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REVIEW ARTICLE

A systematic review on triterpenoids from genus *Schisandra*: Botany, traditional use, pharmacology and modern application

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Review

Abstract The genus *Schisandra* belongs to the family Schisandraceae and grows mainly in south-central and southwestern China. Most of the plants in this genus are used for medicine by their fruits, usually for the treatment of inflammatory diseases. In traditional medicine, *Schisandra* is also used to stop bleeding, relieve pain, and clear heat. Based on this, many domestic and foreign scholars have conducted systematic studies on its chemical composition, and experimental data show that triterpenoid components are the important material basis for the pharmacological effects of this genus. This paper summarizes the relevant literature on triterpenes of the genus *Schisandra* from 1983 to 2023. All information and research about this paper was obtained from libraries and digital databases (SciFinder, Medline PubMed, Google Scholar, and CNKI, etc.). At present, there are 335 different kinds of triterpenes isolated from the genus Schisandra, including lanostanes, cycloartanes, nortriterpenoids and pentacyclic triterpenoids, which are mostly found in fruits and vine stems. They have been found to possess various activities such as antitumor, antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, nephroprotective and hepatoprotective.

This review systematically summarizes the literature on triterpenoid composition, traditional applications, pharmacology, and exploitation of the genus *Schisandra*. We hope this paper will provide a valuable reference for further research and development of the resources of this genus.

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1. Introduction

The Schisandraceae contains *Schisandra* and *Kadsura* with distributions in southeastern Asia and southeastern North America, with 22 species of the genus *Schisandra* in China (See Table 1 for specific names and main distribution). At present, research on the genus *Schisandra* has focused on *S. chinensis*, *S. sphenanthera*, *S. arisanensis*, *S. rubriflora, S. propinqua* and *S. arisanensis*. Research on this genus has been increasing this year, especially on its fruits and vine parts. Among them, the fruit of *S. chinensis* (habitually known as Bei Wu Wei Zi) and the fruit of *S. sphenanthera* (habitually known as Nan Wu Wei Zi) are included in the Chinese Pharmacopoeia (Gao and Liu, 2010). The genus *Schisandra* has the properties of astringent, benefiting the qi, nourishing the kidneys and nourishing the heart (Xu et al., 2008). Its efficacy is documented in *Shennon's Herbal Classic* and the *Compendium of Materia Medica*. It is a traditional medicinal plant with a long history of use in China and other parts of Asia. This herb can be applied to treat a wide range of conditions, including respiratory, digestive, and inflammation, as well as fatigue and stress. In traditional medicine, it is often used as a soup and as a powder to treat illnesses (Zhao, 2008). In comparison with the summary by Zhang et al. (Zhang et al., 2022) this paper focuses on the collation of triterpenoids from the genus *Schisandra*, with a total of 335 compounds, in addition to the traditional uses of the genus and the current status of related exploitation.

In recent years, scientific research has focused on the potential health benefits of this genus, particularly its antioxidant, anti-inflammatory and neuroprotective properties. Pharmacological studies have shown that the triterpenoid component of the genus is one of the important material bases for this pharmacological action. As research continues, some structurally novel triterpenes have also been discovered, and their pharmacological activities and mechanisms of action

Table 1 Names and distribution of species of the genus *Schisandra* in China.

No.	Species	Main distribution	Ref.
a	*Schisandra sphenanthera* (*S. sphenanthera*)	China (Shanxi, Shannxi, Gansu, Shandong, Jiangsu, Guizhou, Yunnan)	(Liu et al., 2023)
b	*Schisandra chinecnsis* (*S. chinensis*)	China (Heilongjiang, Jilin, Liaoning, Inner Mongolia, Hebei), Korea, Japan, Russia	(Liu et al., 2023)
c	*Schisandra arisanensis* (*S. arisanensis,* Subspecies: *S. Viridis*)	China (Taiwan)	(Liu et al., 2023)
d	*Schisandra glaucescens* (*S. glaucescens*)	China (Hubei, Sichuan)	(Liu et al., 2023)
e	*Schisandra rubriflora* (*S. rubriflora*)	China (Gansu, Hubei, Sichuan, Yunnan, Tibet)	(Liu et al., 2023)
f	*Schisandra longipes* (*S.longipes*)	China Southeast	(Liu et al., 2023)
g	*Schisandra bicolor* (*S. bicolor,* Synonym: *S. wilsoniana*)	China (Zhejiang, Jiangxi, Hunan)	(Liu et al., 2023)
h	*Schisandra grandiflora* (*S. grandiflora*)	China (Tibet, Yunnan), Nepal, Bhutan, Sikkim,	(Liu et al., 2023)
i	*Schisandra henryi* (*S. henryi*)	China (Zhejiang, Jiangxi, Fujian, Henan), Vietnam	(Liu et al., 2023)
j	*Schisandra incarnata* (*S. incarnata*)	China (Hubei), East Himalaya	(Liu et al., 2023)
k	*Schisandra lancifolia* (*S. lancifolia*)	China (Sichuan, Yunnan)	(Liu et al., 2023)
l	*Schisandra micrantha* (*S. micrantha*)	China (Guangxi, Guizhou, Yunnan), Assam, Myanmar	(Liu et al., 2023)
m	*Schisandra neglecta* (*S. neglecta*)	China (Sichuan, Yunnan, Tibet), Assam, Bangladesh, China South-Central, East Himalaya, Myanmar, Nepal	(Liu et al., 2023)
n	*Schisandra plena* (*S. plena*)	China (Yunnan), India, East Himalaya	(Liu et al., 2023)
o	*Schisandra propinqua* (*S. propinqua*)	China (Yunnan, Tibet), Bhutan, Assam, Himalaya, Jawa, Lesser Sunda Is, Myanmar, Nepal, Thailand	(Liu et al., 2023)
p	*Schisandra pubescens* (*S. pubescens*)	China (Sichuan)	(Liu et al., 2023)
q	*Schisandra sphaerandra* (*S. sphaerandra*)	China (Sichuan, Tibet)	(Liu et al., 2023)
r	*Schisandra tomentella* (*S. tomentella*)	China (Sichuan)	(Liu et al., 2023)
s	*Schisandra macrocarpa* (*S. macrocarpa*)	China (Yunnan)	(Liu et al., 2023)
t	*Schisandra parapropinqua* (*S. parapropinqua*)	China South-Central	(Liu et al., 2023)
u	*Schisandra pubinervis* (*S. pubinervis*)	China South-Central	(Liu et al., 2023)
v	*Schisandra repanda* (*S. repanda*)	China Southeast	(Liu et al., 2023)

are gradually becoming a hot topic of interest for researchers. The triterpenoids micranoic acid B (**319**) isolated from *S. pubescens* have been used in the preparation of anti-tumor drugs with significant pharmacological activity against human lung cancer (A549) and nasopharyngeal carcinoma (KB) (Lu et al., 2016). Notably, the triterpenoids from this genus can also be used to develop food and beverages as well as health products, which have good market prospects (Li and Chen, 2013; Cao and Zhang, 2012).

Accordingly, this paper aims to systematically classify the triterpenes in the genus *Schisandra* and to present the progress made in their traditional applications, pharmacology and development, to provide an important scientific basis for the subsequent comprehensive development of the triterpenoids in this genus. All species queries in Table 1 are from Catalogue of Life China: 2023 (Liu et al., 2023).

2. Search strategy

This paper presents a comprehensive study and analysis of the previously published literature to investigate the traditional uses, phytochemistry and pharmacological activities of plants of the genus *Schisandra*. Articles from 1987 to 2023 were searched using databases such as Medline PubMed, Science Direct, Sci Finder, Baidu Scholar, Google Scholar and CNKI by using the keywords such as genus *Schisandra*, *S. chinensis*, Triterpenoids and uses of *Schisandra*. Part of the analyzed studies was got by a manual search of articles in the reference lists of the included studies. The chemical structures were drawn using Chem Draw Professional 20.0 software.

3. Physiology, description and distribution

Woody vines, glabrous throughout (branches, leaf backs, and petioles of *S. chinensis*, *S. pubescens* and *S. sphaerandra* pubescent), branchlets with petioles decurrent on both sides of the base into longitudinal stripes or sometimes narrowly winged; with long branches and spur-like short branches growing from axillary buds on long branches. Bud scales 6–8, imbricate, bud's axillary alone or two together or many clustered in leaf axils or at the tips of short branches. Leaves papery, margins membranous decurrent to petiole into narrow wings, flesh with hyaline dots; leaf scars rounded, slightly elevated. Flowers are unisexual, dioecious, rarely monoecious, borne singly in leaf axils or bract axils, often on short branches, in clusters of several due to dense internodes. Tepals 5–12(20), usually the largest in the middle whorl, smaller in the outer and inner whorls; male flowers: stamens 5–60, filaments slender or short, or adnate to the receptacle without filaments. Female flowers: pistils 12–120, free, spirally and densely arranged on the receptacle, which gradually elongates and becomes sparse after pollination. Ovules 2 (3) per locule, superimposed on the ventral suture. The mature carpels are small berries, arranged on the receptacle, forming sparse or dense long spikes of aggregated fruit. The seeds are 2 (3) or sometimes only 1 developed, with a conspicuous hilum, usually U-shaped, Testa smooth or rugose or tuberculate-like projection (Yang et al., 2002; Guo et al., 2015; Sun, 2006).

The entire genus has about 30 species, mainly in eastern and south-eastern Asia, with only one species (*Schisandra glabra*) in the American continent (Jose and Patricia, 1998). 22 species in China, distributed throughout the country (except Xin Jiang), mostly growing in valleys and among jungles (Schisandra in Flora of China @ efloras.org, 2020). Fig. 1 illustrates the distribution of the genus *Schisandra*.

4. Traditional use of *Schisandra*

The genus *Schisandra* is widely distributed throughout China and has a long history of use in China for its rich biological and pharmacological activity, which is why it is often used to treat a variety of diseases. In the genus *Schisandra*, the fruit is the main part of the medicine. In different regions, the fruits of many species are used as a substitute for "*S chinensis*" (the fruit of *S. chinensis*). In Yunnan Province, the fruits of *S. propinqua*, *S. rubriflora*, *S. neglecta*, *S. lancifolia*, and *S. micrantha* are used as substitutes. In Sichuan Province, the fruits of *S. henryi* and *S. rubriflora* are used as substitutes; in Zhejiang Province, the fruits of *S. viridis* are used as substitutes. In the Ming Dynasty, Li Shizhen recorded the difference between the efficacy of the northern and southern species of *Schisandra*, describing that there are northern and southern varieties of *Schisandra*, with the southern variety being red and the northern variety black, with the northern variety being more tonic. In the *Tang Materia*, it is recorded that *Schisandra* has the effect of stopping loss, sweating and diarrhea. It is worth mentioning that its wide distribution has also given rise to ethnic uses with regional characteristics. In Tibetan areas of China, the fruit of *Schisandra* is often used to treat indigestion and diarrhea from enteritis. In addition, similarly distinctive ethnomedicines include Mongolian medicine and Miao medicine. Its development to date has also been helpful to modern medicine, being used to treat rheumatism, stomach pain, gastritis, dysentery and urticaria. Table 2 describes the applications of different plants of the genus *Schisandra* in traditional medicine.

Therefore, in this article, we have collected information on the characteristic folk uses of the *Schisandra* genus, including empirical prescriptions and hospitalized preparations for folk use (Liu et al., 2012b; Jiang, 2005; Zhang et al., 2014; Wei et al., 2009).

5. Triterpenoids

Structurally diverse triterpenoids have been isolated from the genus *Schisandra*. There are **335** triterpenoids in total, and these compounds are divided into four major groups: **72** lanostanes, **42** cycloartanes, **207** nortriterpenoids and **14** pentacyclic triterpenoids. Compound names and sources are shown in Table 3, and their chemical structures are shown in Figs. 2-15.

5.1. Lanostane

5.1.1. Intact lanostanes

The structural features of this type (**1**–**19**) of triterpenoids: the C-3 position is mainly substituted by carbonyl or hydroxyl group, and the double bonds in the ring are mostly in C-8 (9), C-9, and C-12 positions are mostly substituted by –OH. And most of the compounds are substituted by carbonyl group at C-3 position (Fig. 2).

5.1.2. 3,4-Secolanostanes

The structure of these compounds is characterized by the breakage of the carbon bond at the C-3 and C-4 positions to open the ring, the formation of carboxylic acid at the C-3 position, in a few cases, the formation of carboxylic acid deriva-

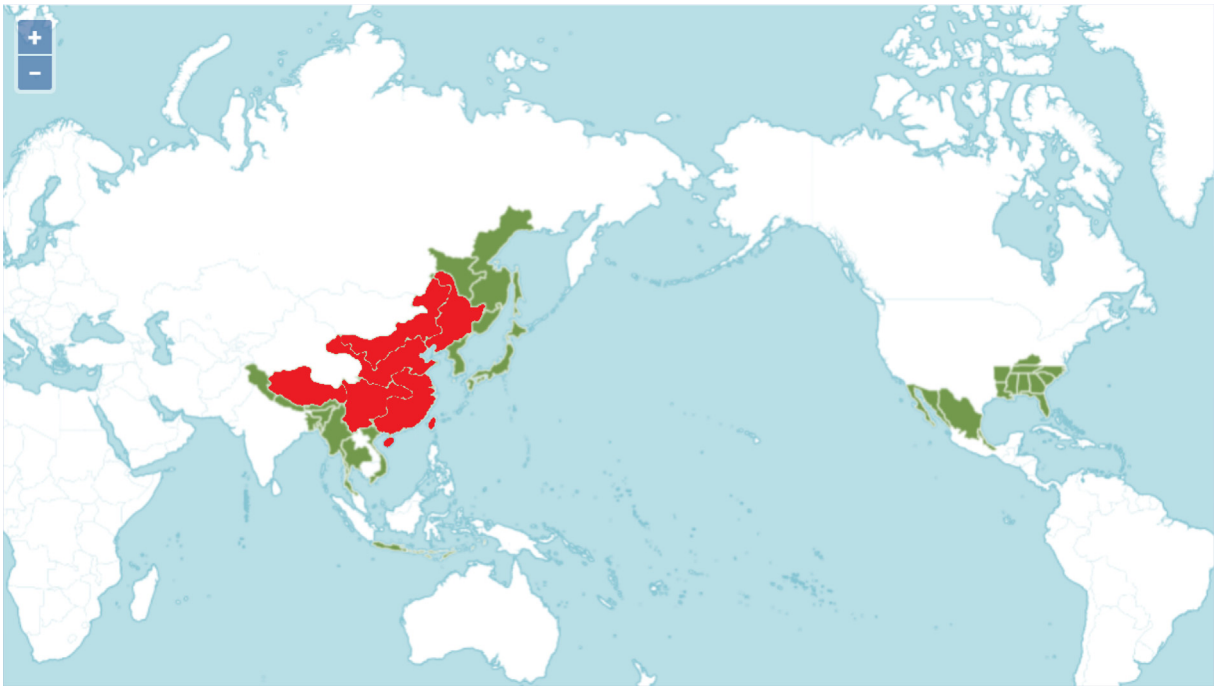

Fig. 1 Distribution of the genus *Schisandra* (the distribution of this genus in China is marked in red).

tives (**20**–**72**). The side chains are mainly 24(*Z*)-ene-26-acids or 22, 26-lactone rings. Most of the lanostane compounds isolated so far belong to this type (Fig. 3).

5.2. Cycloartane

The cycloartane triterpenes (**73**–**79**) are typically characterized by the ternary ring formed by C9 and C19 in their structural skeleton, and are distinguished from other types of triterpene structures by this. In this paper, we classify them into two categories, intact cycloartanes (Fig. 4) and 3,4-seco-cycloartanes (Fig. 5). The structural difference between these two types of cycloartanes is that the former has a carbonyl or hydroxyl group at the C-3 position, while the latter has a broken carbon bond at the C-3 and 4 positions to form a carboxylic acid or a carboxylic acid derivative at the C-3 position (**80**–**114**).

5.3. Nortriterpeonids

5.3.1. Schiartane

Schiartane (**115**–**140**) is the simplest class of nortriterpenes with a 7/6/5 ring system skeleton and possessing 29 carbon atoms. 26 compounds were obtained and their structures are shown in Fig. 6. The differences in the structure of the skeleton are: C-2 or C-16 are easily substituted with hydroxyl groups. Side chain ring formation: The hydroxyl group of C-22/C-23 and the carboxyl group of C-26 are dehydrated to form a six or five-membered lactone ring.

5.3.2. 18-Norschiartane

The 18-Norschiartane type triterpenes (**141**–**161**), with a 7/6/5 carbon shelf parent nucleus, are presumably derived from the oxidative decarboxylation of the schiartane type Me-18 (Fig. 7). So far, 23 compounds of this type have been isolated. The difference between its structural features and those of schiartane: the hydroxyl group at C-13 can form a five-membered oxygen ring by intramolecular dehydration with the hydroxyl group at C-22, in addition to a six-membered oxygen ring by intramolecular dehydration with the hydroxyl group at C-23. The C-23 position has methoxy substitution of different orientations.

5.3.3. Wuweiziartane and lancischiartane

The wuweiziartane type (**162**–**178**) has a 7/5 carbon frame parent nucleus and the differences in skeletal structure are: Me-21 has a different conformation. 24,25 Carbon-carbon double bonds are partially present. C-30 has hydroxyl substitution. lancischiartane and wuweiziartane have the same planar structure, except for the absolute C-13 configuration, which is β- for wuweiziartane and α- for lancischiartane (Fig. 8).

5.3.4. Preschisanartane

Preschisanartane type (**179**–**210**), with a 7/8/3 carbon frame parent nucleus, are presumably derived from schiartane type triterpenes undergoing oxidative rearrangement of C-13, C-14, and cyclization of C-13, C-16 (Fig. 9). The structure is characterized by the easy introduction of hydroxyl groups at C-2, C-19, C-30 and the hydroxyl group introduced at the C-19 position has two conformations. Compound 94 has no oxygen bridge fragment.

5.3.5. 16,17-Secopreschisanartane and 14,15-secopreschisanartan

The 16,17-secopreschisanartane type (**211**–**225**), presumably derived from preschisanartane type triterpenes by C-16, C-17 oxidative rearrangement (Fig. 10), is the only backbone type with a 7/8-carbon parent core and a 9-carbon side chain at present. C-2, C-8, C-19, C-30 are generally hydroxyl substituted.

Table 2 The traditional uses of genus *Schisandra*.

Species	Local name	Dosage form	parts	Traditional clinical uses	Ref
S. sphenanthera	Man shan xiang, Yan pi pa, Hong ling zi	Decoction, Liquor, Powder (orally)	fruits	insomnia, palpitations, calming and tranquilizing, cough.	(Jiang, 2005; Zhang et al., 2014)
		Powder (external application)	stem, root	dysmenorrhea.	
S. chinensis	Xuan ji, Hui ji, Shan hua jiao, Wu wei, Wu mei zi	Decoction, Liquor, Powder (orally), Liniment (external application)	fruits	palpitations, night sweating, rheumatism, cough.	(Jiang, 2005; Zhang et al., 2014)
			stem, root	chronic gastritis, acute gastroenteritis, stomachache.	
S. arisanensis	Jin bei teng, Jin la ba	Liquor (orally)	fruits	insomnia, palpitations, calming and tranquilizing.	(Jiang, 2005; Zhang et al., 2014)
S. glaucescens	Xi wu wei, Cheng gan ma	Fruits, Decoction (orally)	fruits	cough, rheumatism, gall tumors, goiter.	(Liu et al., 2012b)
S. rubriflora	Dian wu wei, Hong xue teng, Guo shan long, Xiang xue teng	Decoction(orally), Fruits	fruits	rheumatism, neurological disorders.	(Jiang, 2005; Zhang et al., 2014)
			stem	rheumatism, stomachache, indigestion.	
S. bicolor	Xiang su zi, Er se nei feng xiao	Decoction, Liquor (orally)	fruits	chest tightness, gastrointestinal distress.	(Jiang, 2005; Zhang et al., 2014)
		Wine(orally)	stem, root	traumatic injuries, excessive fatigue.	
S. grandiflora		Decoction(orally)	fruits	analgesic, cough, tonics for the kidneys.	(Liu et al., 2012b; Zhang et al., 2014)
			stem, root	tonics for the kidneys.	
S. henryi	Da feng teng, Yao wu wei, Huang zuan	Decoction, Wine (orally)	fruits	back pain, lumbar strain.	(Liu et al., 2012b; Wei et al., 2009)
			stem, root	soreness in the limbs, irregular menstruation, stomachache.	
S. incarnata	Xi wu wei	Fruits	fruits	lumbar strain, gastrointestinal discomfort, cough, night sweating.	(Liu et al., 2012b)
S. lancifolia	Diao diao xiang	Decoction(orally)	stem, root	bruises and injuries, fractures, hemostasis.	(Liu et al., 2012b)
		Fruits	fruits	Neurasthenia.	
S. micrantha	Xiang shi teng, Da shen jin, Jie jin teng	Decoction, Wine (orally)	fruits	nephrosis, menstrual irregularities.	(Liu et al., 2012b)
			stem, root	rheumatism, abdominal pain.	
S. neglecta	Xiao xue teng	Decoction, Wine (orally), External application, Fruits	fruits	cough, clears heat.	(Liu et al., 2012b)
			stem	diarrhea, relieving pain.	
S. plena	Fu ban huang long teng	Decoction	whole plant	clears heat, relieving pain.	(Liu et al., 2012b)
S. propinqua	Zhong jian wu wei zi	Decoction(orally), External application	fruits	stops bleeding, clears heat.	(Liu et al., 2012b)
			stem, root	stomach pain, gastritis, menstrual disorders, fractures, blood clots.	
S. pubescens	Mao mai wu wei zi	Fruits Decoction(orally)	fruits	cough, night sweating.	(Liu et al., 2012b)
			stem	exertional injuries, diarrhea.	
S. sphaerandra	Shan bao gu, Shan hua jiao, Xiao xue pian	Fruits, Liquor (orally)	stem, root	rheumatic arthritis, joint pain, abdominal distension, dysentery.	(Jiang, 2005;)
S. tomentella	Mao bei wu wei zi	vinum, wine (orally)	fruits	diarrhea, palpitation, insomnia.	(Jiang, 2005)
S. viridis	Guo shan feng, Nei feng xiao, Bai zuan	Decoction (orally or external application)	fruits	urticaria, zoster, rheumatism, stomachache.	(Jiang, 2005)

hydroxyl and methoxy are easily introduced at the C-15 position. The 14,15-Secopreschisanartan type (**226**–**230**) has a 1-oxospiro [6.6] tridecane system.C-22,23-position double bond conformation has both Z and E conformations.

5.3.6. Lancifoartane and 12,22-Cyclopreschisanartane

Lancifoartane (**231**–**232**), which possesses a 7/7-carbon nucleus and has a lactone bridge between C-9 and C-14, may be derived from 16,17-secopreschisanartane-type triterpenes by

Table 3 Triterpenoids isolated from genus *Schisandra*.

NO.	Compound	Source	Parts	Ref
5.1.1. Intact lanostanes				
1	schiglausin R	g	stems	(Liu, 2018)
2	schisandronic acid	b	stems	(Suh, 2014)
3	3*β*-hydroxy-lanosta-8,24*Z*-dien-26-oic acid	o	stems	(Liu and Tao, 1992)
4	schipropinqua acid E	o	stems and leaves	(Ding, 2018)
5	schipropinqua acid F	o	stems and leaves	(Ding, 2018)
6	schipropinqua acid G	o	stems and leaves	(Ding, 2018)
7	schipropinqua acid H	o	stems and leaves	(Ding, 2018)
8	schiglausin R	d	furits	(Yu et al., 2016)
9	(24*E*)-3*α*,12*α*-dihydroxy-lanost-24-en-26-oic acid	d	stems	(Wu, 2016)
10	coccinic acid	d	stems	(Wu, 2016)
11	anwuweizonic acid	d	stems	(Wu, 2016)
12	*iso*-anwuweizic acid	a	furits	(Zhang, 2008)
13	schisactone D	a	furits	(Zhang, 2008)
14	schisanlactone	a	furits	(Zhang, 2008)
15	3*β*-hydroxyl-5*α*,8*α*-*epi*-dioxyergosta-6,22-diene	a	furits	(Li and Sun, 2004)
16	12*β*-hydroxycoccinic acid	a	furits	(Du, 2007)
17	*iso*-schizandrlic acid	a	furits	(Du, 2007)
18	schizandronic acid	a	furits	(Du, 2007)
19	schisanol	c	leaves	(Hou et al., 2016)
5.1.2. 3,4-secolanostane				
20	manwuweizic acid	g	stems	(Liu, 2018)
21	schiglausin G	g	stems	(Liu, 2018)
22	kadsuric acid	b	stems	(Guo et al., 2019)
23	schipropinqua acid N	o	stems and leaves	(Ding, 2018)
24	kadcoccinic acid O	j	stems	(Zhou, 2018)
25	29-hydroxyl schiglausin D	c	stems	(Wang et al., 2021)
26	6-hydroxyl schiglausin G	c	stems	(Wang et al., 2021)
27	schisanlactone A	b	furits	(Liu et al., 1983)
28	schinalactone D	b	stems and leaves	(Qiu et al., 2018)
29	schisanchinlactone B	b	stems and leaves	(Zhao et al., 2020)
30	schisanlactone C	b	stems and leaves	(Qiu et al., 2018)
31	schisphenthin C	a	furits	(Liu et al., 2017a)
32	schisanlactone I	b	stems and leaves	(Qiu et al., 2018)
33	schiglausin P	d	furits	(Yu et al., 2016)
34	schiglausin Q	d	furits	(Yu et al., 2016)
35	schisanlactone H	a	furits	(Du, 2007)
36	schinchinenlactone D	b	roots	(Song et al., 2015)
37	schisphendilactone B	b	stems and leaves	(Qiu et al., 2018)
38	schinchinenlactone B	b	stems and leaves	(Song et al., 2013)
39	schinchinenlactone C	b	stems and leaves	(Song et al., 2013)
40	schisanchinlactone A	b	stems and leaves	(Zhao et al., 2020)
41	schisanchinlactone C	b	stems and leaves	(Zhao et al., 2020)
42	schinchinenin B	b	stems and leaves	(Song et al., 2013)
43	schinchinenin C	b	stems and leaves	(Song et al., 2013)
44	schinchinenin D	b	stems and leaves	(Song et al., 2013)
45	schinchinenin E	b	stems and leaves	(Song et al., 2013)
46	schinchinenin F	b	stems and leaves	(Song et al., 2013)
47	henrischinin A	b	stems and leaves	(Song et al., 2013)
48	henrischinin B	b	stems and leaves	(Song et al., 2013)
49	schinchinenin G	o	stems	(Liu and Tao, 1992)
50	schipropinqua acid k	o	stems and leaves	(Ding, 2018)
51	schipropinqua acid L	o	stems and leaves	(Ding, 2018)
52	schipropinqua acid M	o	stems and leaves	(Ding, 2018)
53	schipropinqua acid M 3-methyl ester	o	stems and leaves	(Ding, 2018)
54	kadsuric acid 3-methyl ester	d	stems	(Wu, 2016)
55	kadsuricacid	a	furits	(Du, 2007)
56	kadpolysperin J	d	stems	(Wu, 2016)
57	schinalactone E	j	stems	(Zhou, 2018)
58	12-hydroxyschiglausin B	d	stems	(Liu et al., 2018)
59	sphendilactone	a	stems	(Huang and Qin, 2016)
60	sphenantherain A	a	furits	(Zhang, 2008)
61	sphenantherain B	a	furits	(Zhang, 2008)

Table 3 (*continued*)

NO.	Compound	Source	Parts	Ref
62	sphenantherain C	a	furits	(Zhang, 2008)
63	schiglausin A	a	furits	(Liu et al., 2017a)
64	6-hydroxyl schiglausin A	c	stems	(Wang et al., 2021)
65	schisanlactone E	a	furits	(Du, 2007)
66	schisphenthin A	a	furits	(Liu et al., 2017a)
67	schisphenthin B	a	furits	(Liu et al., 2017a)
68	schiglausin C	a	furits	(Liu et al., 2017a)
69	schisanlactone G	a	furits	(Ren, 2012)
70	schisanlactone B	a	furits	(Liu et al., 2012a)
71	henrischinin A	i	stems and leaves	(Xue et al., 2011)
72	henrischinin B	i	stems and leaves	(Xue et al., 2011)
5.2.1. Intact cycloartanes				
73	ganwuweizic acid	b	stems	(Guo et al., 2019)
74	schipropinqua acid I	o	stems and leaves	(Ding, 2018)
75	schipropinqua acid J	o	stems and leaves	(Ding, 2018)
76	schiglausin S	d	furits	(Yu et al., 2016)
77	cycloart-23-ene-3,25-diol	a	furits	(Li and Sun, 2004)
78	schinensin D	a	roots	(Tanaka et al., 2021)
79	lancifodilactone H	k	stems and leaves	(Xiao et al., 2006b)
5.2.2. 3,4 secocycloartane				
80	schisanbilactone A	g	stems	(Ma et al., 2009)
81	schisanbilactone B	g	stems	(Ma et al., 2009)
82	kadsulactone A	g	stems	(Ma et al., 2009)
83	kadsudilactone C	b	roots	(Song et al., 2015)
84	schisphendilactone A	a	stems	(Liang et al., 2013a)
85	schinensin C	a	roots	(Tanaka et al., 2021)
86	kadsudilactone B	j	stems	(Zhou, 2018)
87	kadsuphilactone B	b	stems and leaves	(Qiu et al., 2018)
88	renchanglactone A	a	furits	(Liu et al., 2017a)
89	wuweizilactone acid	b	stems and leaves	(Huang et al., 2008)
90	schisanlactone J	b	stems and leaves	(Qiu et al., 2018)
91	propiniclactone A	b	roots	(Song et al., 2015)
92	schinchinenin G	b	stems and leaves	(Song et al., 2013)
93	schinchinenin H	b	stems and leaves	(Song et al., 2013)
94	henrischinin C	b	stems and leaves	(Song et al., 2013)
95	schipropinqua acid A	o	stems and leaves	(Ding, 2018)
96	schipropinqua acid B	o	stems and leaves	(Ding, 2018)
97	schipropinqua acid B 3-methyl ester	o	stems and leaves	(Ding, 2018)
98	schipropinqua acid C	o	stems and leaves	(Ding, 2018)
99	schiglausin O	d	stems	(Wu, 2016)
100	6*β*-hydroxyl nigranoic acid	d	stems	(Wu, 2016)
101	3,4-seco(24*Z*)-cycloart-4(28),24-diene-3,26-dioic-3-methyl ester	d	stems	(Wu, 2016)
102	abiesatrine O	j	stems	(Zhou, 2018)
103	nigranoic acid	p	stems	(Sun et al., 1996)
104	schipropinqua acid D	o	stems and leaves	(Ding, 2018)
105	schiglausin T	d	furits	(Yu et al., 2016)
106	lancifoic acid A	d	stems	(Wu, 2016)
107	propindilactone Z	o	stems and leaves	(Ding, 2018)
108	12-hydroxykadsuphilactone B	d	stems	(Liu et al., 2018)
109	kadsudilactone A	j	stems	(Zhou, 2018)
110	20*R*-hydroxyschinalactone C	d	stems	(Liu et al., 2018)
111	propinic lactone A	a	furits	(Liu et al., 2017a)
112	3-*O*-methylchangnanic acid	a	roots	(Tanaka et al., 2021)
113	henrischinin C	i	stems and leaves	(Xue et al., 2011)
114	propinic lactone C	j	stems	(Zhou, 2018)
5.3.1. Schiartane				
115	wuweizidilactone C	b	aerial parts	(Huang et al., 2007b)
116	wuweizidilactone D	b	aerial parts	(Huang et al., 2007b)
117	wuweizidilactone E	b	aerial parts	(Huang et al., 2007b)
118	wuweizidilactone F	b	aerial parts	(Huang et al., 2007b)
119	2*β*-hydroxy-micrandilactone C	b	leaves and stems	(Wang et al., 2011)
120	schinchinenlactone A	b	stems and leaves	(Qiu et al., 2018)
121	schinchinenin A	b	stems and leaves	(Song et al., 2013)

(*continued on next page*)

Table 3 (*continued*)

NO.	Compound	Source	Parts	Ref
122	rubriflordilactone B	e	stems and leaves	(Xiao et al., 2006c)
123	schinensin B	a	roots	(Tanaka et al., 2021)
124	henridilactone J	i	stems and leaves	(He et al., 2020)
125	henridilactone k	i	stems and leaves	(He et al., 2020)
126	lancifodilactone F	k	stems and leaves	(Xiao et al., 2005a)
127	micrandilactone B	l	stems and leaves	(Li, 2005)
128	micrandilactone C	l	stems and leaves	(Li, 2005)
129	propindilactones k	o	stems	(Lei, 2009)
130	propindilactone L	o	stems	(Lei, 2009)
131	propindilactone M	o	stems	(Lei, 2009)
132	propindilactone O	o	stems	(Lei, 2009)
133	propindilactone P	o	stems	(Lei, 2009)
134	hydroxymicrandilactone C	b	stems	(Wang et al., 2011)
135	propincilactone E	o	stems	(Lei et al., 2008)
136	propincilactone F	o	stems	(Lei et al., 2008)
137	propincilactone G	o	stems	(Lei et al., 2008)
138	propincilactone H	o	stems	(Lei et al., 2008)
139	propincilactone I	o	stems	(Lei et al., 2008)
140	propincilactone J	o	stems	(Lei et al., 2008)
5.3.2. 18-Norschiartane				
141	wuweizidilactone A	b	aerial parts	(Huang et al., 2007b)
142	wuweizidilactone B	b	aerial parts	(Huang et al., 2007b)
143	wuweizidilactone G	b	stems and leaves	(Huang et al., 2008)
144	wuweizidilactone H	b	stems and leaves	(Huang et al., 2008)
145	wuweizidilactone I	b	furits	(Xue et al., 2010)
146	19(*R*)-hydroxylwuwei-zidilactone H	b	furits	(Li et al., 2017)
147	propindilactone W	o	stems and leaves	(Ding, 2018)
148	propindilactone X	o	stems and leaves	(Ding, 2018)
149	propindilactone Y	o	stems and leaves	(Ding, 2018)
150	schirbidilactone F	e	stems and leaves	(Xiao et al., 2010a)
151	rubriflordilactone A	e	stems and leaves	(Xiao et al., 2006c)
152	schinensin A	a	roots	(Tanaka et al., 2021)
153	wilsonianadilactone F	g	stems and leaves	(Yang et al., 2011)
154	henridilactone F	i	stems and leaves	(He et al., 2020)
155	henridilactone G	i	stems and leaves	(He et al., 2020)
156	henridilactone H	i	stems and leaves	(He et al., 2020)
157	henridilactone I	i	stems and leaves	(He et al., 2020)
158	wuwezidilactone Q	k	stems	(Liu et al., 2015)
159	wuwezidilactone R	k	stems	(Liu et al., 2015)
160	lancifodilactone A	k	stems and leaves	(Li et al., 2002)
161	wuweizidilactone Q	c	stems and leaves	(Liu et al., 2017b)
5.3.3. Wuweiziartane and Lancischiartane				
162	schintrilactone A	b	furits	(Huang et al., 2007c)
163	schintrilactone B	b	furits	(Huang et al., 2007c)
164	schintrilactone C	a	furits	(Jiang, 2011)
165	schintrilactone D	a	furits	(Jiang, 2011)
166	propintrilactone A	o	stems	(Lei et al., 2010)
167	propintrilactone B	o	stems	(Lei et al., 2010)
168	propintrilactone C	a	stems	(Jiang et al., 2011)
169	arisandilactone A	a	furits	(Cheng et al., 2010a)
170	schicagenin C	a	stems	(Liang, 2013)
171	arisanlactone A	c	furits	(Cheng et al., 2010b)
172	propinqtrilactone A	o	stems and leaves	(Ding, 2018)
173	propinqtrilactone B	o	stems and leaves	(Ding, 2018)
174	schilancitrilactone A	a	stems	(Liang, 2013)
175	schilancidilactone A	k	stems and leaves	(Luo et al., 2009)
176	schilancidilactone B	k	stems and leaves	(Luo et al., 2009)
177	schilancitrilactone B	k	stems	(Luo et al., 2012)
178	schilancitrilactone C	k	stems	(Luo et al., 2012)
5.3.4. Preschisanartane				
179	2β-hydroxyarisanlactone C	c	furits	(Cheng et al., 2010b)
180	schindilactone D	c	furits	(Cheng et al., 2010b)
181	schindilactone E	c	furits	(Cheng et al., 2010b)

Table 3 (*continued*)

NO.	Compound	Source	Parts	Ref
182	preschisanartanin A	c	furits	(Cheng et al., 2010b)
183	preschisanartanin B	c	furits	(Cheng et al., 2010b)
184	pre-schisanartanin A	b	aerial part	(Huang et al., 2007a)
185	pre-schisanartanin B	b	stems and leaves	(Huang et al., 2008)
186	preschisanartanin Q	e	stems and leaves	(Hu et al., 2019)
187	preschisanartanin R	e	stems and leaves	(Hu et al., 2019)
188	preschisanartanin S	e	stems and leaves	(Hu et al., 2019)
189	preschisanartanin T	e	stems and leaves	(Hu et al., 2019)
190	preschisanartanin U	e	stems and leaves	(Hu et al., 2019)
191	preschisanartanin X	e	stems and leaves	(Hu et al., 2019)
192	preschisanartanin V	e	stems and leaves	(Hu et al., 2019)
193	preschisanartanin W	e	stems and leaves	(Hu et al., 2019)
194	preschisanartanin Y	e	stems and leaves	(Hu et al., 2019)
195	preschisanartanin Z	e	stems and leaves	(Hu et al., 2019)
196	preschidilactone A	e	stems and leaves	(Hu et al., 2019)
197	pre-schisanartanin C	a	stems	(He, 2009)
198	pre-schisanartanin D	a	stems	(He, 2009)
199	pre-schisanartanin E	a	stems	(He, 2009)
200	pre-schisanartanin H	a	stems	(He, 2009)
201	pre-schisanartanin F	a	stems	(He, 2009)
202	pre-schisanartanin G	a	stems	(He, 2009)
203	pre-schisanartanin I	a	stems	(He, 2009)
204	pre-schisanartanin J	a	stems	(He, 2009)
205	schilancidilactone V	g	furits	(Gao et al., 2013)
206	schilancidilactone W	g	furits	(Gao et al., 2013)
207	henridilactone E	i	stems and leaves	(He et al., 2020)
208	schisanartanin A	j	stems	(Zhou, 2018)
209	schisanartanin B	j	stems	(Zhou, 2018)
210	pre-schisanartanin P	c	stems and leaves	(Liu et al., 2017b)
5.3.5. 16,17-secopreschisanartane and 14,15-secopreschisanartan				
211	schisdilactone H	b	stems	(Li et al., 2013a)
212	schisdilactone I	b	stems	(Li et al., 2013a)
213	schicagenin A	a	rattans	(Li et al., 2013b)
214	schicagenin F	a	stems	(Liang, 2013)
215	schicagenin G	a	stems	(Liang, 2013)
216	schicagenin H	a	stems	(Liang, 2013)
217	isoschicagenin C	a	stems	(Liang, 2013)
218	schicagenin B	a	stems	(Liang, 2013)
219	lancifonin A	k	stems	(Shi et al., 2014)
220	lancifonin B	k	stems	(Shi et al., 2014)
221	lancifonin C	k	stems	(Shi et al., 2014)
222	lancifonin D	k	stems	(Shi et al., 2014)
223	schicagenin D	m	stems	(Liang et al., 2013b)
224	schicagenin E	m	stems	(Liang et al., 2013b)
225	schisdilactone J	a	stems	(Wang et al., 2012)
226	spiroschincarin A	j	furits	(Song et al., 2017)
227	spiroschincarin B	j	furits	(Song et al., 2017)
228	spiroschincarin C	j	furits	(Song et al., 2017)
229	spiroschincarin D	j	furits	(Song et al., 2017)
230	spiroschincarin E	j	furits	(Song et al., 2017)
5.3.6. Lancifoartane and 12,22-Cyclopreschisanartane				
231	lancifonin E	k	stems	(Shi et al., 2014)
232	lancifonin F	k	stems	(Shi et al., 2014)
233	lancolide A	k	stems	(Shi et al., 2013)
234	lancolide C	k	stems	(Shi et al., 2013)
235	lancolide B	k	stems	(Shi et al., 2013)
236	lancolide D	k	stems	(Shi et al., 2013)
5.3.7. 14-Nor-16,17-secopreschis anartane and 15,17-Dicyclolancifoartan				
237	schinesdilactone A	a	stems	(Wang et al., 2012)
238	schinesdilactone B	a	stems	(Wang et al., 2012)
239	schisphenin A	a	stems	(Liang, 2013)
240	schisphenin B	a	stems	(Liang, 2013)
241	schisphenin C	a	stems	(Liang, 2013)

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Table 3 (*continued*)

NO.	Compound	Source	Parts	Ref
242	schisphenin D	a	stems	(Liang, 2013)
5.3.8. Pchisanartane				
243	schinarisanlactone A	c	furits	(Lin et al., 2011)
244	arisanlactone B	c	furits	(Cheng et al., 2010b)
245	arisanlactone C	c	furits	(Cheng et al., 2010b)
246	arisanlactone D	c	furits	(Cheng et al., 2010b)
247	schindilactone A	b	aerial part	(Huang et al., 2007a)
248	schindilactone B	b	aerial part	(Huang et al., 2007a)
249	schindilactone C	b	aerial part	(Huang et al., 2007a)
250	schindilactone F	b	stems and leaves	(Huang et al., 2008)
251	sphenadilactone F	a	stems	(He, 2009)
252	lancifodilactone O	k	stems and leaves	(Xiao et al., 2010b)
253	lancifodilactone P	k	stems and leaves	(Xiao et al., 2010b)
254	lancifodilactone Q	k	stems and leaves	(Xiao et al., 2010b)
255	20-hydroxymicrandilactone D	k	stems and leaves	(Xiao et al., 2010c)
256	schindilactone G	b	stems and leaves	(Huang et al., 2008)
257	schindilactone H	b	furits	(Xue et al., 2010)
258	propindilactone V	o	stems and leaves	(Ding, 2018)
259	schirbidilactone A	e	stems and leaves	(Xiao et al., 2010a)
260	wilsonianadilactone D	g	stems and leaves	(Yang et al., 2011)
261	wilsonianadilactone E	g	stems and leaves	(Yang et al., 2011)
262	wilsonianadilactone B	g	stems and leaves	(Yang et al., 2008)
263	wilsonianadilactone C	g	stems and leaves	(Yang et al., 2008)
264	lancifodilactone L	k	stems and leaves	(Xiao et al., 2006a)
265	lancifodilactone M	k	stems and leaves	(Xiao et al., 2006a)
266	rubriflorin A	e	stems and leaves	(Xiao et al., 2007c)
267	rubriflorin B	e	stems and leaves	(Xiao et al., 2007c)
268	rubriflorin C	e	stems and leaves	(Xiao et al., 2007c)
269	rubriflorin D	e	stems and leaves	(Xiao et al., 2007a)
270	rubriflorin E	e	stems and leaves	(Xiao et al., 2007a)
271	rubriflorin F	e	stems and leaves	(Xiao et al., 2007a)
272	rubriflorin G	e	stems and leaves	(Xiao et al., 2007a)
273	rubriflorin H	e	stems and leaves	(Xiao et al., 2007a)
274	rubriflorin i	e	stems and leaves	(Xiao et al., 2007a)
275	rubriflorin J	e	stems and leaves	(Xiao et al., 2007a)
276	schirbidilactone B	e	stems and leaves	(Xiao et al., 2010a)
277	schirbidilactone C	e	stems and leaves	(Xiao et al., 2010a)
278	schirbidilactone D	e	stems and leaves	(Xiao et al., 2010a)
279	schirbidilactone E	e	stems and leaves	(Xiao et al., 2010a)
280	sphenadilactone A	a	stems and leaves	(Xiao et al., 2006d)
281	sphenadilactone B	a	stems and leaves	(Xiao et al., 2006d)
282	sphenalactone A	a	stems and leaves	(Xiao et al., 2007b)
283	sphenalactone B	a	stems and leaves	(Xiao et al., 2007b)
284	sphenalactone C	a	stems and leaves	(Xiao et al., 2007b)
285	sphenalactone D	a	stems and leaves	(Xiao et al., 2007b)
286	sphenadilactone C	a	stems and leaves	(Xiao et al., 2008)
287	sphenadilactone D	a	stems and leaves	(He et al., 2012)
288	sphenadilactone E	a	stems and leaves	(He et al., 2012)
289	wilsonianadilactone A	g	stems and leaves	(Yang et al., 2008)
290	schigrandilactone A	h	stems	(Xiao et al., 2009)
291	schigrandilactone B	h	stems	(Xiao et al., 2009)
292	schigrandilactone C	h	stems	(Xiao et al., 2009)
293	henridilactone A	i	stems and leaves	(Li et al., 2004a)
294	henridilactone B	i	stems and leaves	(Li et al., 2004a)
295	henridilactone C	i	stems and leaves	(Li et al., 2004a)
296	henridilactone D	i	stems and leaves	(Li et al., 2004a)
297	henridilactone L	i	stems and leaves	(He et al., 2020)
298	henridilactone M	i	stems and leaves	(He et al., 2020)
299	henridilactone N	i	stems and leaves	(He et al., 2020)
300	henridilactone O	i	stems and leaves	(He et al., 2020)
301	lancifodilactone R	k	stems and leaves	(Xiao et al., 2010b)
302	lancifodilactone I	k	stems and leaves	(Xiao et al., 2006a)
303	lancifodilactone J	k	stems and leaves	(Xiao et al., 2006a)

Table 3 (*continued*)

NO.	Compound	Source	Parts	Ref
304	lancifodilactone L	k	stems and leaves	(Xiao et al., 2006a)
305	lancifodilactone N	k	stems and leaves	(Xiao et al., 2006a)
306	lancifodilactone G	k	stems and leaves	(Xiao et al., 2005b)
307	lancifodilactone E	k	stems and leaves	(Li et al., 2004b)
308	micrandilactone A	l	stems and leaves	(Li et al., 2003a)
309	negleschidilactone A	m	stems	(Liang et al., 2013b)
310	negleschidilactone B	m	stems	(Liang et al., 2013b)
311	lancifodilactone D	k	stems and leaves	(Li et al., 2004b)
312	lancifodilactone C	k	stems and leaves	(Li et al., 2004b)
313	lancifodilactone B	k	stems and leaves	(Li et al., 2004b)
5.3.9. 8,9-seco-12,22-cyclopreschisanartane and 9,23:12,22-Dicyclolancischiartane				
314	schincalactone A	j	stems	(Song et al., 2018)
315	schincalactone B	j	stems	(Song et al., 2018)
316	schincalide A	j	stems	(Zhou, 2018)
317	schincalide B	j	stems	(Zhou et al., 2016)
5.3.10. Octanortriterpenoids and others				
318	micranoic acid A	l	stems and leaves	(Li et al., 2003b)
319	micranoic acid B	l	stems and leaves	(Li et al., 2003b)
320	11β-hydroxylkadsuphilactone A	p	stems	(Wang et al., 2016)
321	chinorlactone A	b	stems	(Yang et al., 2022)
5.4. Pentacyclic triterpenoids				
322	oleanolic acid	a	furits	(Du, 2007)
323	β-Amyrin	h	stems	(Zong et al., 2013)
324	taraxerol	h	stems	(Zong et al., 2013)
325	maslinic acid	h	stems	(Zong et al., 2013)
326	ursolic acid	h	stems	(Shi et al., 2012; Zong et al., 2013)
327	acetylursolic acid	h	stems	(Zong et al., 2013)
328	2α, 3α-dihydroxyurs-12-en-28-oic acid	h	stems	(Zong et al., 2013)
329	corosolic acid	h	stems	(Zong et al., 2013)
330	asiatic acid	h	stems	(Zong et al., 2013)
331	2α, 3α, 23-trihydroxyurs-12-en-28-oic acid	h	stems	(Zong et al., 2013)
332	23-hydroxyursolic acid	h	stems	(Zong et al., 2013)
333	granditriol	h	stems	(Shi et al., 2016)
334	lupeol	h	stems	(Zong et al., 2013)
335	betulinic acid	h	stems	(Zong et al., 2013)

keto-alcohol condensation rearrangement. 12,22-Cyclopreschisanartane type (**233**–**236**), possessing a 7/8/3/5 carbon frame parent nucleus, presumably derived from preschisanartane type by oxidation and keto-alcohol condensation rearrangement reaction (Fig. 11).

5.3.7. 14-Nor-16,17-secopreschis anartane and 15,17-Dicyclolancifoartan

The 14-Nor-16,17-secopreschisanartane type (**237**–**238**), which possesses a 7-carbon backbone parent nucleus, is derived from the 16,17-secopreschisanartane type by the removal of the C-14 atom after the 14,15 oxidative rearrangement reaction. 15,17-Dicyclolancifoartan type triterpenes (**239**–**242**), with [9.2.1.$0^{2.8}$] tetradecane system. So far, four of these compounds have been isolated. The specific structures are shown in Fig. 11.

5.3.8. Schisanartane

Schisanartane type (**243**–**313**), possessing a 7/8/5 carbon frame parent nucleus, presumably derived from the cyclic reaction at the C-16, C-22 positions of 16,17-secopreschisanartanes type triterpenes. The hydroxyl group is generally substituted on C-2, C-8, C-19, C-30. Double bond position: generally between C-1 and C-10, C-5 and C-6/C-10, C-8 and C-7/C-14, C-24 and C-25 positions (Fig. 12).

5.3.9. 8,9-Seco-12,22-cyclopreschisanartane and 9,23:12,22-Dicyclolancischiartane

The 8,9-Seco-12,22-cyclopreschisanartane type (**314**–**315**) has a unique 5/5/6/11/3 ring system and is the first type with a characteristic thirteen-membered carbon ring structure found in Schisandraceae. The schincalactone A and B isolated from *S. incarnata* belong to this conformation. 9,23:12,22-Dicyclolanci schiartane type, with a [5.2.1.01,6] decane system. Two compounds (**316**–**317**) of this type, schincalide A-B, were isolated so far and their chemical structures are shown in Fig. 13.

5.3.10. Octanortriterpenoids and others

The compounds micranoic acid A (**318**) and B (**319**) are highly degraded triterpenoids in which the fission of the C-17/C-20 bond is achieved by oxidation. **319** differed from **318** in which the Me-19 was replaced by a cyclopropyl methylene group. In addition, two other classes of triterpenes, **320** and **321**, were isolated. Their chemical structures are shown in Fig. 14.

5.4. Pentacyclic triterpenoids

Pentacyclic triterpenes (**322**–**335**) are widely found in Chinese herbal medicine, which are triterpenoids consisting of five closed rings linked by six isoprene units as the parent, and

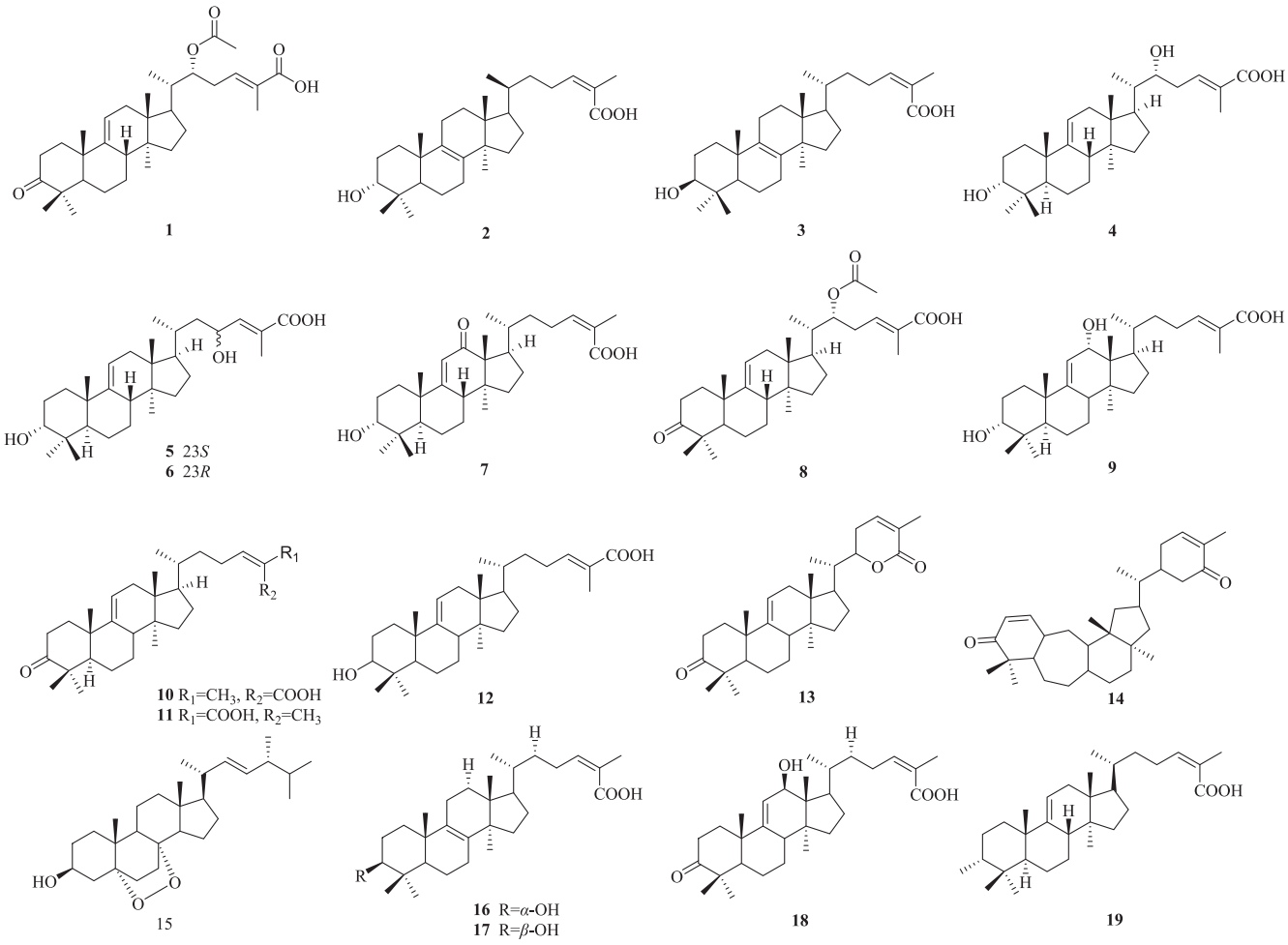

Fig. 2 The chemical structure of 1–19.

the three categories of Oleanane, Ursane and Lupane are summarized in this paper. The structures are shown in Fig. 15.

6. Pharmacology of *Schisandra* spp

In recent years, the medicinal value of the *Schisandra* genus has gradually received attention from scholars, and the research on its chemical components and pharmacological effects has intensified. As one of the components with great potential for development, triterpenes have also received much attention in pharmacological effects, especially in hepatoprotective, neuroprotective and antitumor effects.

6.1. Hepatoprotective and anti-inflammatory effects

Wang et al. explored the effect of triterpenoid derivatives of *S. chinensis* on HDAC and NLRP3 inflammatory vesicle activity and found that the derivatives showed significant inhibition of HDAC with IC_{50} of 1.139–10.558 μM and low cytotoxicity (CC_{50} greater than 20 μM) against J774A.1 compared to HDAC inhibitor class of antitumor drugs, showing potential for development as potential for development as an anti-inflammatory immune drug. In addition, this class of derivatives modulates LPS and Nig levels and reduces IL-1β and caspase-1 expression (Wang, 2021a). A new triterpene, 11β-hydroxylkadsuphilactone A (**320**), was isolated from the stem of *S. pubescens* and the structure of the compound was determined through wave spectroscopy, while the hepatoprotective activity of the new triterpene against D-GalN-induced cell death of QSG7701 cells was later assessed. The test results showed that 11β-hydroxyl kadsuphilactone A (**320**) showed hepatoprotective activity at 10 μM with a survival rate of 60.5% (Silybin served as a positive control with a survival rate of 66.2 ± 4.0%) (Wang et al., 2016). Kang et al. investigated the effect of ethanolic extract of *S. chinensis* fruit (dose of 500 μg/mL) on the expression and production of pro-inflammatory mediators and inflammatory cytokines in RAW264.7 cells and the possibility of SF having anti-inflammatory properties was investigated by determining the effect on the levels of NO, etc. The results showed that it significantly blocked the production of nitric oxide (NO), tumor necrosis factor-α (TNF-α) and IL-1β induced by lipopolysaccharide (LPS) stimulation and that this effect did not trigger a cytotoxic response (Kang, 2014). Similarly, Jeong et al. investigated the anti-inflammatory effect of the ethanolic extract of *S. chinensis* fruit and found that the ethanolic extract of *S. chinensis* fruit inhibited the expression and activity of IL-1β-stimulated matrix proteases in SW1353 cells, and this effect may be related to the expression of nuclear factor-κB and c-Jun N-terminal kinase/p38MAPK (Jeong, 2015).

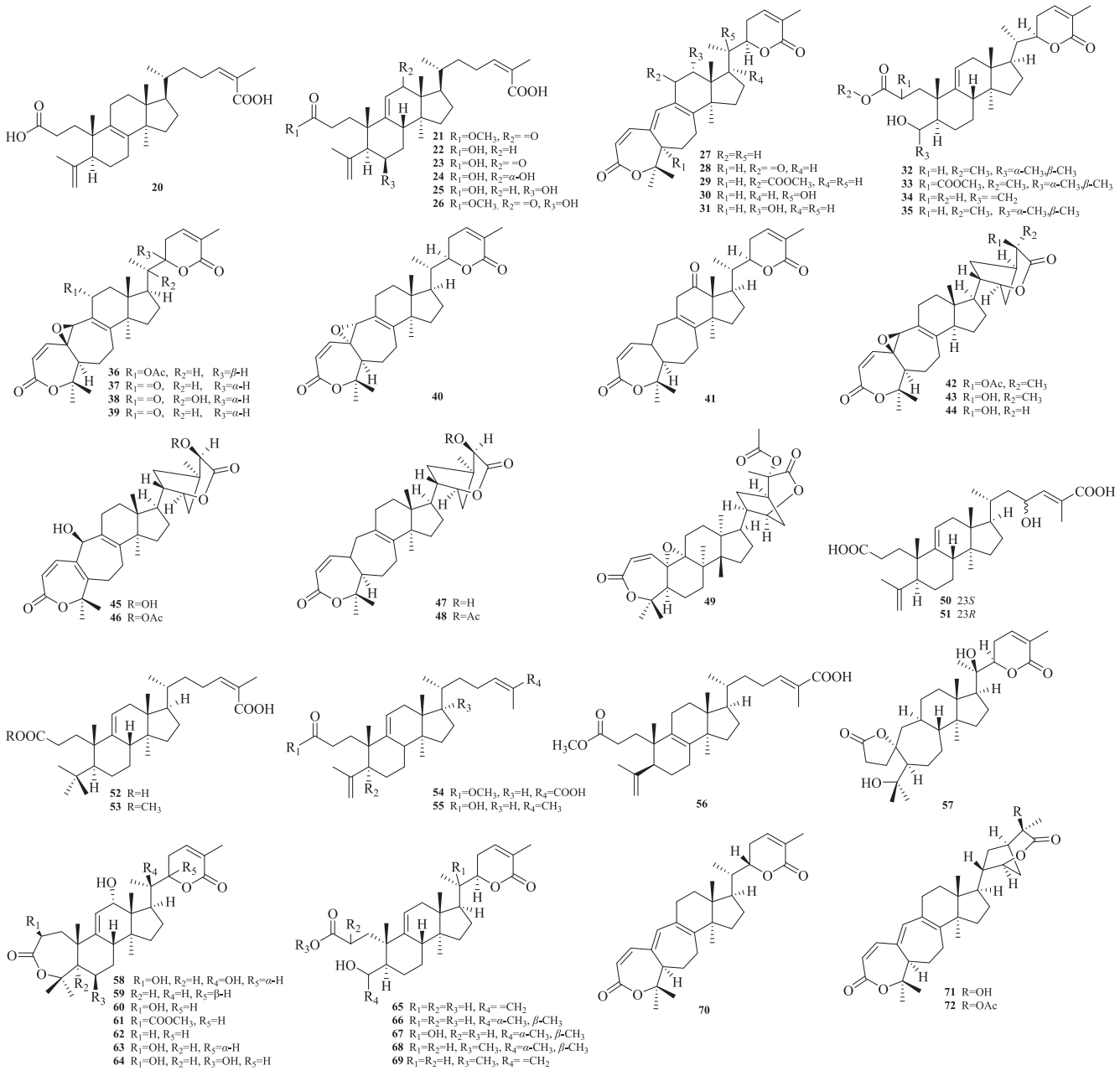

Fig. 3 The chemical structure of 20–72.

A new triterpene propindilactone L (**130**) isolated from *S. propinqua* was found to significantly inhibit hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg), which is the first report on the anti-hepatitis B virus effect of nortriterpenoids, and achieved good therapeutic effect with SI values of 2.68 and 1.11 (Lei, 2009). The compounds arisanlactone B (**244**) and D (**246**) were found to have a slight anti-inflammatory effect, with 22.24% and 18.47% inhibition of elastase at 10 μg/mL, correspondingly (Cheng et al., 2010b).

6.2. Anti-tumor effects

Gao et al. found that schilancidilactone V (**205**) isolated from *S. wilsoniana* had significant cytotoxic activity against oral epithelial carcinoma cells and breast cancer cells MDA-MB-231 cells and was effective in inhibiting the proliferation of cancer cells with IC_{50} values of 3.18 and 5.22 μmol/L in that order (with camptothecin as the positive control, IC_{50} values of 1.62 and 2.18 μmol/L) (Gao et al., 2013). Tanaka et al. tested the anti-proliferative activity of triterpenoids from the roots of *S. chinensis* against human cancer cell lines A549 (lung cancer), RPMI8226 (leukemia), HeLa (uterine cancer) and MCF-7 (breast cancer) cells and showed that propiniclactone A (**91**), schinensin C (**85**), schinensin D (**78**) and schisanbilactone A (**80**), which are triterpenes with α,β-unsaturated δ-lactone moiety, showed more significant anti-proliferative activity against MCF-7 cells with IC_{50} values of 9.3–12.8 μM, and their activity was close to that of the positive drug Cisplatin (IC_{50} of 8.5 μM) (Tanaka et al., 2021). Liu et al. performed human tumor cytotoxicity tests on 12-hydroxyschiglausin B (**58**) and 12-hydroxykadsuphilactone B

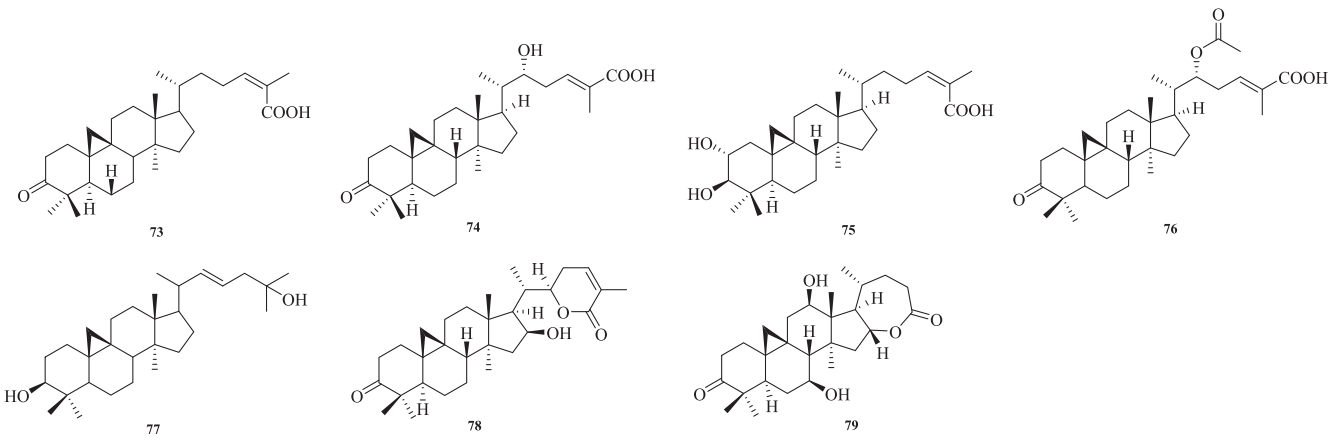

Fig. 4 The chemical structure of 73–79.

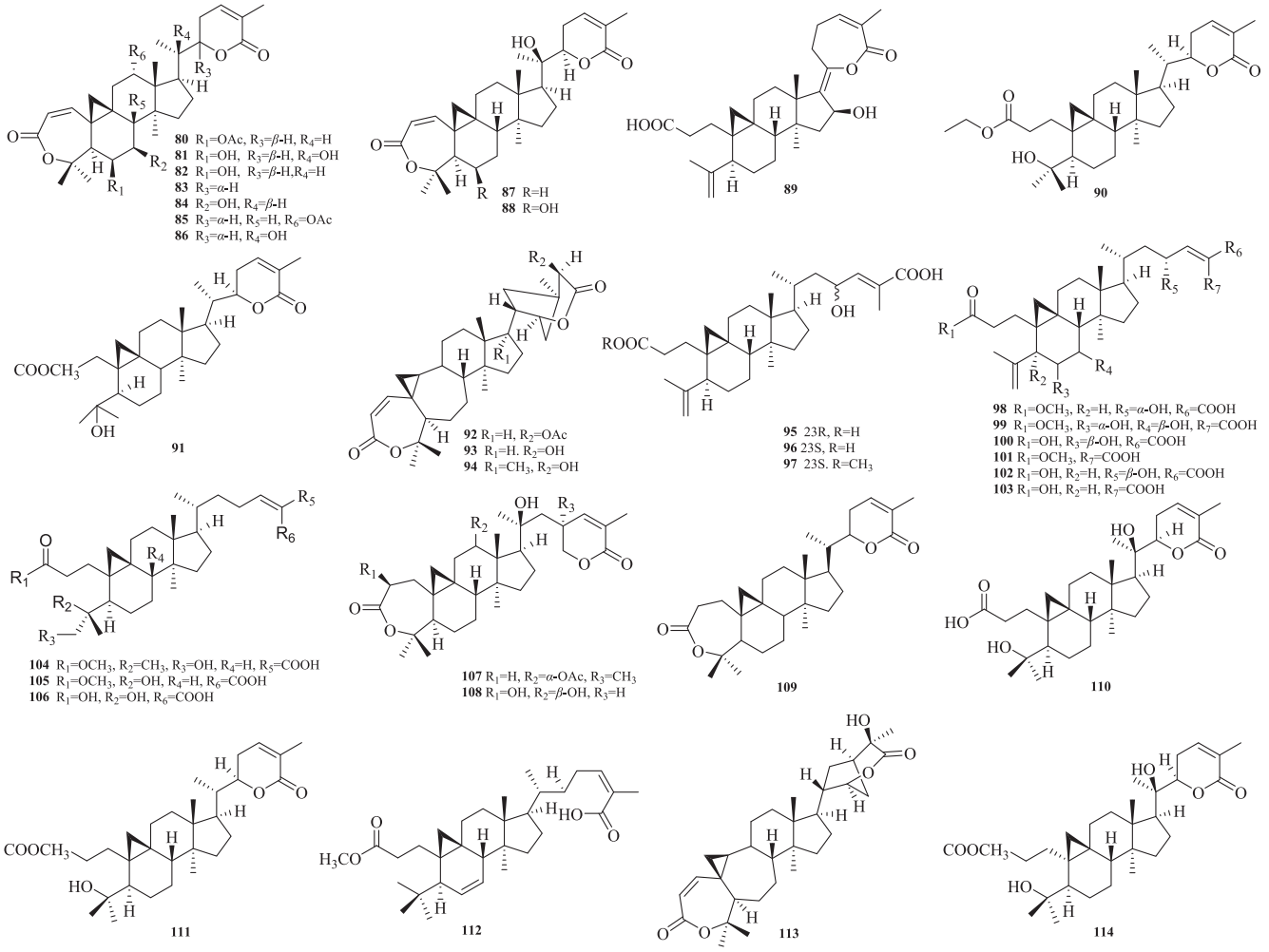

Fig. 5 The chemical structure of 80–114.

(**108**) using the MTT method. The data showed that 12-hydroxykadsuphilactone B (**108**) had higher cytotoxic activity, with the strongest toxicity against $HepG_2$ cells with an IC_{50} of 11.3 μM (Liu et al., 2018). Five new triterpenes, Schiglausins P-T (**33**–**34**, **8**, **76**, **105**), were isolated from *S. glaucescens* fruit and tested for cytotoxicity by YU et al. Pharmacological

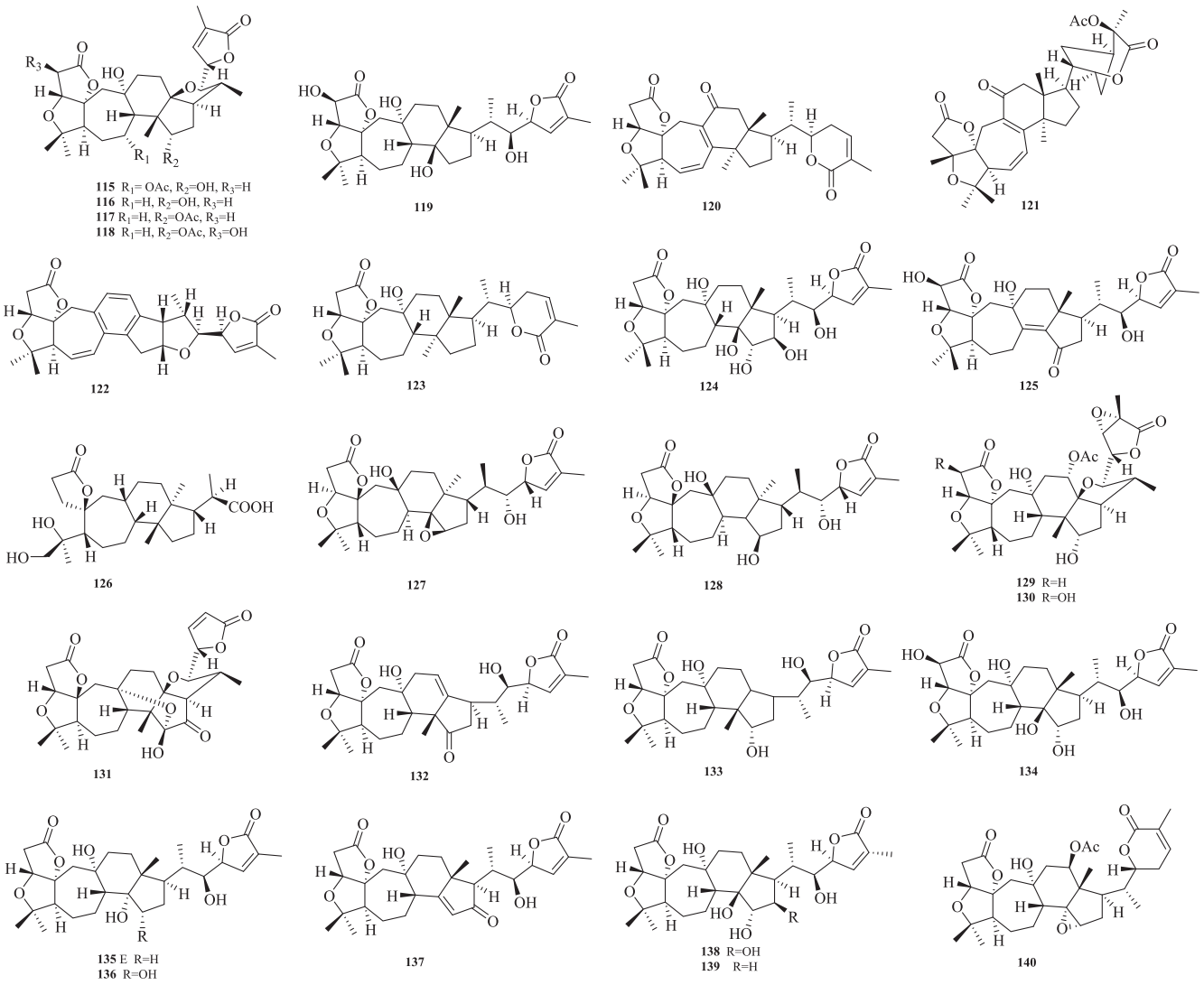

Fig. 6 The chemical structure of 115–140.

experiments confirmed that all five compounds had toxic effects on B16 mouse melanoma cell lines with IC_{50} values ranging from 3.64 to 27.00 μM, exhibiting moderate inhibition of tumor cell proliferation (Doxorubicin hydrochloride as the positive control, IC_{50} values of 2.61 μM) (Yu et al., 2016).

Pharmacological studies have shown that manwuweizic acid (**20**) inhibited lung cancer, brain tumour-22 and solid liver cancer in mice. Additionally, anwuweizonic acid (**11**) and nigranoic acid (**103**) also have been reported to have antitumor activity, showing high inhibition of human decidual cells and rat luteal cells (20 ug/ml for rat luteal cells and 40 ug/ml for human decidual cells). That is the first that a plant from the family *Schisandra*ceae can inhibit these two tumor cells (Chen et al., 2001). *S. chinensis* extract can affect the function of the immune organs of the spleen and thymus and influence the activity of immune cells, thus enhancing the ability of the body to clear cancer cells. Hou et al. studied *S. viridis* as an anti-tumor active ingredient. Using the MTT assay, Fluorouracil (5-FU) was used as a positive control, and Schisanol (**19**) was found to have an inhibitory effect on human tongue cancer CAL27 cells with an IC_{50} of 11.7 mg/mL. In further studies, Schisanol (**19**) was also shown to have toxic activity against human breast cancer MCF7 cells, with significant inhibitory effects on cancer cell proliferation (Hou et al., 2016).

6.3. Anti-HIV effects

At present, the use of anti-AIDS drugs remains the main response to AIDS and therefore anti-AIDS natural products have become the focus of scholarly attention in various countries. In recent years, researchers have conducted numerous studies on the biological activities, pharmacological effects and mechanisms of action of the fruits, roots and leaves of the genus *Schisandra*, leading to the isolation of a series of novel highly oxidized triterpenoids with anti-HIV effects. Xiao et al. isolated three new highly oxidized hypo triterpenoids rubriflorins A-C (**266**–**268**) from *S. rubriflora*, which have a unique A-ring opening feature. Pharmacological experiments showed that rubriflorins A-C (**266**–**268**) exhibited anti-HIV effects with EC_{50} of 10.0–81.3 μg/mL (AZT as a positive control with EC_{50} of 0.0043 μg/mL) (Xiao et al., 2007c). The compounds schisphendilactone A (**84**) and B (**37**) were isolated

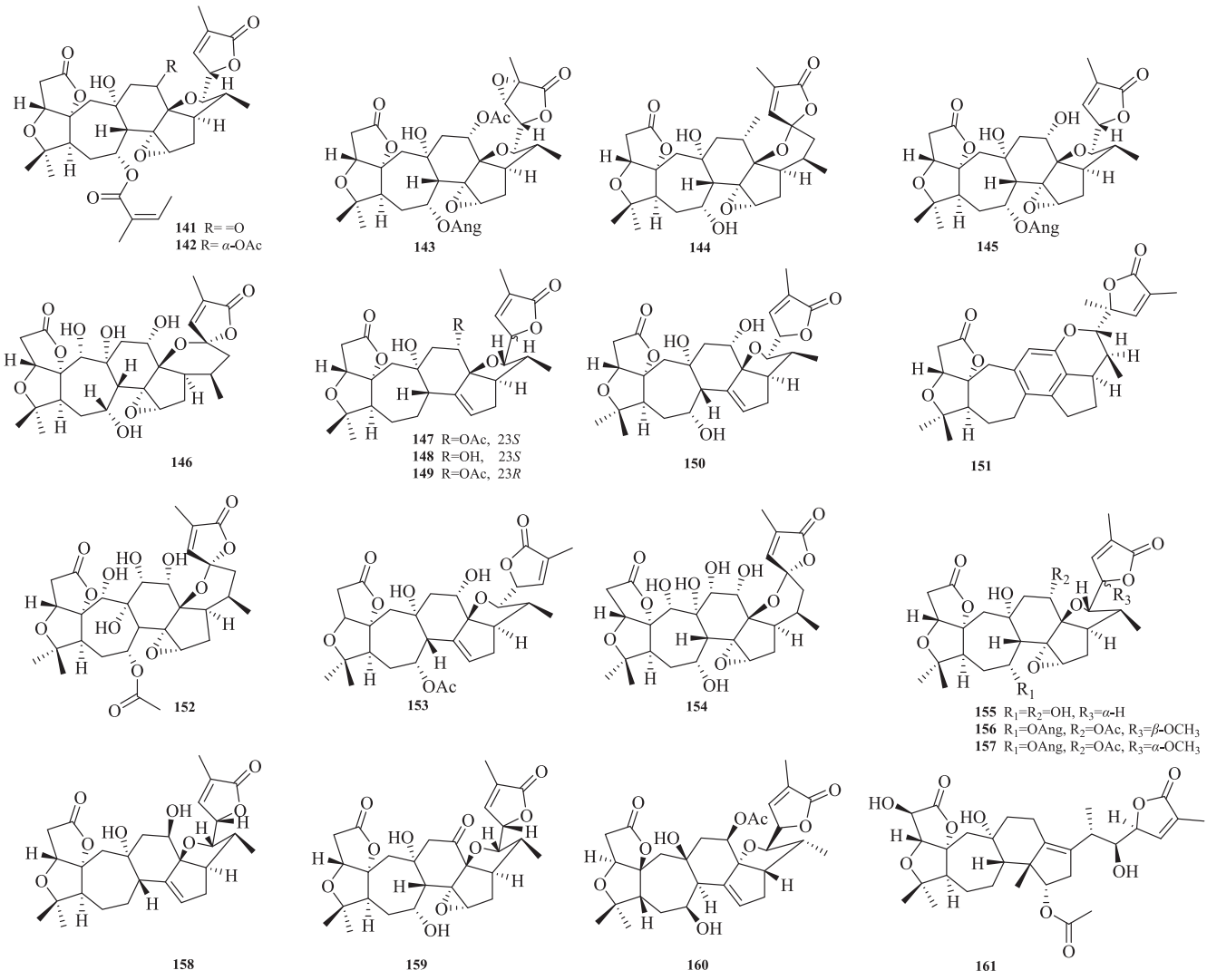

Fig. 7 The chemical structure of 141–161.

from *S. sphenanthera* by Liang et al. In vitro experiments demonstrated their significant anti-HIV effects. Their EC_{50} values were 8.79 and 1.09 μg/mL respectively, while the positive control AZT EC_{50} was 0.0053 μg/mL (Liang et al., 2013a).

Xiao et al. isolated two new triterpenes lancifodilactone F (**126**) and G (**306**) from *S. lancifolia*, and pharmacological experiments showed that both compounds had an anti-HIV activity with EC_{50} values of 20.69 and 95.47 μg/mL, respectively (Xiao et al., 2005a; Xiao et al., 2005b). In 2015, the anti-HIV effect of *S. chinensis* was discovered and identified a lead compound, diphenylamine ester, with potent anti-HIV activity. Diphenylamine esters have low toxicity and a good broad spectrum and are effective against both experimental and clinical strains. It is currently undergoing preclinical studies and is expected to become a new class of anti-HIV drugs.

6.4. Neuroprotective effects

Researchers isolated 11 compounds from *S. henryi* and pharmacological assays revealed that only henridilactone O (**300**) exhibited moderate neuroprotective activity with a cell differentiation rate of 11.1% (He et al., 2020). It has been reported in the literature that *S. chinensis* extract prevents hydrogen peroxide-induced neuronal cell death and improves cognitive dysfunction in rats. The experimental data suggest that this is associated with an increase in brain-derived neurotrophic factor, downstream molecules pERK, pATK and pCREB (Park et al., 2019). Jin et al. investigated the protective effect of an aqueous extract of *S. chinensis* on neuronal cells in the cerebral cortex of mice. The results illustrated that *S. chinensis* aqueous extract could improve the learning ability of APP/PS1 double transgenic mice, enhance the number of nisin bodies, improve the cell quality of the cerebral cortex, and promote the survival of neural cells. In addition, mice treated with *S. chinensis* aqueous extract showed a decrease in MDA content and a significant increase in SOD content in the cerebral cortex. Its neuroprotective effect may be related to the reduction of damage caused by oxidative stress, and its mechanism of action should be further explored (Jin, 2017).

6.5. Immunomodulation effects

The triterpenoids schisanlatone C (**30**) showed selective inhibition of B-lymphocyte proliferation with IC_{50} with 20.51 μM;

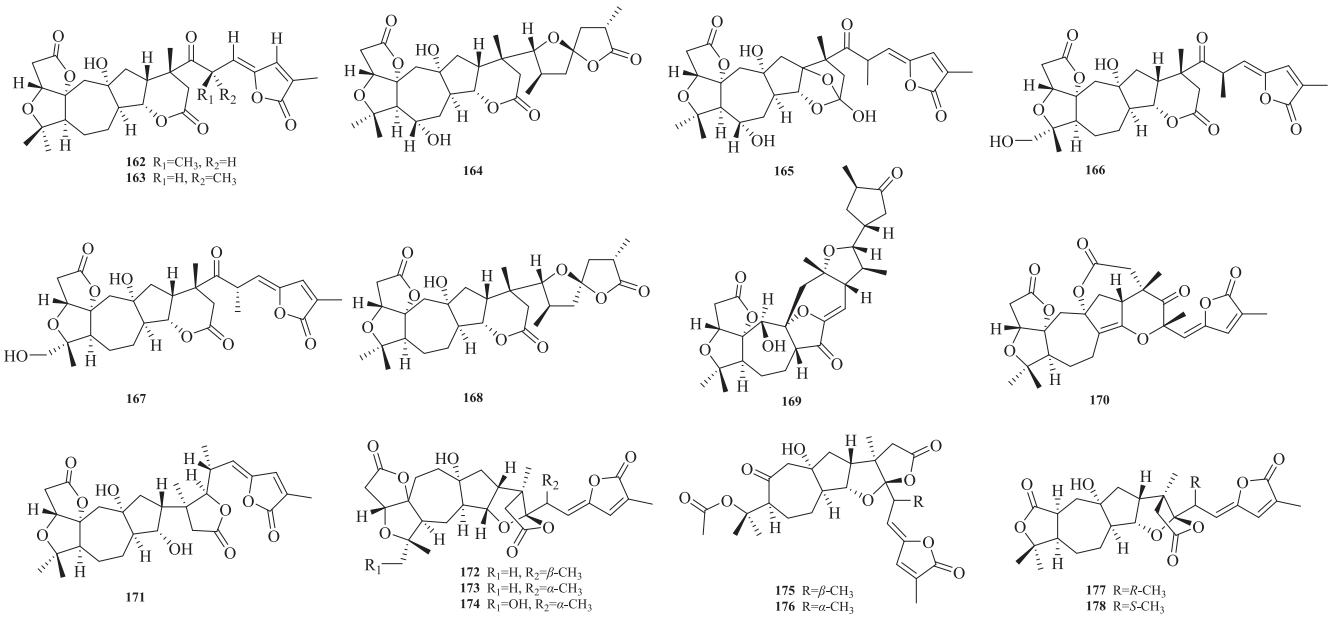

Fig. 8 The chemical structure of 162–178.

the compounds schisanlactone B (**70**) and 3,4-seco-(24*Z*)-*cyclo*-4(28),24-diene-3,26-dioic-3-methyl ester (**101**) had a selective inhibitory effect on T-lymphocyte proliferation with an IC_{50} range of 14.28–19.33 μM (positive control: cisplatin, IC_{50} = 3.16 μg/mL); Propinic lactone A (**111**) had an inhibitory effect on both T- and B-lymphocyte proliferation with an IC_{50} of 6.97–16.93 μM (positive control: 5-Fluorouracil, IC_{50} = 8.48 μM). Among them, schisanlactone B (**70**) and 3,4-seco-(24*Z*)-cycloart-4(28),24-diene-3,26-dioic-3-methyl ester (**101**) specifically inhibited the proliferation of B lymphocytes by more than 90% (Qiu et al., 2018; Zhao et al., 2020; Liu et al., 2017a).

kadsudilactone A (**109**) showed moderate inhibition of ConA-induced T-lymphocyte proliferation with an IC_{50} of 6.32 μM. Significant inhibition of LPS-induced B lymphocyte proliferation was observed with the same intensity as the positive drug mycophenolate mofetil (MMF) with an IC_{50} of 11.49 μM (IC_{50} of MMF was 17.8 μM). Moreover, there was no significant toxicity to mouse spleen lymphocytes at a concentration of 100 μM compared to the positive drugs CsA and MMF (Zhou, 2018). Studies have found that *S. chinensis* extract has a bidirectional immunomodulatory effect, on the one hand enhancing the secretion of immune cells and on the other hand, increasing the activity of related cells and accelerating the clearance of antigens (Chen, 2021).

6.6. Anti-oxidation activity

The intrinsically low levels of catalase (CAT), glutathione peroxidase (POD) and superoxide dismutase (SOD) make immune cells more susceptible to damage from oxidative stress induced by high levels of glucose and free fatty acids. Thus, the high antioxidant activity and free radical scavenging capacity of *S. chinensis* extracts play an invaluable role in protecting cells from dysfunction or death (Jo et al., 2011). The total triterpenoids of *S. chinensis* had a strong antioxidant capacity overall and there was an obvious quantitative-effect relationship. The total triterpene scavenging ability of *S. chinensis* stems and leaves were flowering > spreading > budding > deciduous, and only the total triterpene scavenging ability of vine stems was spreading > flowering > budding > deciduous. The reducing ability of total triterpenes of *S. chinensis* stems and leaves were stronger than VE and weaker than VC, and the antioxidant ability of stems was the strongest compared with other parts (Wang, 2021b). The scavenging ability of *S. chinensis* vine stem triterpenes on DPPH radicals was correlated with the concentration of added triterpenes, the higher the added amount, the stronger the scavenging capacity, with an IC_{50} of 0.077 mg/mL, and the IC_{50} of the positive control VC was 0.692 mg/mL. Besides, there was an inhibitory effect on lipid oxidation (Li, 2012).

6.7. Antimicrobial activity

The ethanolic extract of *S. chinensis* has been reported to have an antibacterial effect. In recent years, it has been found to have a significant inhibitory effect on *Staphylococcus aureus*, *Escherichia coli, Salmonella typhi* and *Escherichia coli*, and the extract has shown good stability to heat treatment (Zou et al., 2011; Chen, 2018). In vitro inhibition experiments showed that the total triterpenes of *S. chinensis* leaves had some inhibitory effect on bacteria, but not on *Candida albicans*. The inhibitory ability against *Bacillus subtilis* and *Pseudomonas aeruginosa* was more pronounced and weaker against *Staphylococcus aureus* and *Escherichia coli*. The MIC of the total triterpenes of the stem and leaves of *S. chinensis* at different periods ranged from 0.63 to 5.00 mg/mL and the MBC from 2.50 to 20.00 mg/mL, and the growth rate and cycle of the bacteria were effectively limited (Zhou, 2018).

6.8. Insecticidal activity

Jiang et al. screened the insecticidal activity of triterpenes from *S. chinensis* and found that manwuweizic acid (**20**) showed toxic to A*phis gossypii* and *Plutella xylostella* with a pest mor-

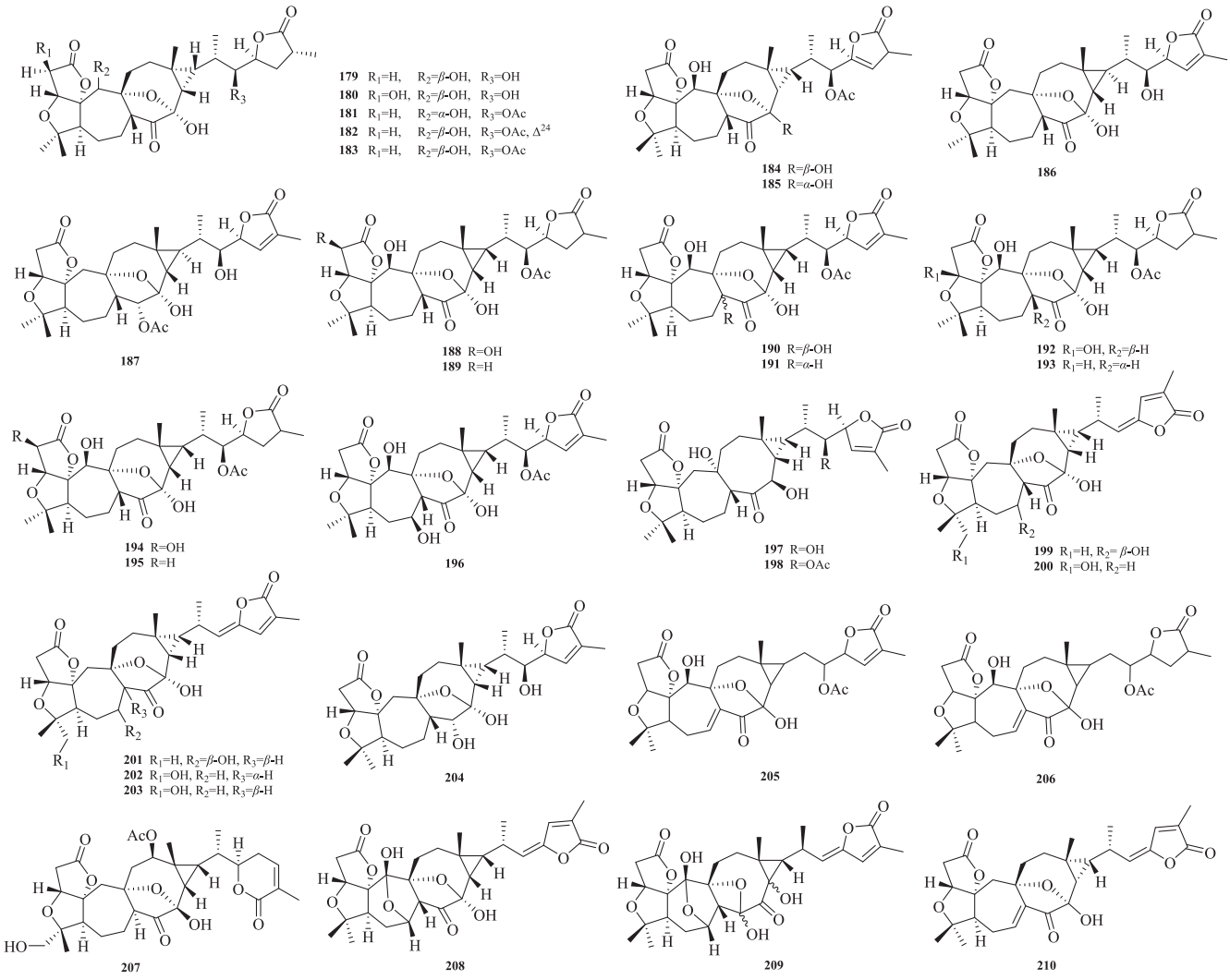

Fig. 9 The chemical structure of 179–210.

tality rate of 66% (Jiang, 2011). The compounds acetyl ursolic acid (**327**), 2α, 3α-dihydroxy urs-12-en-28-oic acid (**328**) and corosolic acid (**329**) exhibited significant cytotoxicity against marine shrimp larvae with IC_{50} of 17.0–25.2 μM. Preliminary structure–activity relationship studies indicated that the 3-position hydroxylation of the arcane-type triterpene acids and acetylation of the urethane-type triterpene acids could greatly enhance their insecticidal activity (Zong et al., 2013).

6.9. Others

Ding et al. isolated a series of triterpenoids with good activity from *S. chinensis*, among which propindilactone Z (**107**) and schipropinqua acid J (**75**) showed moderate inhibitory activity against COLL-induced platelet aggregation in rabbits with 12.6 ± 4.5 and 10.4 ± 9.5, respectively, as inhibition percentage (%) (Ding, 2018). The research reports that the compound manwuweizic acid (**20**) obtained from *S. propinqua* exhibited cholesterol biosynthesis inhibitory activity with 19.2% inhibition (Liu et al., 1989). Scholars conducted in vitro cytotoxicity experiments with anwuweizonic acid (**11**) and manwuweizic acid (**20**). The data showed that the mortality rate of the human metaphase cell line and murine corpus luteum cell line exceeded 98.5% after the addition of 20 and 40 mg/mL of both triterpenes. This indicated that the triterpenes had strong cytotoxic activity against the human metaphase cell line and murine luteal cell line and had anti-reproductive effects (Chen et al., 2002; Chen et al., 2001). All the pharmacological effects of this genus are summarized in Table 4 (active: IC_{50} < 10 μM; moderately active: 10 μM < IC_{50} < 20 μM; not active: IC_{50}-greater than 20 μM).

7. Treatment potential

7.1. Liver injury

Non-alcoholic fatty liver disease (NAFLD) includes simple fatty liver and the evolution of steatohepatitis, cirrhosis and liver cancer from it. Up to now, its pathogenesis is still unclear, and treatment is mainly through lipid-lowering, alleviation of insulin resistance and anti-oxidative stress to alleviate NAFLD. The hepatoprotective active component of *S. chinensis*, triterpenes 19*R*-hydroxylwuwei-zidilactone H (**146**), had significant effects on hepatic lesions, and such components

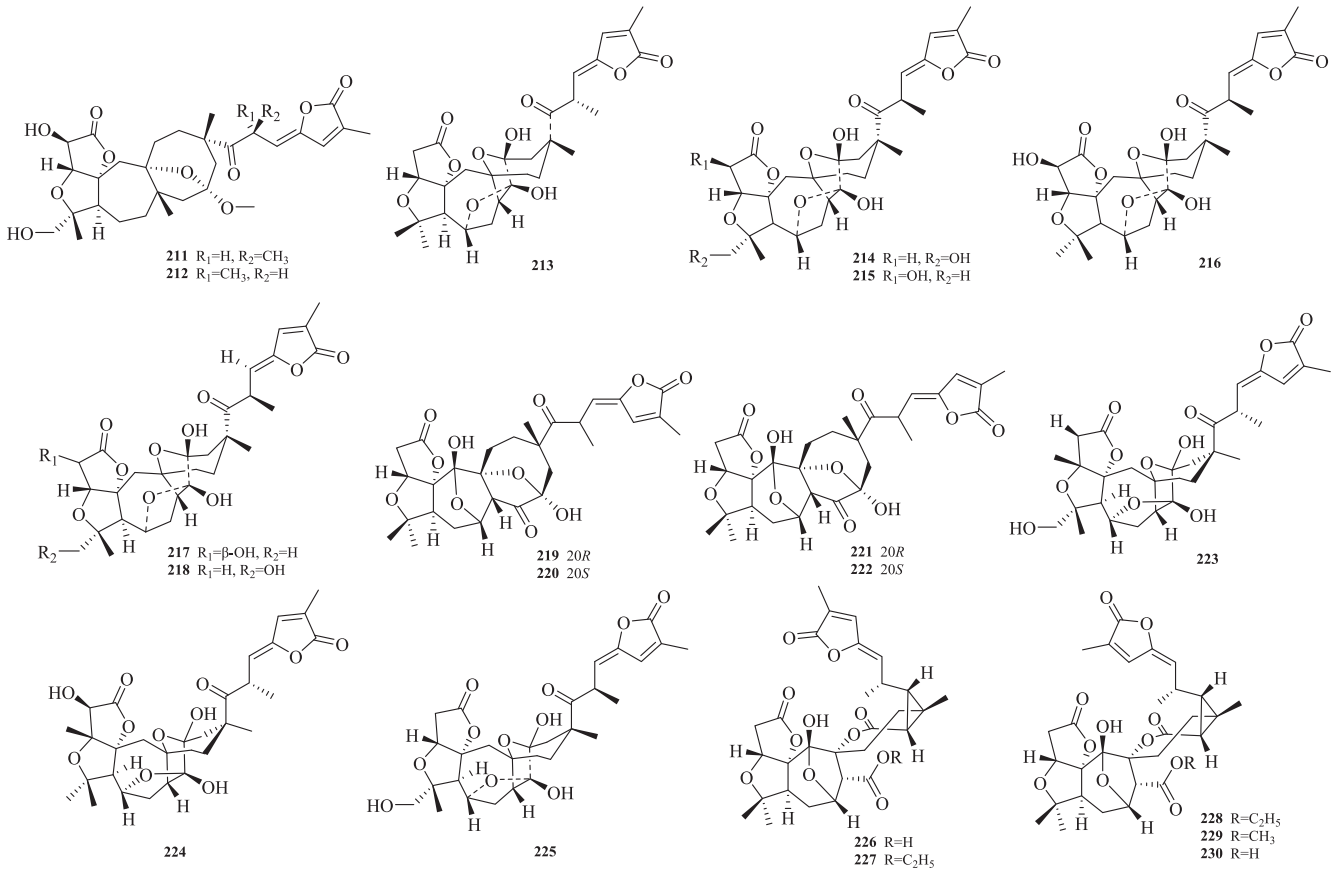

Fig. 10 The chemical structure of 211–230.

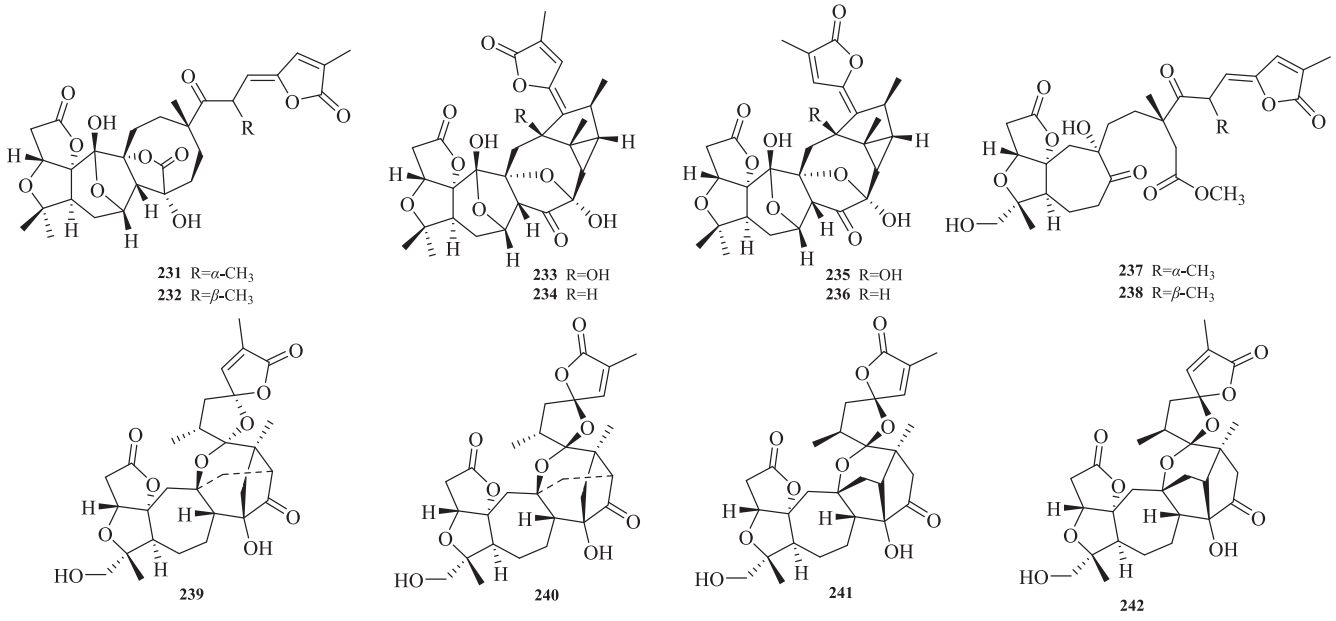

Fig. 11 The chemical structure of 231–242.

showed significant alleviation of high-fat diet-induced NASH in rats and also modulated related enzyme activities, thus providing relief from NAFLD (Li et al., 2017). Researchers found that total triterpenes of *S. chinensis* had significant intervention effects on both acute and chronic liver injury induced by alcohol intake. It is speculated that the mechanism of action may be to alleviate the lipid peroxidation triggered by ethanol metabolism, scavenge oxygen free radicals and protect cellular

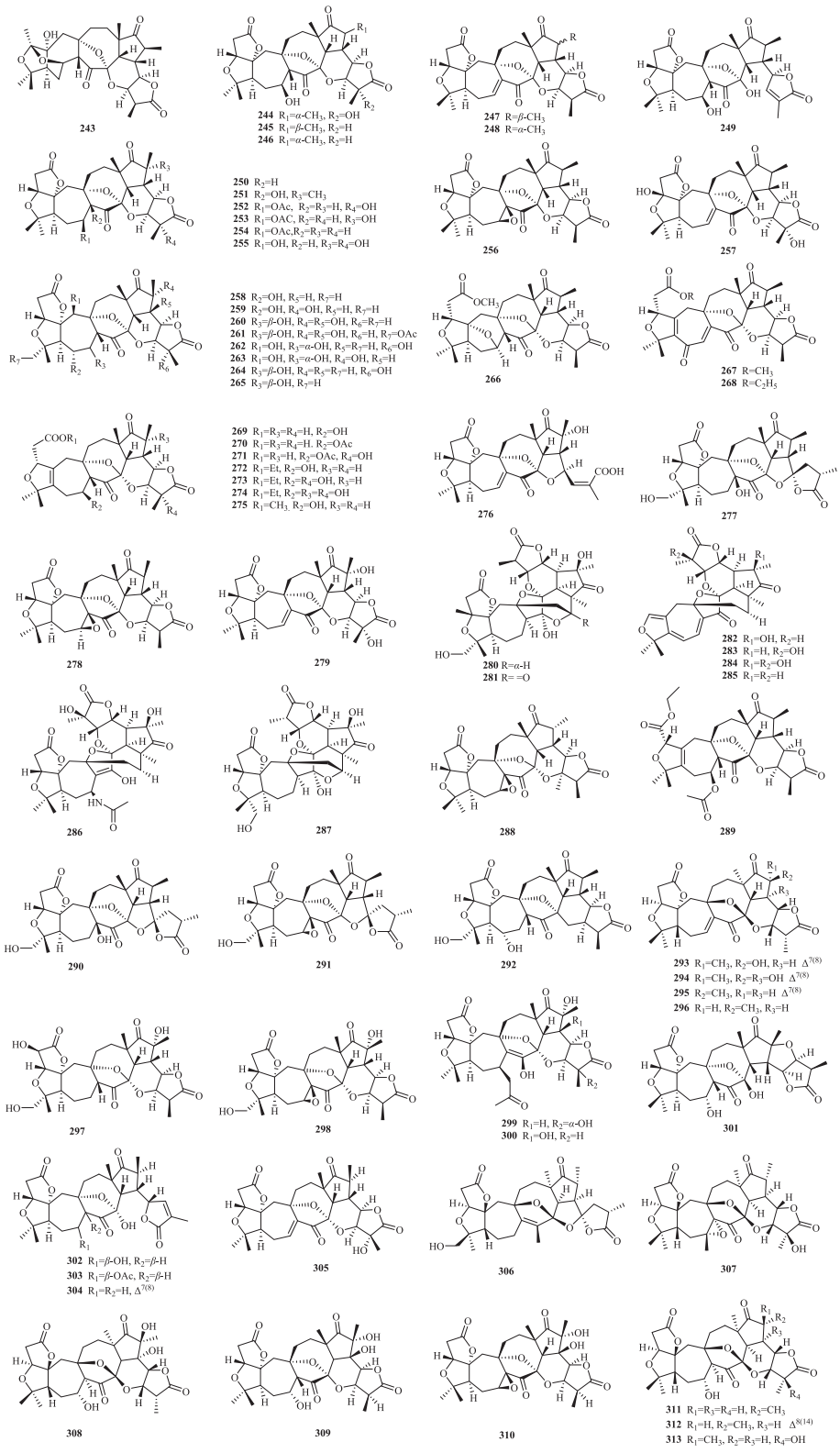

Fig. 12 The chemical structure of 243–313.

organelles. Secondly, it regulates the expression of CYP2E1, a key enzyme in ethanol metabolism, and reduces its activity to improve the liver injury caused by alcohol intake (Zhu, 2014). Leng et al (Leng, 2015). used *S. chinensis* to treat patients with drug-induced liver injury, with *Silybin Meglumine* as the control group, both treated for two courses of treatment (one course of treatment is 30 days). Clinical results showed that the total effective rate of the treatment group (86.67%) was better than that of the control group (73.33%), and there was a significant difference between the two groups, which

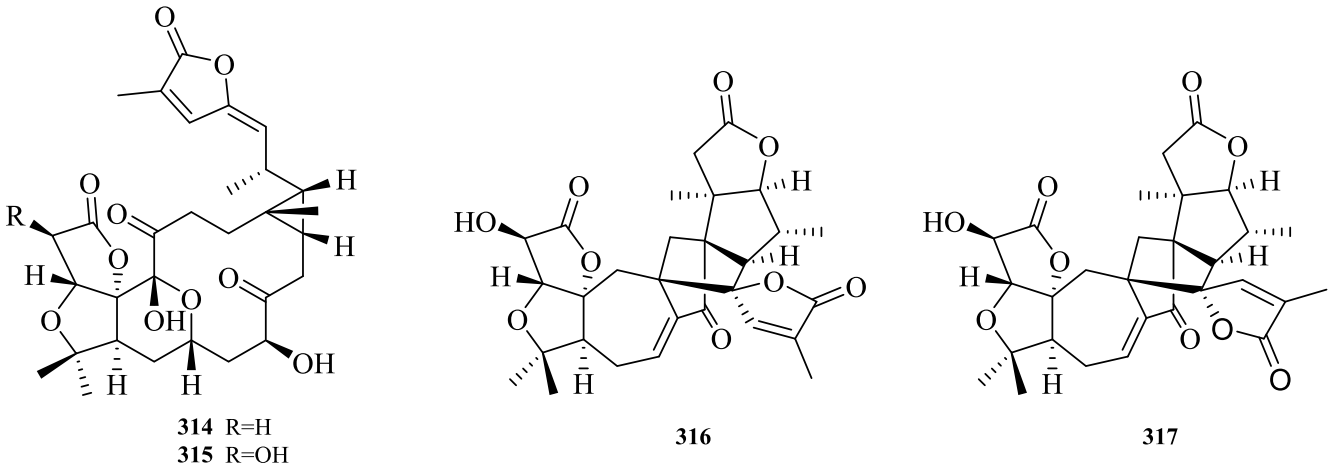

Fig. 13 The chemical structure of 314–317.

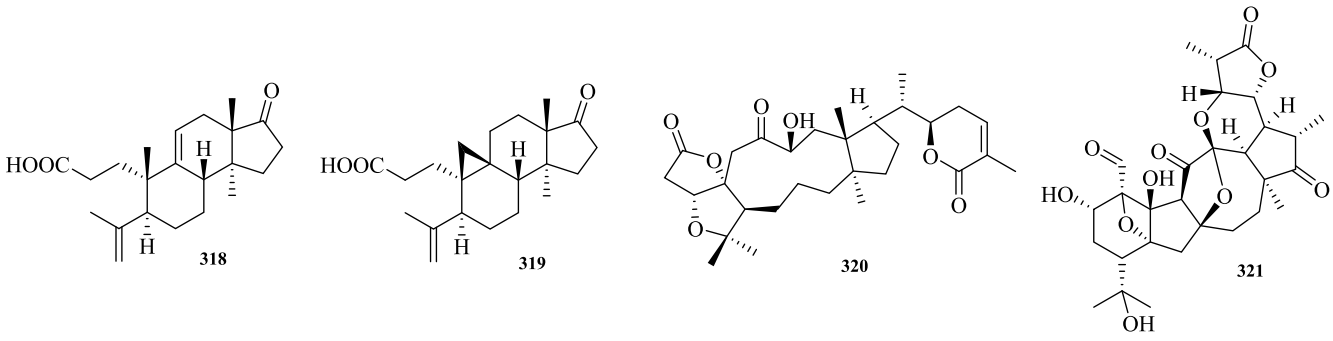

Fig. 14 The chemical structure of 318–321.

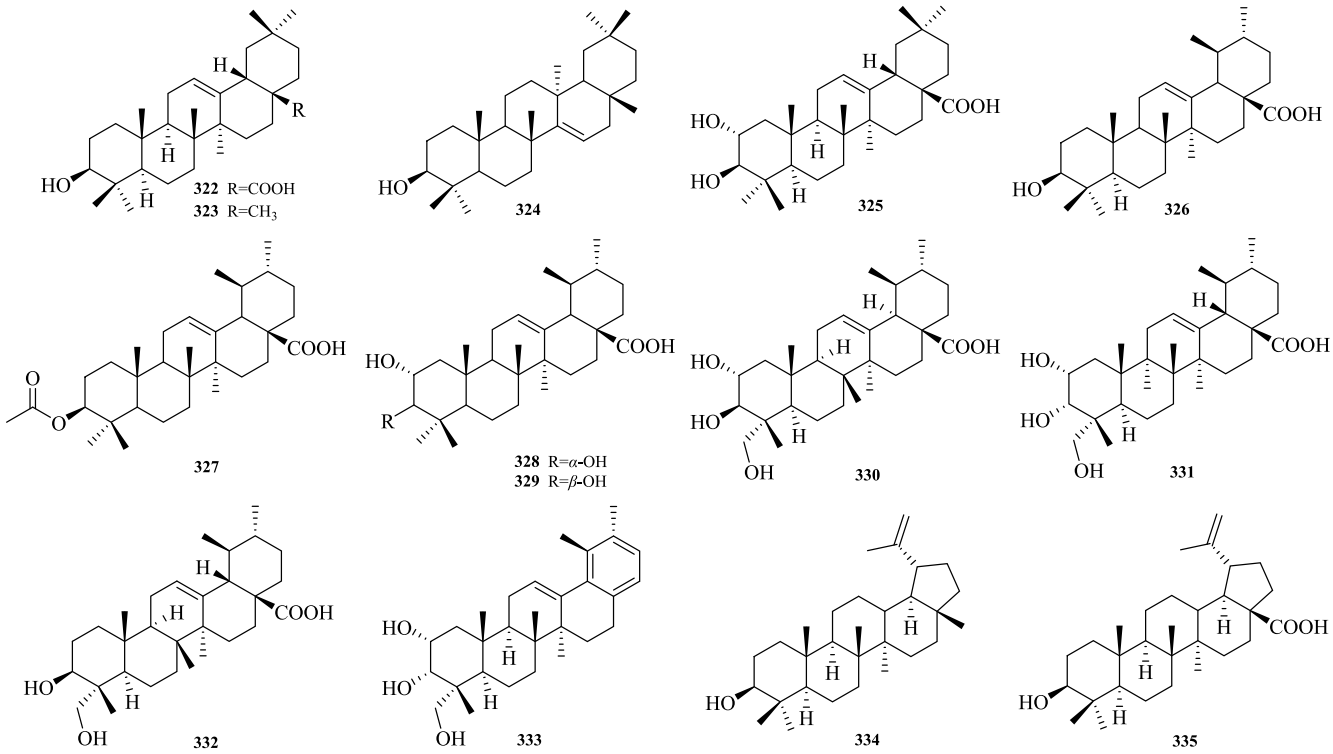

Fig. 15 The chemical structure of 322–335.

Table 4 Pharmacology Activities of *Kadsura*.

Pharmacologic Action	Effective Fraction/ Compounds	Model	Response and Critical Assessment	Target or Possible Mechanism	Ref
Anti-inflammation effects	niqranoic acid derivatives	Macrophage J774A.1	IC_{50} = 1.139–10.558 μM (Inhibition of IL-1β and caspase-1)	LPS and Nig↑, IL-1β and caspase-1↓	(Wang, 2021a)
	11β-hydroxylkadsuphilactone A	QSG7701 cells	survival rates of 60.5%	p38 MAPK↓, Increases intracellular glucocorticoid levels, p38 MAPK-C/EBPβ pathway	(Wang et al., 2016)
	propindilactone L	HepG 2.2.15cells	SI value of 2.68 and 1.11 (Inhibition of HBsAg, HBeAg)	Not mentioned	(Lei, 2009)
	propindilactone N	HepG 2.2.15cells	SI value of 1.62 (HBsAg)		
	arisanlactone B	Human neutrophils	Inhibition rate of 22.24%	Inhibition of superoxide anion production and elastase release by neutrophils	(Cheng et al., 2010b)
	arisanlactone D		Inhibition rate of 18.47% (Inhibition of elastase)		
	schisanbilactone A	LPS-induced NO production	IC_{50} = 10.6 μM	Inhibiting NO	(Song et al., 2015)
Anti-tumor effects	schilancidilactone V	KB	IC_{50} = 3.18 μmol/L	Not mentioned	(Gao et al., 2013)
		MDA-MB-231 cells	IC_{50} = 5.22 μmol/L		
		HL-60	IC_{50} = 11.5 μmol/L (Inhibits tumor cell proliferation)		
	schilancidilactone W	KB	IC_{50} = 8.21 μmol/L		
		MDA-MB-231 cells	IC_{50} = 12.44 μmol/L		
		HL-60	IC_{50} = 4.15 μmol/L		
	propinic lactone A schinensin C schinensin D schisanbilactone A	MCF-7 cells	IC_{50} = 9.3–12.8 μM (Inhibits tumor cell proliferation)	Key groups: α, β-unsaturalted δ-lactone moiety	(Tanaka et al., 2021)
	12-hydroxy schiglausin B	HepG2 cells	IC_{50} = 14.0 μM	Not mentioned	(Liu et al., 2018)
	12-hydroxy kadsuphilactone B		IC_{50} = 11.3 μM (positive control: Doxorubicin 0.02 μM)		
	anwuweizonic acid nigranoic acid	human decidual cells and rat luteal cells	Effective inactivation rate: 98.5–100 %	Not mentioned	(Chen et al., 2001)
	schisanol	human tongue cancer CAL27 cells	IC_{50} of 11.7 mg/mL	C-2 and C-3 positions and removal of hydroxyl at C-7 greatly enhancedthe activity	(Hou et al., 2016)
		human breast cancer MCF7 cells	IC_{50} of 10.6 mg/mL (Medium activity)		
	schisphenthin A schisphenthin C schisanlactone H propinic lactone A	HepG2 cells	IC_{50} = 18.12–49.52 μM (Medium activity)	Not mentioned	(Liu et al., 2017a)
	3β-hydroxy-lanosta-8,24*Z*-dien-26-oic acid	Cdc25A phosphatase	inhibitory rates of 85.5% (significant inhibition)	Not mentioned	(Zhao et al., 2020)
	3,4-seco-(24*Z*)-cycloart-4 (28),24-diene- 3,26-dioic-	Lung cancer A-549 cells	IC_{50} = 28.11 ± 1.49 μM	Not mentioned	(Ding, 2018)

Table 4 (*continued*)

Pharmacologic Action	Effective Fraction/ Compounds	Model	Response and Critical Assessment	Target or Possible Mechanism	Ref
	3-methyl ester	Liver cancer SMMC-7721 cells	IC_{50} = 25.33 ± 1.39 μM		
	schigrandilactone A	K562 cells	IC_{50} = 0.13 μg/mL	Not mentioned	(Xiao et al., 2009)
		HepG2 cells	IC_{50} = 0.19 μg/mL		
	schigrandilactone B	K562 cells	IC_{50} = 3.19 μg/mL		
		HepG2 cells	IC_{50} = 0.20 μg/mL (significant cytotoxicity)		
	6-hydroxyl schiglausin A	BGC-823 cells	IC_{50} = 7.3 μM	Not mentioned	(Wang et al., 2021)
		W480 cells	IC_{50} = 7.9 μM (significant cytotoxicity)		
Anti-HIV effects	rubriflorin A rubriflorin B rubriflorin C	C8166 cells	EC_{50} of 10.0–81.3 microg/mL	Not mentioned	(Xiao et al., 2007c)
	schisphendilactone A	C8166 cells	EC_{50} = 8.79 μg/mL	Not mentioned	(Liang et al., 2013a)
	schisphendilactone B		EC_{50} = 1.09 μg/mL		
	lancifodilactone F	C8166 cells	EC_{50} = 20.69 μg/mL	Not mentioned	(Xiao et al., 2005a; Xiao et al., 2005b)
	lancifodilactone G		EC_{50} = 95.47 μg/mL		
	lancifodilactone G	C8166 cells	EC_{50} = 95.47 ± 14.19 μg/mL (Low activity)		
	rubriflorin D	C8166 cells	EC_{50} = 19.1 μg/mL AZT as apositive control (EC_{50} = 0.0043 ug/mL)	Not mentioned	(Xiao et al., 2007a)
Neuro-protective effects	henridilactone E	PC12 cells	survival rate is 67.39%		(He et al., 2020)
	henridilactone O	PC12 cells	survival rate is 64.52% positive control: desipramine (DIM)	Not mentioned	
	S. chinensis extract	PC12 cells	75, 150, or 300 mg/kg/day	Increase in downstream molecules pERK, pATK and pCREB	(Park et al., 2019)
	S. chinensis extract	C57BL/6 mice	10、30、50 mg/kg	MDA content decreased and SOD content increased	(Jin, 2017)
Immunomodulation effects	schisanlatone C	B lymphocytes	IC_{50} = 20.51 μM	Inhibits proliferation of T and B lymphocytes	(Chen, 2021)
	schisanlactone B 3,4-seco-(24*Z*)-cycloart-4 (28),24-diene- 3,26-dioic-3-methyl ester	T lymphocytes	IC_{50} = 14.28–19.33 μM (moderate inhibitory)		
	kadsudilactone A	ConA-induced T-lymphocyte	IC_{50} of 6.32 μM	Inhibits proliferation of T and B lymphocytes	(Zhou, 2018)
		LPS-induced B lymphocytes	IC_{50} of 11.49 μM		
Anti-bacterial activity	ethanolic extract of *S. chinensis*	*Staphylococcus aureus* *Trichoderma* *Salmonella typhi* *Escherichia coli*	The diameter of the inhibition circle is 11.3–19.3 mm	Not mentioned	(Zou et al., 2011; Chen, 2018)
	total triterpenes of *S. chinensis* leaves	*Staphylococcus aureus* *Escherichia coli*	MIC was 0.63–5.00 mg/mL and MBC was 2.50–20.00 mg/mL	Not mentioned	(Zhou, 2018)
Insecticidal activity	manwuweizic acid	*Aphis gossypii* *Plutella xylostella*	Mortality rate of 66% (moderate inhibitory)	Not mentioned	(Jiang, 2011)
	acetylursolic acid 2α, 3α-dihydroxyurs-12-en-28-oic acid	marine shrimp larvae	IC_{50} of 17.0–25.2 μM	Not mentioned	(Zong et al., 2013)

(*continued on next page*)

Table 4 (*continued*)

Pharmacologic Action	Effective Fraction/ Compounds	Model	Response and Critical Assessment	Target or Possible Mechanism	Ref
	corosolic acid micranoic B	*Plutella xylostella* *Cotton worms*	mortality rate of 66% (Medium activity)	Not mentioned	(Jiang, 2011)
Anti-platelet aggregation	propindilactone Z	rabbits	Inhibition rate = 12.6 ± 4.5%	Not mentioned	(Ding, 2018)
	schipropinqua acid J		Inhibition rate = 14.2 ± 11.0%		
	23-hydroxyursolic acid		Inhibition rate = 10.4 ± 9.5% (moderate inhibitory)		
	lancolide A	PAF-induced aggregation	IC_{50} = 79.95 μg/mL	Best activity at 100 μg/ml	(Shi et al., 2013)
	lancolide D		IC_{50} = 52.56 μg/mL		
Anti-oxidation activity	lancifonin E	Caco-2 cells	EC_{50} = 0.26 mM	Blocking phosphorylation of JNK 1/2/3 MAPK in CaCO-2 cells	(Shi et al., 2014)
cytotoxicity	henrischinin A	HSV-2	SI = 23.31	The acetyl and hydroxyl groups of C-25 may be crucial for the role of triterpenoids in the inhibition of HSV-2 and adenovirus.	(Song et al., 2013)
	henrischinin B		SI = 29.55		
	henrischinin C		SI = 19.49		
	schinchinenin A	Adenovirus	SI = 13.75		
	schinchinenin G		SI = 11.43		
	henrischinin A		SI = 13.67		
	henrischinin B		SI = 11.45 (most active inhibitor of HSV-2)		
	kadsuphilactone A	SMMC-7721 cell lines	IC_{50} = 29.9 μM	Not mentioned	(He et al., 2012)
		A549 cell lines	IC_{50} = 32.5 μM		
		MCF-7 cell lines (modest cytotoxicity)	IC_{50} = 24.4 μM		

was statistically significant ($P < 0.05$). In addition, it can effectively reduce alanine transferase, aspartate transferase and alkaline phosphatase, and significantly improve liver function, which is worth applying and popularizing in the clinic.

7.2. Diabetes

The production of reactive oxygen species (ROS) and the accumulation of glycosylation end-products in the body cause apoptosis in kidney cells, leading to hyperglycemia in diabetes. It was found that ursolic acid (**326**) could scavenge early ROS production and prevent apoptosis due to hyperglycemia. In addition, ursolic acid (**326**) has mimetic and insulin-sensitizing activities and promotes insulin receptor tyrosine phosphorylation. It has a positive effect on insulin-mediated signaling and the translocation of glucose transporter 4 in 3 T3-L1 adipocytes for the treatment of type 1 and type 2 diabetes (Oh et al., 2007; Jung et al., 2007).

7.3. Cardiovascular disease

The literature reports that oleanolic acid (**322**) and corosolic acid (**329**) are the main pentacyclic triterpenes against cardiovascular diseases. Scholars conducted experiments using ex vivo perfusion of rat atria. The results showed that oleanolic acid (**322**) treated with 10–30 mg/kg-d could increase the secretion and synthesis of ANP induced by atrial myocardial traction and achieve the purpose of regulating cardiovascular homeostasis. It also reversed the ox-LDL-induced cell proliferation inhibition and exerted anti-atherosclerotic effects (Kim et al., 2013; Pan et al., 2018). Sun et al. obtained derivatives by hydroxyl esterification of corosolic acid (**329**), which have different degrees of inhibition on glycogen phosphorylase and play a role in the prevention and treatment of atherosclerosis and other diseases (Sun et al., 2009). Xu et al. explored the clinical effect of *S. chinensis* in the treatment of cardiac arrhythmia, and the results showed that the number of premature beats of patients treated with *S. chinensis* was significantly less than that of the control group (*Amiodarone Hydrochloride Tablets*), the total effective rate of treatment in the treatment group was 97.06%, which was higher than that of the control group (82.35%), and the difference was statistically significant. Demonstrates its potential for the treatment of arrhythmia (Xu et al., 2018). The main pharmacological activities and mechanisms of the triterpenes of *S. chinensis* and the related therapeutic potential are shown in Fig. 16.

8. Exploitation

The genus *Schisandra* is named after the fruit's sweet, sour, pungent, bitter, and salty flavors. It is native to China and other parts of East Asia. The fruits of most species in this genus are edible and have cough-relieving properties. Its leaves and seeds can extract aromatic oil, which can be used as industrial raw materials and lubricants. The stem bark is pliable and can be used for rope. Due to their attractive leaves and flowers, these plants are also popular as ornamental plants. In addition, *Schisandra* plants are valued for their medicinal properties. They have been used for centuries in traditional Chinese medicine to treat a variety of ailments, including coughs, asthma and liver disease.

8.1. New drug development

A variety of monomeric compounds in the genus *Schisandra* are rich in the structural skeleton, and their pharmacological activities are also rich and diverse, which are important discoveries beyond the traditional functions. It is of great significance to the clinical practice of TCM and the development of new drug varieties in Chinese medicine. Modern studies have shown that micranoic acid B (**319**), a cyclic pineapple alkane type hypo triterpene isolated from the stem of *S. pubescens*, has good antitumor activity, with significant cytotoxic effects against several types of human cancer cells, including lung cancer (A549), prostate cancer (PC-3), and nasopharyngeal carcinoma (KB and KBvin), with GI50 of 4.07 ~ 4.40 μg/mL. It is shown to have potential as a chemotherapeutic agent for the treatment of cancer and has positive implications for the preparation of antitumor drugs. This finding highlights the potential of *S. pubescens* as a source of natural compounds with significant antitumor properties (Lu et al., 2016). Li et al. isolated a new 3,4-secolanostane from *S. sphenanthera*, which has a novel structure, easy extraction and isolation method, and relatively high content of the obtained compound, which is conducive to its further pharmacological study and creates conditions for the development of new antitumor and anti-AIDS drugs with good efficacy and low side effects (Li et al., 2008).

8.2. Economic importance

Schisandra genus is a dual-use food material with nutritional value and healthcare effects and has been widely used in the food industry. Yang et al. investigated the application of extracts of *S. wilsoniana* in cigarettes and found that various components of *S. wilsoniana*, such as triterpenes, their lactones, and flavonoids, are commonly used as aroma components in tobacco. In this regard, a preliminary analysis of the extraction process optimization and the effect of the additive on harmful substances in a cigarette was carried out, and the results showed that the additive can improve cigarette quality, scavenge free radicals and reduce the content of harmful components in cigarette smoke (Yang, 2008; Li et al., 2016). According to a study by Russian scholar Vikorov, the fruit of *Schisandra* contains 1.1 mg of anti-aging substances in 100 ml of juice, indicating its high nutritional value (Wang and Zhang, 2003). Therefore, *Schisandra* fruit is becoming an important raw material for food and beverage production

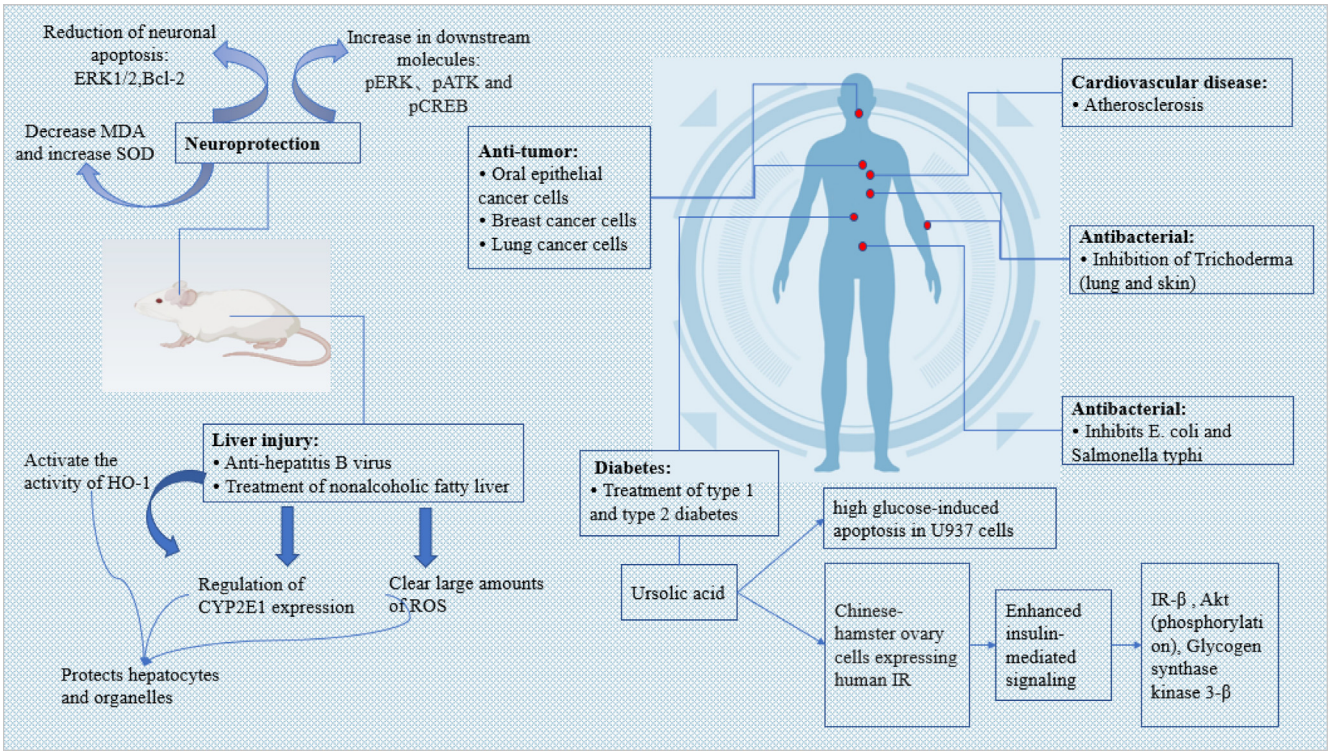

Fig. 16 Major pharmacological activities and therapeutic potential of triterpenes from genus *Schisandra*.

abroad, and there are precedents for its application in Eastern Europe. In addition, it is also used in the dye and cosmetic industries (Wang and Chen, 2007; Zheng et al., 2020).

With the continuous research on the *Schisandra* genus, its functions and values are increasing with each passing day, and with its wide distribution and abundant resources, it shows enormous exploitation value for exploitation. On the whole, *Schisandra* spp. has economic and cultural importance in China and other parts of Asia.

9. Discussion, development status and prospects

Schisandra genus is widely distributed in East Asia that has a long history of use in traditional medicine and has given rise to many related medical prescriptions in Chinese folklore. The best-known and most widely studied species of this genus are *S. sphenanthera* and *S. chinensis*, renowned for their adaptogenic and hepatoprotective properties. Among them, triterpenoids are dominant in *S. sphenanthera* and *S. chinensis* and also represent an essential component of compounds in the genus *Schisandra*, which have been investigated broadly for their potential health benefits. After years of research, more than **335** triterpenoids have been identified from the genus *Schisandra* with diverse chemical structures, especially in recent years, a large quantity of highly oxygenated descending triterpenes have been extracted and isolated from this genus, greatly enriching the composition of triterpenoids. It can be seen from Fig. 17 that nortriterpeonids have the largest percentage of triterpenoids in the genus *Schisandra*. This class of compounds has good anti-tumor and anti-HIV activities. It has been developed and explored by several scholars for new drugs and has received patents. Moreover, its hypolipidemic, enzyme activity-regulating and kidney cell-protecting effects have positive effects on the prevention and treatment

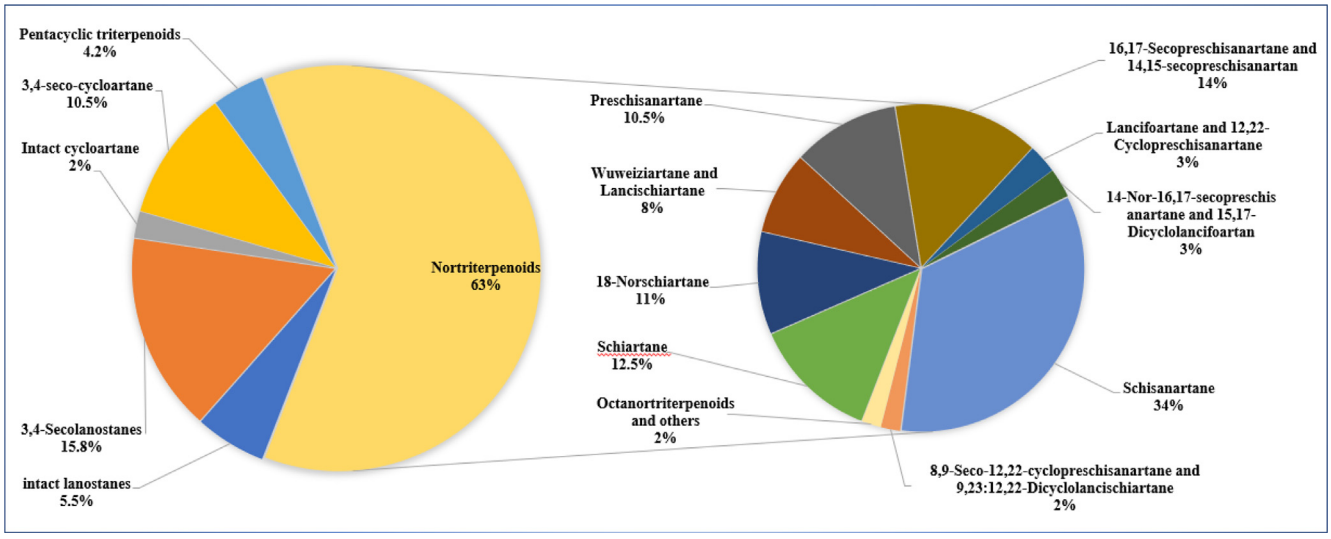

Fig. 17 Distribution of triterpenoids in the *Schisandra* genus.

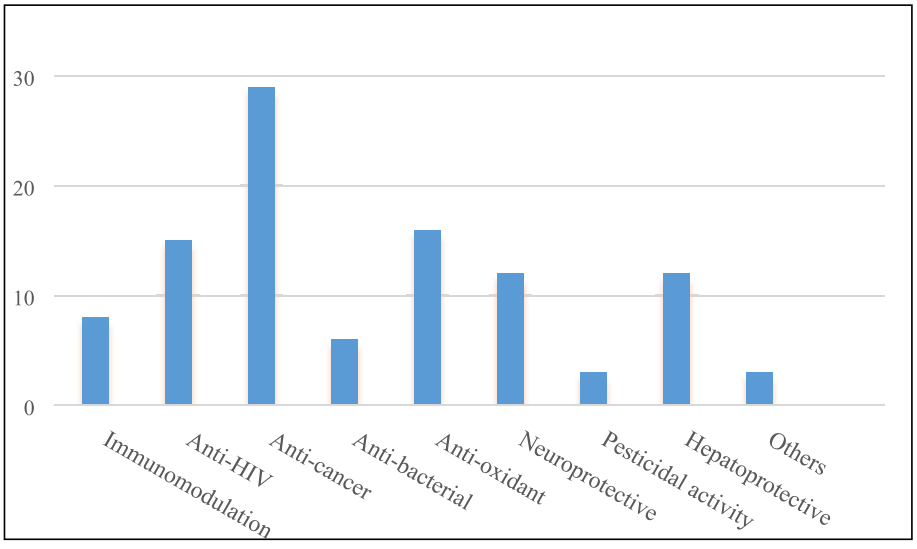

Fig. 18 Major biological properties of the triterpenoids of the genus *Schisandra*.

of liver damage and diabetes. Triterpenoids have proved to be a promising source of valuable natural compounds that deserve further research and development.

The pharmacological activities of the triterpenoid components in the *Schisandra* genus are mainly antitumor, anti-HIV, antioxidant and hepatoprotective (Fig. 18). Some studies suggest that it may also help improve cognitive function, enhance immunity, and reduce symptoms of depression and anxiety disorders. One area of focus is the anti-inflammatory and antioxidant properties of the *Schisandra* genus, which have been shown to exert anti-inflammatory effects by modulating inflammatory signaling pathways and reducing the production and release of inflammatory factors such as TNF-α, IL-6 and IL-1β, in combination with protecting cells from oxidative stress. These properties make it effective in the treatment of liver disease, acute inflammation and Alzheimer's disease. In clinical practice, it is often found in the form of traditional formulations. Its roots, stems, leaves and fruits are used as raw materials and are commonly available in the dosage forms of wine, pills and tablets.

Although research on the genus *Schisandra* is promising, however, there are several areas still in need of further study. First, the genus is rich in triterpenoid species and has been extensively reported in the literature, but there are few kinds of literature reports on *S. plena* and *S. tomentella* in this genus (Fig. 19 and Fig. 20). Besides, the vine stems, roots and fruits from this genus have been well studied, while the study of other parts is relatively blank. Therefore, a comprehensive research program should have built to systematically study this genus to enrich the chemical composition of triterpenoids of this genus. Secondly, to strengthen the research on monomeric compounds, schisanlactone H from *S. sphenanthera* has significant inhibitory activity against either HIV or tumor cells, which is expected to be the next generation of anti-tumor drugs. Therefore, in-depth exploration of monomeric compounds with good physiological activity is an essential source of avenues for new drug development and drug preparation, which plays an essential role in the development of innovative drugs. Third, although the activity of triterpenoids of this genus has been widely studied, it is necessary to note that most of its activity tests have been performed in animal models or in vitro, while the mechanism of its action is still unknown (As shown in Table 4, there are relative gaps in mechanistic studies for most compounds). In this regard, more research data are necessary to confirm the confidence of its activity and to continue exploring its mechanism of action and potential side effects. Fourth, its clinical application has some limitations, and its therapeutic potential can be improved by using modern technological tools and developing new formulations and delivery systems. Its potential interactions with other drugs should also be investigated to ensure the safety of *Schisandra*'s use. Fifthly, the genus *Schisandra* is rich in

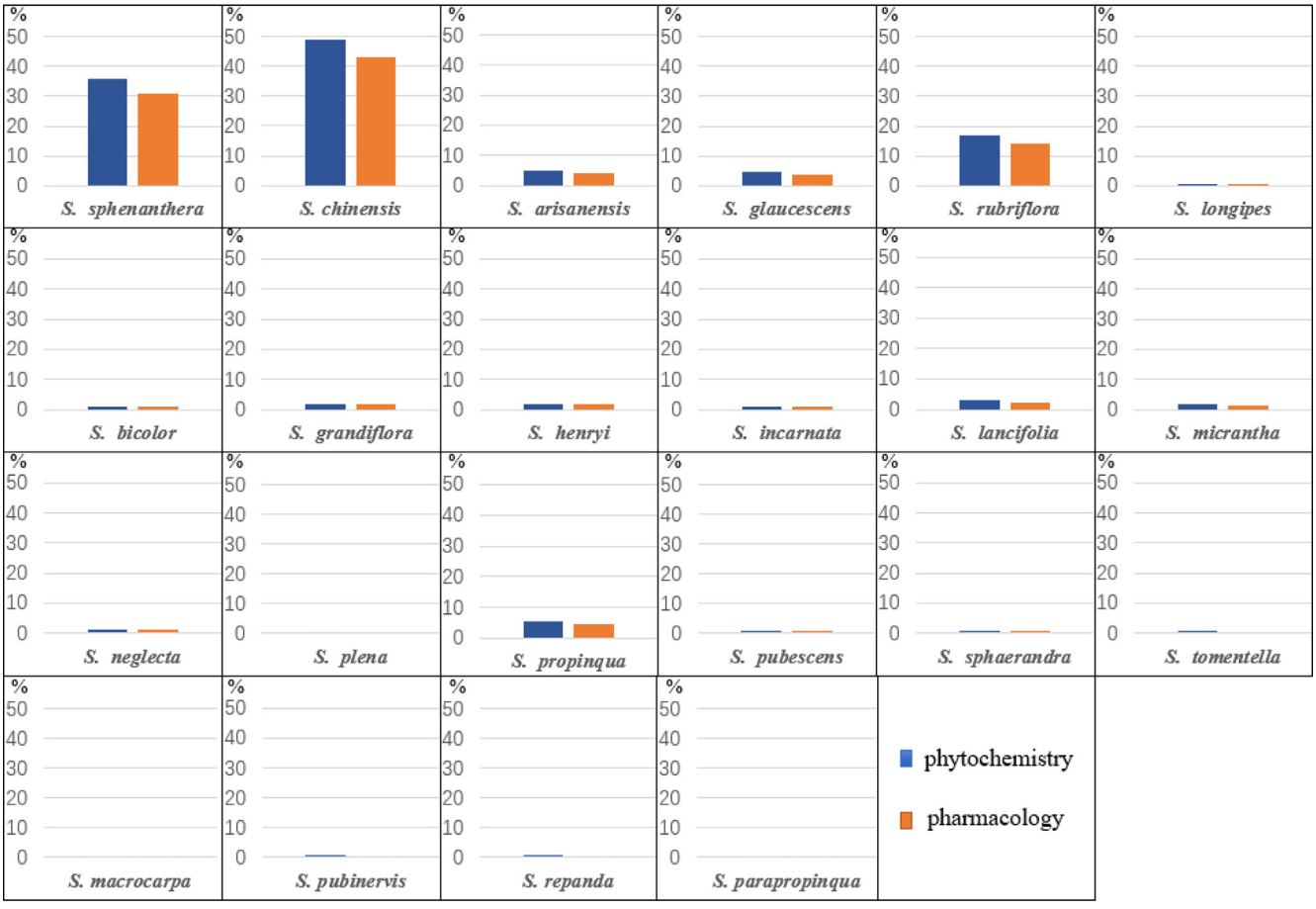

Fig. 19 Relative percentages of all published chemical and biological reports for each species.

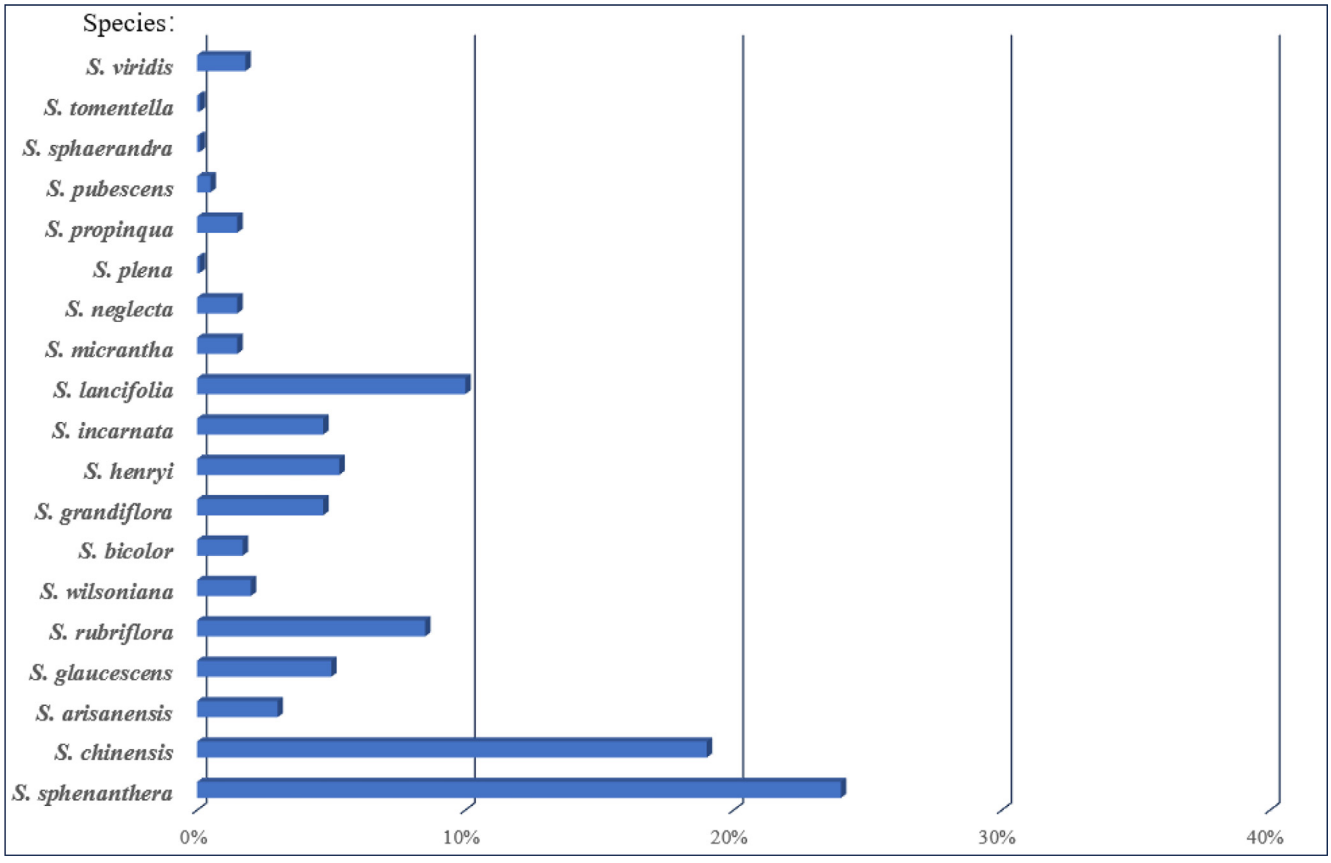

Fig. 20 Percentage distribution of triterpenoids in each species.

resources, most of the plants are for medicinal or edible purposes and have received scholarly attention for their potential health effects. Appropriate commercial products can be developed, such as health products, beverages, skin care products, etc.

All of the above shows that triterpenoids have an indispensable position in the genus *Schisandra*, with a variable chemical structure and rich biological activity, which has long been the focus of researchers' attention. It has been used in clinical treatment, drug development and the food industry, contributing well to human health and economic development. In this paper, we systematically introduce the recent research on triterpenoids and present our views, hoping to provide scientific data to further explore their potential biological activities and develop first-in-class drugs and novel commercial products in the future.

Author contributions

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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