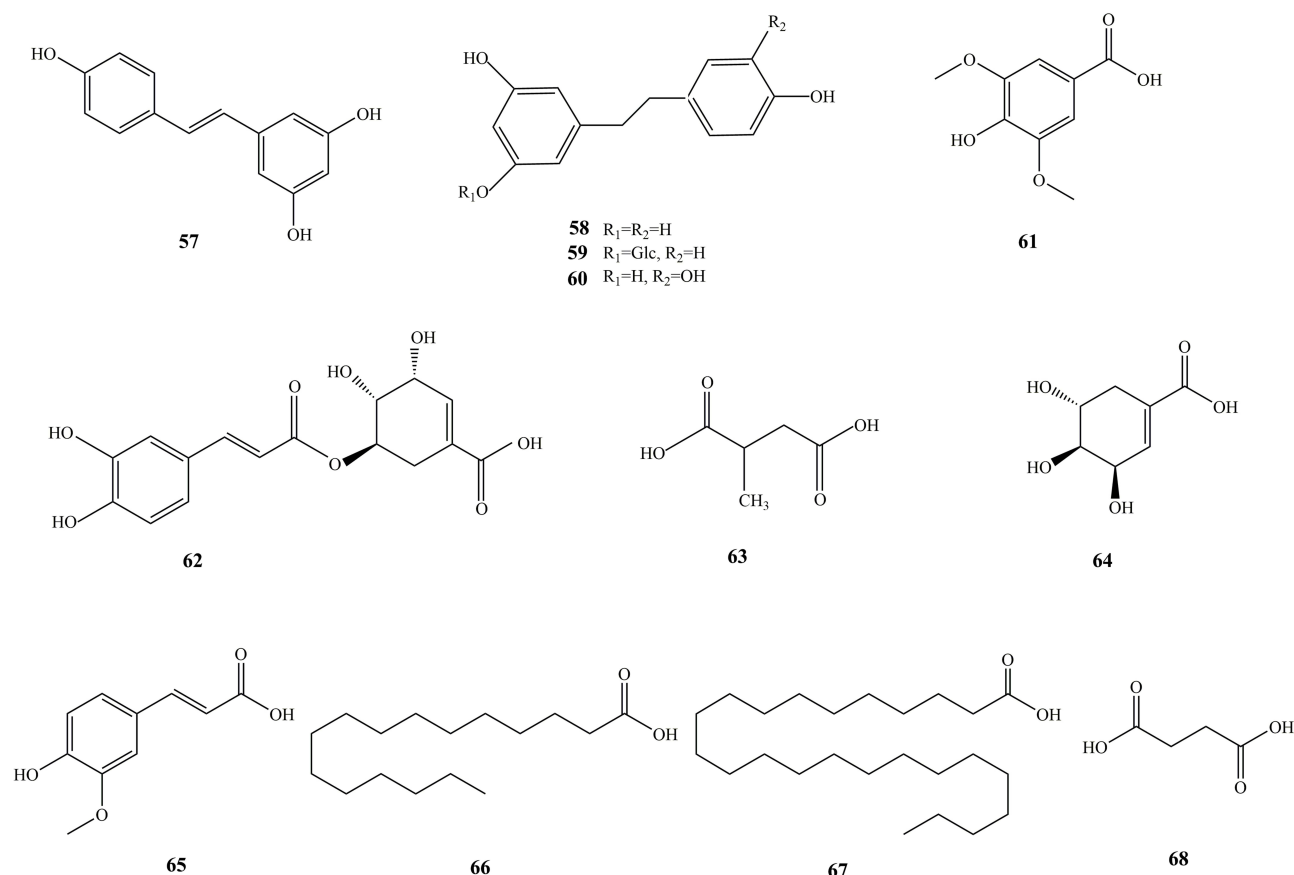
Phenylpropanoids

Phenylpropanol is a naturally occurring compound composed of a benzene ring connected with three straight-chain carbons (C6-C3 groups). It generally has a phenol structure and is a phenolic substance. Studies have shown that the phenylpropanoids with a core structure in SGB include Smilax in A, B, C, D, E (Smiglaside A-E), Helonioside A, and so on. Mainly include anti-tumor, anti-oxidation, anti-inflammatory, and other biological activities (Figure 5).[13,14]

1 R$_1$=R$_3$=OH, R$_2$=H 2*R*,3*R*
2 R$_1$=R$_2$=R$_3$=H, 2*S*
3 R$_1$=OH, R$_2$=R$_3$=H 2*R*,3*R*
4 R$_1$=R$_3$=H, R$_2$=CH$_3$ 2*S*
5 R$_1$=ORha, R$_2$=H, R$_3$=OH 2*R*,3*S*
6 R$_1$=ORha, R$_2$=H, R$_3$=OH 2*R*,3*R*
7 R$_1$=ORha, R$_2$=H, R$_3$=OH 2*S*,3*S*
8 R$_1$=ORha, R$_2$=H, R$_3$=OH 2*S*,3*R*
9 R$_1$=ORha, R$_2$=R$_3$=H 2*R*,3*R*
10 R$_1$=OGlc, R$_2$=R$_3$=H 2*R*,3*R*
11 R$_1$=OH, R$_2$=Glc, R$_3$=H 2*R*,3*R*
12 R$_1$=OH, R$_2$=H, R$_3$=OGlc 2*R*,3*R*
13 R$_1$=OGlc, R$_2$=H, R$_3$=OH 2*S*,3*S*
14 R$_1$=ORha,R$_2$=R$_3$=H 2*R*,3*S*
15 R$_1$=OH, R$_2$=H, R$_3$=OGlc

16

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25

26 R=H
27 R=OH

28

29

30 R$_1$=R$_2$=R$_5$=R$_6$=H, R$_3$=R$_4$=OMe
31 R$_1$=R$_5$=R$_6$=OH, R$_2$=R$_3$=R$_4$=H

32 R$_1$=R$_5$=Me, R$_2$=OH, R$_3$=H, R$_4$=R
33 R$_1$=R$_2$=R$_4$=H, R$_3$=OR, R$_5$=Me

Figure 2 The structures of flavonoids and flavonoid glycosides isolated from SGB.

Figure 3 The structures of phenolic and phenolic acids isolated from SGB.

Figure 4 The structures of stilbene and organic acids isolated from SGB.

Lignans

Lignans are a class of natural compounds polymerized by two molecules of phenylpropanoid derivatives. The lignins in SGB mainly include (-)-secoisolariciresinol, 4-ketopinoresinol, smiglabranol, (+)-lyoniresinol, kompasinolA, Amphenol, including anti-tumor, anti-HIV, anti-oxidation, and liver protection effects, etc (Figure 5).[94–96]

Steroids and Steroid Glycosides

Sterols are a large group of compounds with cyclopentane perhydrophenanthrene (steroid nucleus) as the basic skeleton. They are widely present in biological tissues and are synthesized by acetyl-CoA and play an essential role in the life process of organisms. In nature, sterols exist in different forms. The sterols isolated from SGB mainly include β-Sitosterol, stigmasterol, stigmasterol-3-O-β-D-gulofuranoside, sitosterol-3-O-β-D-gulofuranoside, etc. The sterols in SGB have pharmacological activities such as cholesterol-lowering, anti-tumor, anti-inflammatory, and immune-regulating effects (Figure 6).[97–99]

Volatile Oils

GC-MS is usually used to analyze the volatile oil components in SGB. The chemical components of volatile oil compounds are complex, and terpenoids, small molecular aliphatic, and aromatic compounds are more common. The volatile oil has a wide range of pharmacological activities and has good biological activities in the cardiovascular system, gastrointestinal system, respiratory system and antibacterial, anti-inflammatory, anti-cancer, anti-viral, and promoting drug absorption. The volatile oil compounds isolated are mainly palmitic acid (17.87%), terpinene-4-ol (7.533%), linoleic
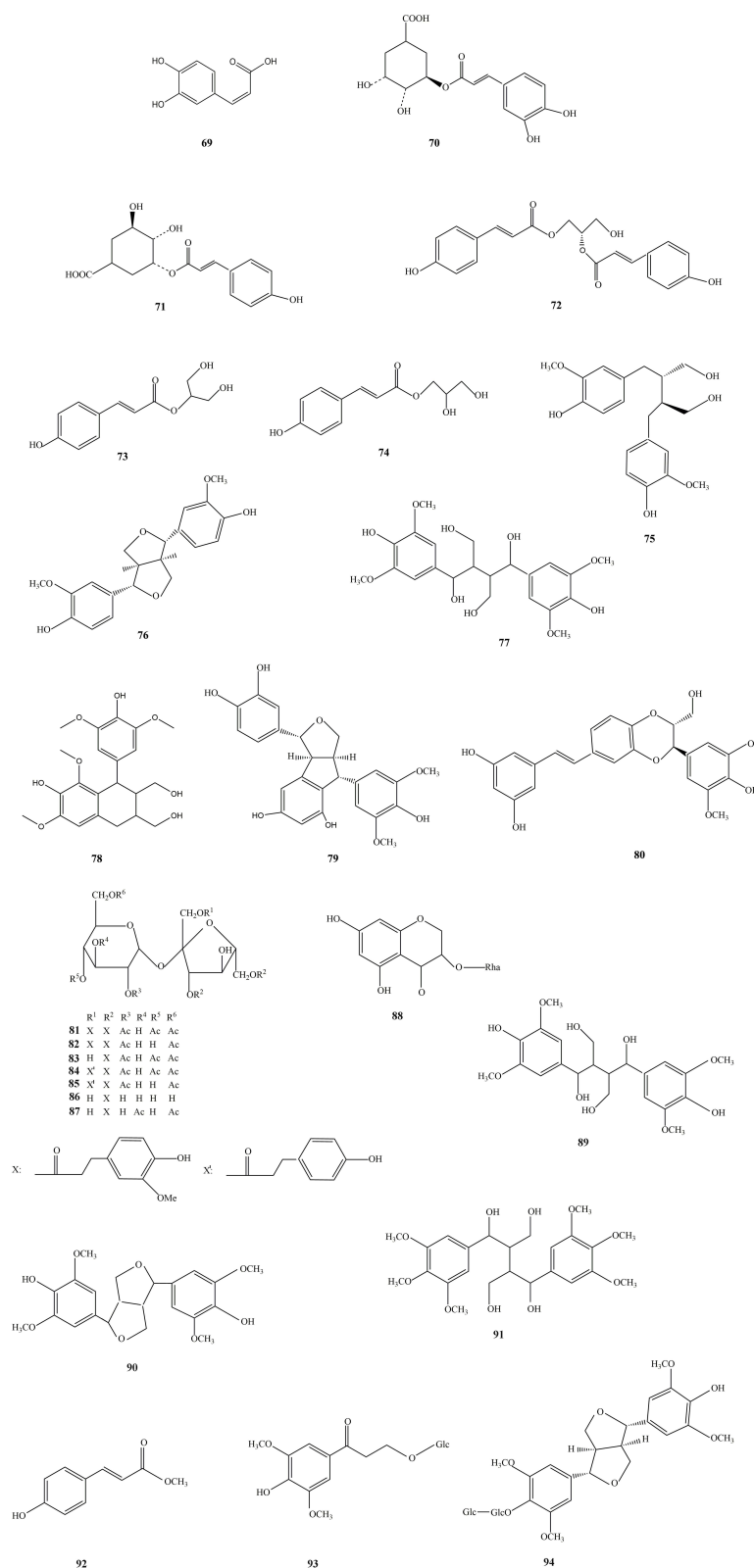
Figure 5 The structures of phenylpropanoids and lignans isolated from SGB.
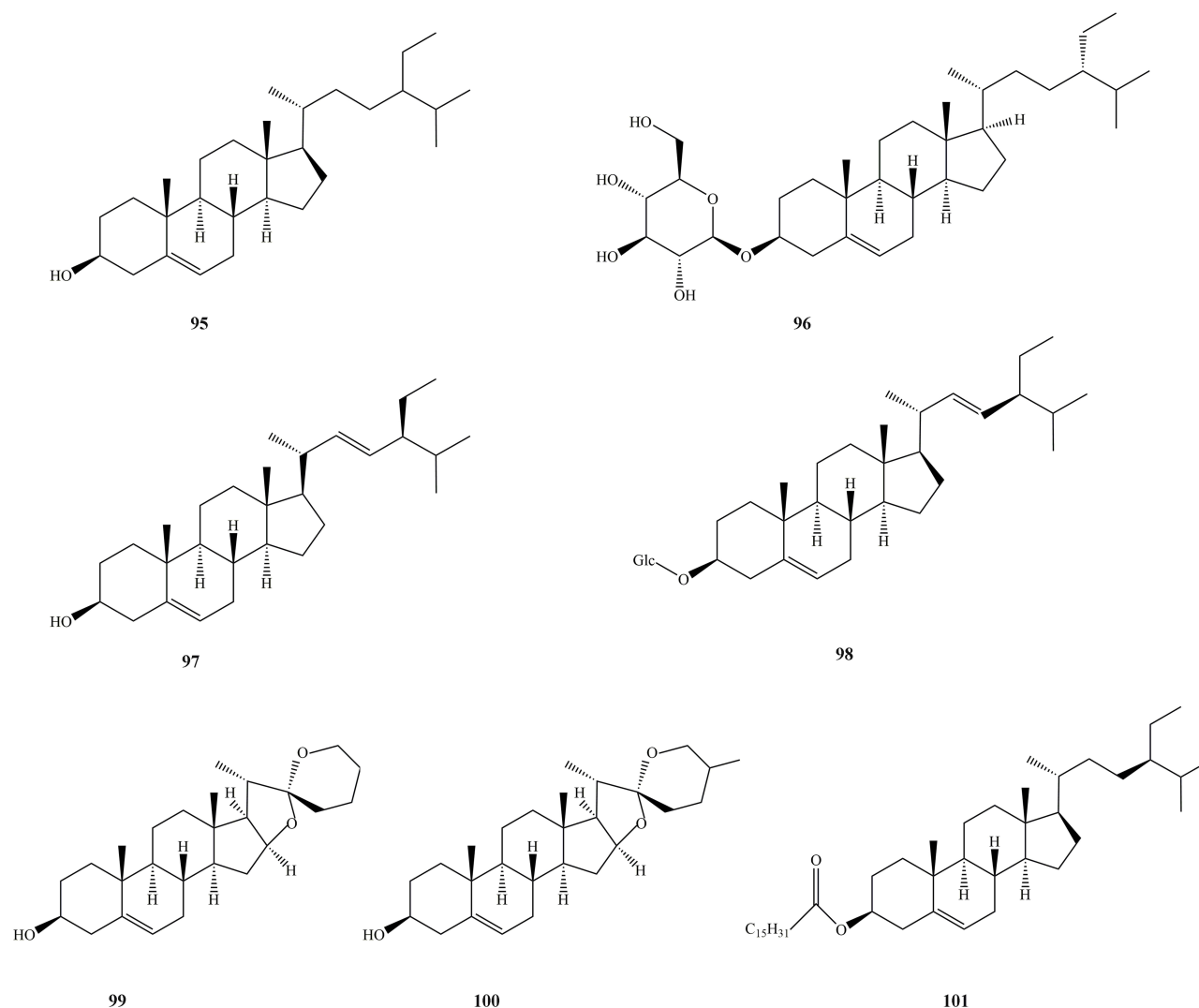
Figure 6 The structures of steroids and steroid glycosides isolated from SGB.

acid (6.775%), nonane (4.509%), 8, 11-octadecadienoic acid, methyl ester (2.215%), α-cedrol (1.810%), methyl palmitate (1.293%), and L-aromatic alcohols, I-terpineol, etc in SGB.[15,100]

Others

The experiment found that the content of alkaloids in the rhizomes of SGB is 0.0349%, the content of tannins is 20.77 mg/g, the range of inorganic elements such as Ca, Mg, Fe, Mn, Cd is relatively high, and the content of components such as K, Cu, Zn is relatively high. Low. The study first discovered 14 alkaloids in the supernatant of water-soluble extracts of SGB in 2015 and verified their anti-cancer properties but failed to isolate and identify these 14 compounds.[101] The protein components of SGB were heterodimers, non-mannose binding lectins, etc. It shows the effects of SGB extracts and main active compounds (Table 2).

Pharmacological Properties

Over the past decades, SGB has been increasingly investigated due to its broad pharmacological activities. SGB extracts (alcoholic extracts, water extracts) and their compounds possess various biological and pharmacological activities, such as anti-infective, anti-cancer, anti-inflammatory, antioxidant, cardiovascular protection, hepatoprotective activity, lower uric acid, and other effects (Figure 7).

Table 2 Characteristics of Chemical Constituents Isolated from SGB

Classes	Chemical Constituents	Biological Activities	References
Flavonoids and flavonoid glycosides	Astilbin, Taxifolin, Neoastilbin, Isoastilbin, Engeletin, Isoengeletin, Taxifolin, Astilbin, Neoastilbin, Isoastilbin, Engeletin, Isoengeletin, Naringenin, Epicatechin	Anti-infective, antibacterial, and antiviral	[11,14,35–62]
Phenolic and phenolic acids	Syringic acid, Eurryphin, Kelampayoside A, Osmanthuside F	Anti-inflammatory, antioxidant, and antibacterial	[9,10]
Phenylpropanoids and lignans	Smiglaside A, Smiglaside B, Smiglaside C, Smiglaside D, Smiglaside E, Helonioside A	Anti-tumor, antioxidant, and anti-inflammatory	[13,14,94–96]
Stilbene and organic acids	Resveratrol, Resveratrol-3-O-β-D-pyranoglucoside, Succinic acid, Palmitic acid, Ferulic Acid, Shikimic acid, Oleic acid, Linoleic acid, 2-Methylsuccinic acid, Oxalic acid	Anti-oxidant, anti-inflammatory, anti-cancer, antibacterial, anti-inflammatory, and hypoglycemic, antioxidant	[63–93]
Steroids and steroid glycosides	Stigmasterol, Beta-Sitosterol, Stigmasterol-3-O-β-D-gulofuranoside, Sitosterol-3-O-β-D-gulofuranoside	Lower cholesterol, anti-tumor, anti-inflammatory	[97–99]
Volatile oils	N-nonane, 8,11-Methyl octadecadienoate, α-Cedarwood oil, L-Aromatic alcohols, I-Terpineol	Antibacterial, anti-inflammatory, anti-cancer, anti-viral	[15,100]
Others	Heterodimeric, Non-mannose-binding agglutinin, Mannose-binding lectin	Support body metabolism, immunity of antibodies, and catalysis of enzymes	[101]

Anti-Infective

There are numerous investigations on the anti-infective activities of the SGB. Studies have explored the inhibitory effects of SGB on HIV-1 protease (HIV-PR) and HIV-1 integrase (HIV-1 IN). The results showed that both the ethanol extract (2μL) and water extract (2μL) of SGB showed anti-HIV-1 IN activity, with IC50 values of 6.7μg/mL and 8.5μg/mL, respectively. In general, ethanol extracts and water extracts of SGB have significant anti-HIV activity.[13]

It found that the minimum inhibitory concentration (MIC) obtained from the antibacterial evaluation of the SGB extract was effective against Staphylococcus aureus ATCC6538 (50μg/mL) in the ethanol extract ethyl acetate component and n-butanol component. The ethyl acetate component shows considerable activity and has significant antibacterial activity against *Candida albicans* SC5314 and *Staphylococcus aureus* ATCC6538, and the MIC value is 200μg/mL. It is the first study on the antifungal activity of SGB.[3] To further study the antibacterial activity of SGB, this study used two kinds of gram-positive bacteria, including Staphylococcus aureus and Bacillus subtilis, and it evaluated two types of gram-negative bacteria, including Escherichia coli and Salmonella typhi, and the antibacterial activity of different extracts of SGB rhizome. The research results show that the rhizome extract of SGB is effective against gram-positive bacteria.[18]

Anti-Viral Activities

Growing research suggests that SGB has antiviral activity. A new mannose-binding lectin was isolated from SGB, called SGM2. Studies have shown that SGM2 has an excellent antiviral effect on herpesvirus type 1 (HSV-1) and respiratory syncytial virus (RSV), and the antiviral activity has the same EC50. HSV-1 was used to increase Vero cells, RSV was used in Hep-2 cells, and the cytopathic effect (CPE) reduction assay was used to determine the antiviral activity. The IC50 of glycoprotein and RSV antiviral activity was 62.5μg/mL, and the IC50 of HSV-1 was 31.3μg/mL, indicating that SGB has a specific antiviral effect.[19] Studies have shown that SGB has a better anti-HCMV (human cytomegalovirus) effect in vitro. The cytopathic and MTT methods were used to detect the maximum nontoxic concentration, minimum effective concentration and therapeutic index of SGB against HCMV in vitro and compared with ganciclovir. The cytotoxicity of SGB is much lower than that of ganciclovir, and its anti-HCMV effect is similar to that of ganciclovir. It may become a drug for the treatment of active HCMV infection.[102]
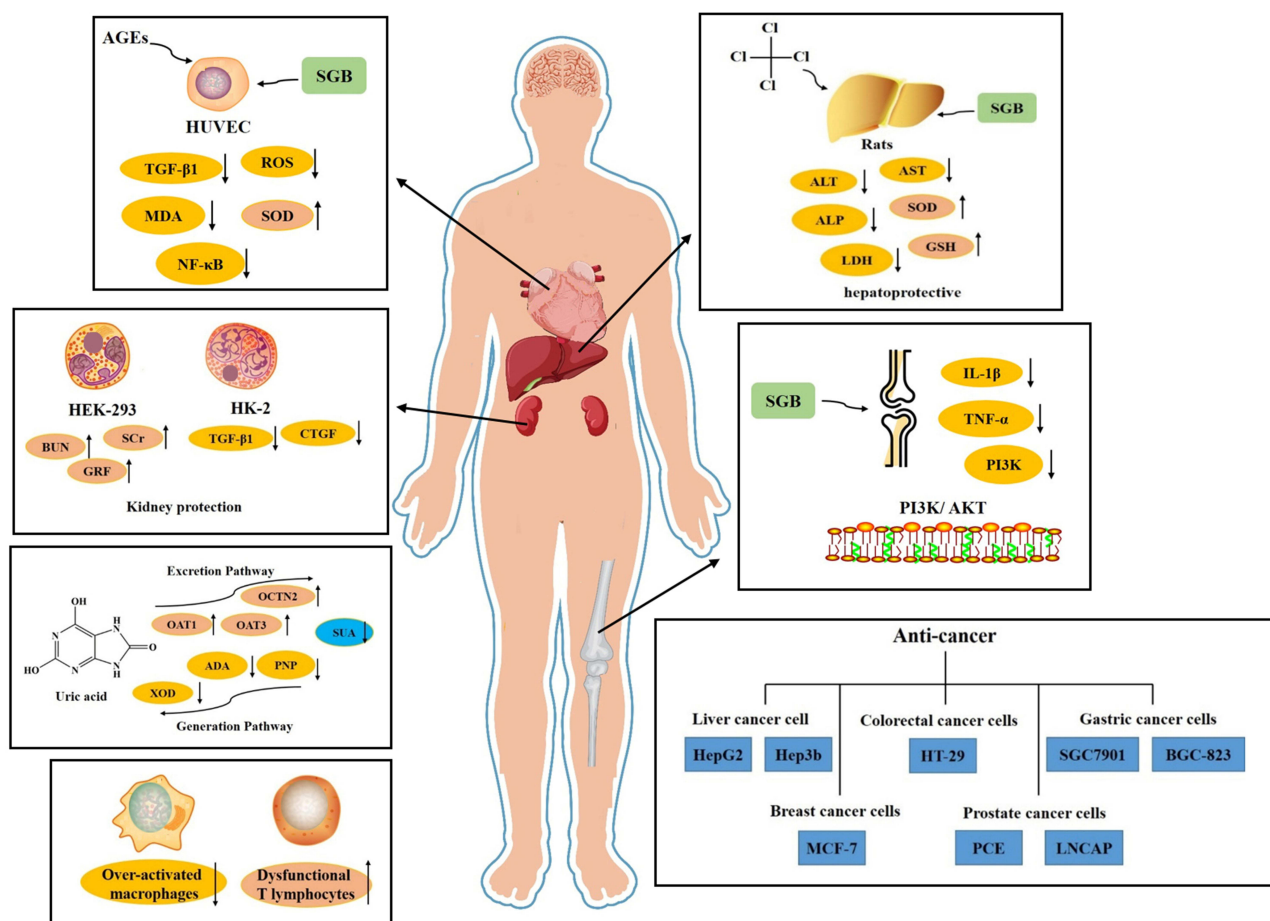
Figure 7 The major pharmacological effects of SGB.

Anti-Cancer

Various compounds isolated from SGB have been shown to affect the growth and proliferation of cancer cells, including human liver cancer cells (HepG2, Hep3b), colorectal cancer cells (HT-29), gastric cancer cells (SGC7901, BGC-823), breast cancer cells (MCF-7) and gastric mucosal epithelial cells (GES 1).[16] Similarly, the study also provides research on the anticancer effects of SGB. SGB can inhibit tumor growth in HT-29 and mouse liver cancer H22 cells. Research results show that cells treated with SGB can inhibit the proliferation of cancer cells, which is related to the apoptosis pathway.[17]

The extracts isolated from SGB showed anti-proliferative effects on human liver cancer HepG2 and Hep3B cells. The results showed that the extract could cause cell cycle arrest and inhibit the growth of HepG2 and Hep3B cells. SGB-mediated apoptosis pathway is mainly involved in activating P38, JNK, and ERK mitogen-activated protein kinase signal transduction, indicating that SGB has specific anticancer activity in HepG2 and Hep3B cells.[98]

This study explored the inhibitory effect of SGB water extract on prostate cancer. Research results show that 5-O-caffeoylquinic is one of the active ingredients of SGB to play an anti-prostate cancer effect. In addition, it further explored the molecular mechanism of SGB's anticancer to provide a reference for the research of SGB in the treatment of prostate cancer.[18] It has been reported that two glycoproteins isolated from SG rhizomes also have anticancer effects in human breast cancer cells (MCF-7). They affect the apoptosis of MCF-7 cells, mainly through the in vitro cell cycle, which is the g1 stage.[103]

Anti-Inflammatory and Cellular Immunosuppressive

Studies have shown that SGB extract has anti-inflammatory and immunomodulatory effects. The study found that rat adjuvant arthritis (AA) induced by Freund's complete adjuvant (FCA) showed the anti-inflammatory and

immunomodulatory effects of SGB. SGB extract showed significant inhibitory activity on primary and secondary paw swelling. By selectively inhibiting the cellular immune response to inflammation and inhibiting the direct anti-inflammatory mechanism of PGE2, SGB extract can be used as a therapeutic agent for immune-inflammatory diseases.[19] This research further studied the mechanism of SGB on the inflammatory condition of AA. The results show that SGB can exert a therapeutic effect on AA by regulating over-activated macrophages and dysfunctional T lymphocytes.[20]

It used molecular biology techniques to analyze and evaluate the effects of SGB polysaccharides on mice. The immunotoxicity and mechanism of Raw264.7 macrophage immunity. The results indicate that SGB polysaccharides can effectively inhibit cell viability by inducing cell apoptosis. SGB polysaccharides can also affect the mRNA expression of apoptotic factors, including Bax and Caspase-8. Studies have shown that SGB polysaccharide has good immunomodulatory activity on Raw264.7 cells.[21]

Antioxidant Effect

Studies have found that phenol-containing extracts in SGB exhibit excellent antioxidant properties. The phenolic extract of SGB shows strong free radical scavenging ability and a dose-dependent manner. At the same time, it also has a significant reduction ability. In this study, the phenolic extract of SGB showed good antioxidant capacity, and the scavenging degree of ABTS was significantly higher than that of ascorbic acid ($P<0.01$).[22]

Not only are phenolic compounds but the flavonoids of SGB also show good peroxide properties. The study extracted six flavonoids from SGB and evaluated their antioxidant activity. The results show that the flavonoids of SGB have vigorous antioxidant activity, which is manifested in DPPH and ABTS+ free radical scavenging ability.[23]

Lower Uric Acid

Studies have shown that the flavonoids in SGB have a good effect on lowering uric acid. The research analyzed the total flavonoids in SGB and studied the effects on serum uric acid indicators and the uric acid production and excretion pathways. It also examined the effects of SGB on renal transporters (OAT1 and OCTN2) and their mRNA. The results showed that SGB could significantly reduce the serum uric acid content in mice ($P<0.01$) and reduce the activity of XOD ($P<0.05$), and it indicates that SGB has a uric acid-lowering effect.[104]

Detoxification Effect

SGB has been proven to have good detoxification effects, mainly including toxicity to heavy metals such as Pb, As, Cd and Hg. The results of acute toxicity test showed that compared with model group, Pb contents in blood, liver and kidney of mice in the total extract from SGB group were significantly lower than that of the model group (P < 0.05). The slow toxicity test showed that compared with the model group, Pb contents in blood, liver and kidney of mice in total flavonoids of SGB group were significantly reduced in a dose-dependent manner (P < 0.05). And liver and kidney damages were ameliorated.[105,106] In the screening experiments to reduce the bioavailability of As and Hg, SGB can significantly reduce the bioavailability of total as by 21.1–43.1%, mainly in the gastric digestion stage. SGB can also reduce the bioavailability of Hg (9.3–80.2%), and it mainly occurs in the intestinal digestion stage. It shows that SGB can reduce the impact of heavy metal pollutants on human health.[107]

Protection of Cardiovascular System

To study the endothelial dysfunction caused by human umbilical vein endothelial cells (HUVECS) exposed to 200μg/mL advanced glycation end products (AGEs). SGB extract significantly reduced the endothelial cell apoptosis induced by AGEs and the down-regulated TGF-β1 protein expression in HUVEC. In addition, SGB extract can reduce ROS, MDA content, and TGF-β1 expression and can significantly increase SOD activity. SGB extract can exert a protective effect on HUVECS by affecting the NF-κB signaling pathway.[24]

SGB flavonoids have been shown to have anti-cardiac hypertrophy effects. 2μmol/L Ang II was used to induce a rat model of primary cardiomyocyte hypertrophy. Still, after SGB treatment, it restored the protein and mRNA expressions of JP2 and RyR2 in cardiomyocytes, indicating that SGB affects the anti-hypertrophy of cardiomyocytes.[16]

This study investigated the inhibitory effect of SGB on the intracellular Ca^{2+} release of rat cardiomyocytes (H9C2). The results show that SGB can significantly inhibit intracellular Ca^{2+} release induced by phenylephrine or angiotensin II. It can also inhibit the Ca^{2+} release caused by the ryanodine receptor (RyR) agonist caffeine and the Ca^{2+} release induced by phenylephrine (PE). The results show that SGB exerts a protective effect by targeting inhibition of intracellular Ca^{2+} release.[25]

Hepatoprotective Activity

The protective effect of flavonoids in SGB on the liver has been studied. Carbon tetrachloride (CCL4) is used to induce liver toxicity in rats. The results showed that compared with CCL4, SGB significantly reduced ALT, AST, ALP, and lactate dehydrogenase activities. In addition, flavonoids significantly increase the activities of SOD, glutathione peroxidase, glutathione reductase, glutathione-S-transferase, and glutathione. The results show that SGB has a protective effect on liver injury in rats.[108]

Protection of Kidney System

Various studies have been conducted to evaluate the potential of SGB to protect the renal system. The effect of total flavonoids from SGB on renal interstitial fibrosis (RIF) and explored the mechanism. After adding TGF-β1 to induce the passage of HK-2 cells after EMT, they were treated with different concentrations of SGB. The results show that SGB treatment can reduce the expression of α-smooth muscle actin and inhibit EMT through the miR-21/PTEN/PI3K/AKT signaling pathway.[109]

The flavonoid extract in SGB can inhibit the nephrotoxicity of rat and human embryonic kidney (HEK)-293 cells. SGB can increase renal function indexes, BUN, and CRE content. Histopathological results show that SGB has a protective effect on rats with renal injury. SGB can affect caspase-3 mediated apoptosis in HEK-293 cells stimulated by Pb. It indicates that SGB has a specific protective effect on the kidneys and treats lead-induced kidney injury.[110]

The flavonoid astilbin was isolated from the rhizome of SGB. To observe the therapeutic effect of astilbin on renal injury, astilbin was added to HK-2 cells stimulated by high glucose. The results showed that astilbin could inhibit the expression of TGF-β1 and connective tissue growth factor (CTGF) in HK-2 cells stimulated by high glucose in vivo and in vitro. Histopathological examination showed that astilbin could protect against kidney damage. This study indicates that astilbin in the total flavonoids of SGB may be a potential target for DN treatment.[111]

Effects of a Joint System

It has been proven that SGB affects joints. The effect of astilbin, the main active ingredient of SGB, on osteoarthritis OA and its mechanism were studied. The rat OA model uses astilbin, PBS, OA, control group, and in vivo experiments. To evaluate the pathological status of cartilage tissue and analyze the expression levels of interleukin (IL)-1β, tumor necrosis factor (TNF)-α, IL-6, AKT, PI3K, and other related proteins. It was found that astilbin can significantly inhibit the expression of IL-1β, TNF-α, and PI3K and play a protective role in joints.[112] It studied the mechanism of SGB on secondary inflammation of AA. The results show that SGB can exert a therapeutic effect on AA by regulating macrophages and T lymphocytes. SGB may be used for clinical rheumatoid arthritis to produce beneficial and long-term treatment.[24]

Clinical Application and Therapeutic Effect

Since 1963, SGB has been listed in the Pharmacopoeia of the People's Republic of China. And SGB has been useful for treating syphilitic, poisoned sores, pathological leucorrhea, eczema itching, carbuncle poisoning, and other infectious diseases for a long time all over the world.

There are many clinical reports on the treatment of infectious diseases by SGB, and all of them have shown sound therapeutic effects.[2] Observe the changes in serum responsive elements in patients with syphilis serum resistance treated by SGB and explore the clinical value of SGB in treating syphilis serum resistance. A total of 42 patients with serum resistance admitted to the STD clinic were randomly divided into treatment group (treated with SGB and benzathine penicillin) and control group (treated with benzathine penicillin), with 21 cases each. The negative conversion rates of serum regaining in the treatment and control groups were 61.90% and 23.81%, respectively. The comparison between the

two groups was *P*<0.05, and the difference was statistically significant. SGB has a good effect in treating syphilis serum resistance and can effectively promote syphilis serum resistance serotonin turns negative.[113]

Some proprietary Chinese medicines with SGB have been included in the pharmacopeia, including *Fuyankang Pian, Shenfukang Jiaonang, Miaoji Wan* et al (Table 3). And *Fufang Qingdai Wan* and *Yinxieling Gao* have been widely used clinically for infectious skin diseases, etc, and have shown sound therapeutic effects.[114–117]

Summary and Perspective

This article reviews the traditional use, chemical composition, pharmacological effects and clinical application of SGB (Figure 8). SGB has complex chemical components and extensive pharmacological effects. It has broad clinical application prospects. However, the relationship between the pharmacological basis and pharmacological activity of

Table 3 The Preparations, in Which SGB is the Main Composition, Used in TCM

Preparation Name	Types	Main Compositions	Traditional and Clinical Uses	References
Fuyankang Pian	Tablet	*Smilax glabra* Roxb., *Paeonia lactiflora* Pall., *Sparganium stoloniferum, Melia azedarach* L., *Curcuma longa* L., *Corydalis yanhusuo, Euryale ferox* Salisb., *Angelica sinensis* (Oliv.) Diels, *Sophora flavescens* Aiton, *Cyperus rotundus* L., *Phellodendron amurense* Rupr., *Salvia miltiorrhiza* Bunge, *Dioscorea oppositifolia* L.	Leukorrheal diseases	Chinese Pharmacopoeia Commission (2020)
Shenfukang Jiaonang	Capsule	*Smilax glabra* Roxb., *Dioscorea oppositifolia* L., *Imperata cylindrica* (L.), *Leonurus cardiaca* L., *Pogostemon cablin* (Blanco) Benth.	Croupous nephritis edema, acute attack of chronic glomerulonephritis	Chinese Pharmacopoeia Commission (2020)
Miaoji Wan	Pill	*Smilax glabra* Roxb., *Pogostemon auricularius* (L.), *Angelica sinensis* (Oliv.), *Conioselinum anthriscoides* "Chuanxiong", *Chaenomeles lagenaria* (Loisel.), *Eucommia ulmoides* Oliv., *Dipsacus asper* Wall. ex DC., *Achyranthes bidentata* Blume, *Atractylodes lancea* (Thunb.) DC., *Foeniculum vulgare* Mill., *Aucklandia costus* Falc., *Syzygium aromaticum* (L.), *Boswellia carteri* Birdw., *Potentilla reptans* L.	Liver and kidney disease, rheumatoid arthritis	Chinese Pharmacopoeia Commission (2020)
Fufang Qingdai Wan	Pill	*Smilax glabra* Roxb., *Isatis tinctoria* L., *Prunus mume* (Siebold)., *Taraxacum officinale* F.H.Wigg., *Arnebia euchroma* (Royle ex Benth.) I.M.Johnst., *Angelica dahurica* (Hoffm.) Benth., *Salvia miltiorrhiza* Bunge., *Dictamnus dasycarpus* Turcz., *Silene banksia* (Meerb.) Mabb., *Dryopteris crassirhizoma* Nakai., *Portulaca oleracea* L., *Dioscorea spongiosa, Crataegus monogyna* Jacq., *Schisandra sphenanthera*.	Universal eczema caused by blood-heat	Chinese Pharmacopoeia Commission (2020)
Yinxieling Gao	Ointment	*Smilax glabra* Roxb., *Sophora flavescens* Aiton., *Glycyrrhiza glabra* L., *Dictamnus dasycarpus* Turcz., *Saposhnikovia divaricata* (Turcz. ex Ledeb.) Schischk., *Cyperus esculentus* L., *Phellodendron chinense* C.K.Schneid., *Rehmannia glutinosa* (Gaertn.) DC., *Lonicera confusa* DC., *Paeonia lactiflora* Pall., *Forsythia suspensa* (Thunb.) Vahl., *Angelica sinensis* (Oliv.) Diels.	Lepra alphos and psoriasis	Chinese Pharmacopoeia Commission (2020)
Tongfengding Jiaonang	Capsule	*Smilax glabra* Roxb., *Gentiana macrophylla* Pall., *Phellodendron chinense* C.K.Schneid., *Corydalis yanhusuo, Paeonia lactiflora* Pall., *Cyathula officinalis* K.C.Kuan., *Alisma plantago-aquatica* L., *Plantago asiatica* L.	Bi-diseases caused by damp heat and blood stasis	Chinese Pharmacopoeia Commission (2020)
Shiduqing Jiaonang	Capsule	*Smilax glabra* Roxb., *Rehmannia glutinosa* (Gaertn.) DC., *Angelica sinensis* (Oliv.) Diels., *Salvia miltiorrhiza* Bunge., *Cyperus esculentus* L., *Sophora flavescens* Aiton., *Dictamnus dasycarpus* Turcz., *Glycyrrhiza glabra* L., *Scutellaria baicalensis* Georgi.	Pruritus cutanea	Chinese Pharmacopoeia Commission (2020)
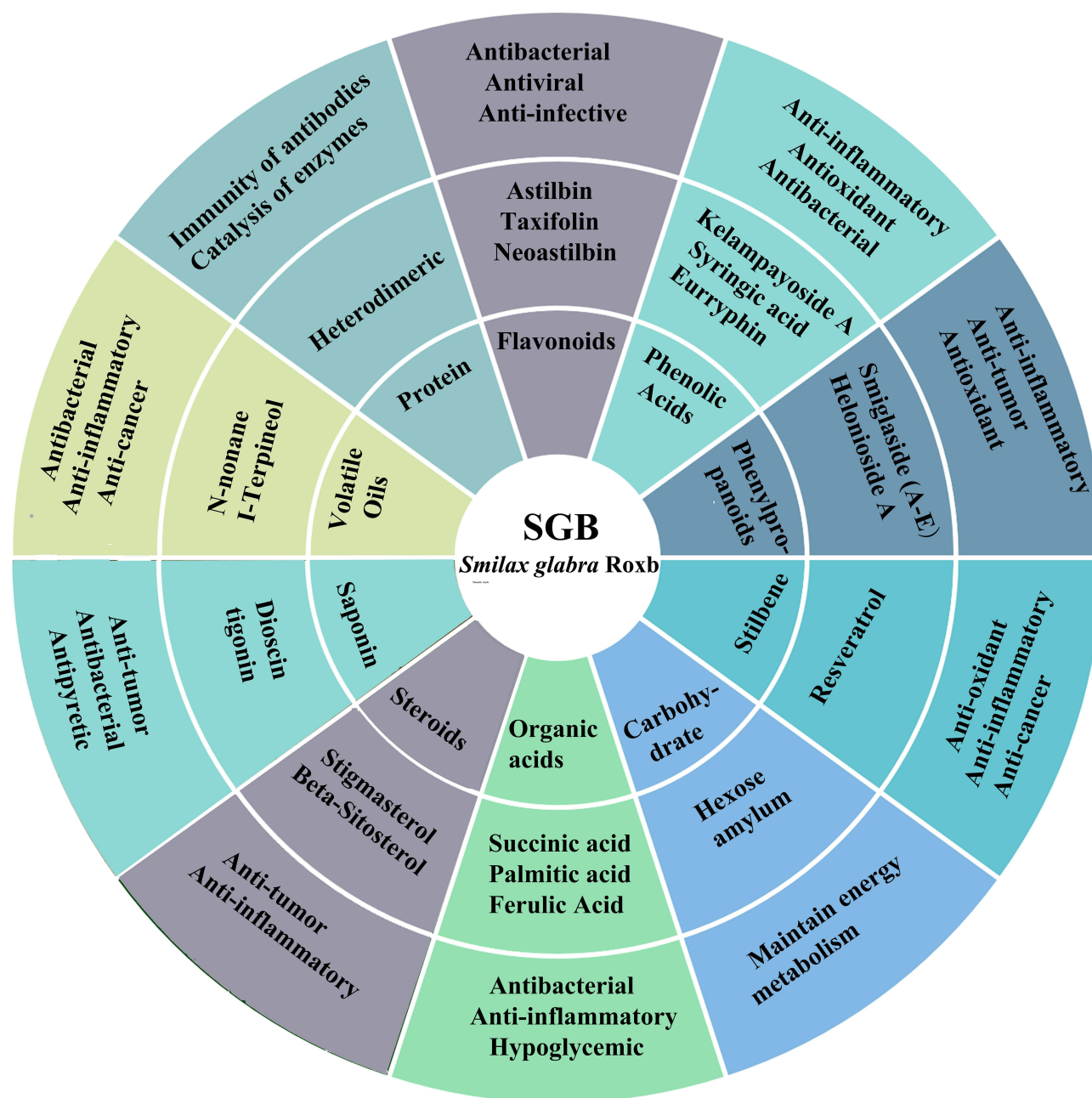
Figure 8 Representative chemical constituents isolated from SGB and their corresponding biological activities.

Smilax glabra is still unclear. The pharmacologically active ingredients of SGB can be explored, which is also of great significance for the clinical medication and drug development of SGB. In addition, domestic and foreign research on SGB is limited to rhizomes, and the exploration of other parts of SGB, such as above-ground stems, leaves, flowers and fruits, should be intensified to fully interpret the organic integrity of the plant.

At the same time, for different isomers, their pharmacological activities are different, which may be determined by the positions of substituents on different C bonds, such as astilbin and neoastilbin in SGB. Further discussion on the influence of the changes of different chemical components on the pharmacological effects will help us to carry out more in-depth research on SGB.

SGB has many clinically proven pharmacological activities, including anti-infection, anti-cancer, anti-inflammatory, antioxidant, etc, but there is still a lack of further research to confirm this conclusion and apply it in clinical treatment.

For example, in anti-infective activity, SGB was considered a folk medicine against infection. Future research needs to conduct in-depth research on the anti-infective mechanism of SGB and its main active ingredients and carry out relevant clinical trial design, in order to make SGB play a better anti-infective effect. Therefore, the evaluation of clinical trials of SGB anti-infectives needs to be carried out urgently. SGB has the potential for the development of anti-infective drugs. However, there are still few anti-infective studies on SGB and its main components. A large amount of long-term clinical treatment evidence shows that SGB has excellent anti-infective pharmacological activity. Therefore, SGB and its main components should be comprehensively studied, especially the potential anti-infective mechanism, to support its anti-infective use. Finally, SGB is a natural product as a potential treatment for life-threatening infections and helps develop anti-infective drugs from natural resources.

Current research shows that a large number of chemical substances have been isolated and identified from SGB, but there is a lack of further material basic research on SGB pharmacological effects. Therefore, in-depth phytochemical research on SGB and its pharmacological properties, especially the mechanism of its biologically active ingredients, will undoubtedly become the focus of further research. The broad pharmacological properties of SGBs may provide an explorable new avenue for our future drug design, development, therapeutic research, and possibly new perspectives for disease management.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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