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Review

Phytochemical and pharmacological progress on *Syringa oblata*, a traditional Mongolian medicine

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ABSTRACT

Syringa oblata is a traditional Mongolian medicine mainly distributed in the Helan Mountains (the boundaries of Inner Mongolia and Ningxia, China) and the north of Yan Mountains (Aohan Qi, Inner Mongolia, China). It is clinically used to treat diseases caused by *Heyi*, such as heartache and heat pathogen in the heart. Phytochemical studies on *S. oblata* revealed the presence of iridoids, lignans, triterpenes, phenylpropanoids, phenylethanoids, and volatile components. Pharmacological investigations revealed a broad spectrum of bioactivities, such as antimicrobial, antioxidant, antiproliferative, and hepatoprotective effects. This article summarized the chemical components and pharmacological activities of *S. oblata*, providing a scientific rationale for its bioactive constituents, quality control, and utilization as an important medicine.

Contents

1. Introduction

Syringa oblata Lindl. is a species belonging to the Oleaceae family and its heartwood is used as a traditional Mongolian medicine

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named A-La-Ge-A-Ga-Ru (Inner Mongolia Mongolian Medicine Standard, 2015). *S. oblata* has several synonyms in China, such as Zidingxiang, Dingxiang, and Huabei Dingxiang in Chinese and Gao-Li-De-Bao-Ri in Mongolian. *S. oblata* and *S. oblata* Lindl. var. *alba* Rehderis are recorded as medicines in *Herbal Materials of Inner Mongolia*, with the spicy and bitter flavor and the nature of cold in Chinese medicine. Due to their pharmacological effects, such as clearing heat and inhibiting *Heyi*, pain, and cough, they are clinically used to treat heat pathogens in the heart, heartache, head dizziness, insomnia, palpitation, asthma, and other diseases caused by *Heyi* (Inner Mongolia Mongolian Medicine Standard, 2015; Wu, Wang, & Sui, 2014; Zhao, Zhao, & Cao, 2020). *S. oblata* is distributed in East Asia, such as China and Korea (Wu, Wang, & Sui, 2014; Liu, 1996). In China, it is widely distributed from the Northeast to the Southwest, including Shandong, Shanxi, and Sichuan provinces. Natural resources are rich in the Helan Mountains and the north of Yan Mountains (Dahei Mountain in Aohan Qi, Inner Mongolia). Usually, their habits are shaded foothills or valleys with an altitude of 2000 m.

There are over 400 species belonging to 28 genera in Oleaceae family. Among them, about 20 are from *Syringa* genus. To our best known, at least 16 species, including 10 endemic species, are distributed in Southwest and North China (Jilin Provincial Drug Standards, 1997; Jilin Institute of Traditional Chinese Medicine, 1982). In Inner Mongolia, there are six *Syringa* species including two cultivators.

S. oblata is a medicinal, edible, and ornamental plant with multiple values. As a well-known ornamental plant, it is usually cultivated in parks, roadsides, and homegardens. Due to its potent ability to clear SO_2, it is also widely planted as an eco-friendly plant in urban areas (Jiangsu Institute of Botany, 1990). In addition, for edible purposes, the tender leaves are made into herbal teas and the flowers are raw materials for producing essential oils. Different plant parts including leaves, barks, flower buds, seeds, roots, and heartwoods of *S. oblata* have been recorded as traditional medicines in Chinese and Mongolian medicinal documents as well. In the *Drug Standard of Jilin Province*, the leaf is used as a hepatoprotective and anti-dysentery medicine with the flavor of bitter and nature of cold, for treating bacterial dysenteries and infectious hepatitis (Xing, 2006). The leaves and barks are both recorded as folk medicines for treating diarrhea and hepatitis in *Herbal Materials in Changbai Mountain* (Gao, 2010). In *Xinhua Bencao Gangyao*, *S. oblata* leaves are recorded as Chinese medicines with a spicy flavor and a warm nature, which are used for detoxification, clearing heat, and inhibiting inflammation. Clinical uses with an external application include treating acute icteric hepatitis, microbial infections, conjunctivitis, sores ulceration, and inflamed disorders (Ma, 1980). In *Chinese Medicines of Ningxia*, similar medicinal uses are documented, and the leaves and barks are both recorded as medicinal materials (Cui, Gao, & Liu, 2009). In *Medicinal Plants of Chifeng*, the roots and heartwoods, possessing spicy and bitter flavors and the nature of cold, are used as Mongolian medicines for treating diseases such as heat pathogens in the heart, heartache, dizziness, insomnia, palpitation, and asthma (Alashan Medicinal Plants Color Atlas, 2016). The flower buds, leaves, and seeds are recorded as medicines in *Chinese Medicines of Liaoning*. With a bitter flavor and being cold in nature, they have pharmacological effects including clearing heat, detoxification, and anti-diarrhea activities and are used for treating dysentery, enteritis, upper respiratory tract infection, tonsillitis, and hepatitis (Mengke, 2018). Records describing the medicinal uses of *S. oblata* are similar in other books including *Color Atlas of Medicinal Plant in Alashan* and *Illustrated Book of Medicines in Wushenqi* (Su et al., 2015b; Zhang & Zhang, 2007).

S. oblata is often used as a substitute for agarwood in Alashan, Inner Mongolia. In Mongolian medicine, it is also used as a substitute for agarwood or *S. pinnatifolia* in A-Ga-Ru prescriptions, which are used for treating heartache and disorders caused by *Heyi*. For example, when used as an ingredient in the Mongolian prescription Chenxiang Anshen San as a substitute for *S. pinnatifolia*, it showed potent pharmacological effects in clinic. Recent phytochemical studies on the leaves, barks, seed coats, stems, twigs, flowers, and flower buds of *S. oblata* have been conducted. These raw plant materials were usually extracted by methanol, ethanol, or aqueous. Leaves and flowers were also made into essential oils. Chemical profiling of these extracts was conducted by various chromatographic methods including silica gel, Sephadex LH-20,

Table 1
Iridoids isolated from *S. oblata* (**1**–**22**).

No.	Compounds	Plant parts	References
1	Syringopicrogenin B	Seed coats, flower buds, leaves	Wang, Zhang, Dong, Zhao, & Zhang, 2010; Dong, Wang, Zhao, & Zhang, 2011; Zhang et al., 2018
2	Syringopicroside B	Leaves	Zhang et al., 2018
3	Fliederoside B	Leaves	Zhang et al., 2018
4	Syringopicroside A	Leaves	Wang, 2008
5	7-Methyl-1-oxo-octahydro-cyclopenta[c] pyran-4-carboxylic acid	Leaves	Li, Xu, Hao, Yang, & Li, 2009
6	Syringopicrogenin A	Seed coats, leaves	Wang, Zhang, Dong, Zhao, & Zhang, 2010; Han, 2012; Zhang et al., 2018
7	Syringopicrogenin C	Leaves	Han, 2012; Zhang et al., 2018
8	Syringopicrogenin D	Leaves	Han, 2012; Zhao et al., 2016; Zhang et al., 2018
9	Syringopicrogenin E	Leaves	Han, 2012; Zhao et al., 2016; Zhang et al., 2018
10	Syringopicrogenin F	Leaves	Zhang et al., 2018
11	(8*E*)-Ligstroside B	Leaves	Zhang et al., 2018
12	(8*E*)-Ligstroside A	Leaves	Zhang et al., 2018
13	7-Dehydrologanin	Leaves	Zhang et al., 2018
14	(8*E*)-Ligstroside	Seed coats, leaves, twigs	Wang, Zhang, Dong, Zhao, & Zhang, 2010; Zhao, Han, Lv, & Zhang, 2012; Zhang et al., 2018
15	Oleuropein	Barks, twigs, leaves	Zhang, Zhang, & Wang, 2006; Zhao, Han, Lv, & Zhang, 2012; Zhang et al., 2018
16	(8*E*)-Gstroside	Barks	Zhang, Zhang, & Wang, 2006
17	8*E*-Nüzhenide	Seeds	Zhang, Guo, Han, Zhao, & Wang, 2011
18	2-(*p*-Hydroxyphenyl)-ethyl-2,6-bis(2*S*,3*E*,4*S*)-3-ethylidene-2-(*β*-D-glucopyranosyloxy)-3,4-dihydro-5-(methoxycarbonyl)-2H-pyran-4-acetate	Seeds	Zhang, Guo, Han, Zhao, & Wang, 2011
19	4-*O*-11-Methyloleoside-*p*-hydroxyphenyl-(6–11-methyloleoside)-*β*-D-glucopyranoside	Seeds	Zhang, Guo, Han, Zhao, & Wang, 2011
20	Syringalactone B	Leaves	Wang, 2008
21	2-(3,4-Dihydroxyphenyl) ethyl(1*R*,4a*S*,8*R*,8a*S*)-8-methyl-6-oxo-1-[(2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethy)oxan-2-yloxy-4a,5,8,8a-tetrahydro-1H-pyrano[3,4-c]pyran-4-carboxylate	Leaves	Tian, Li, Lv, Zhang, & Liu, 2013
22	7*β*-D-Glucopyranosyl-11-methyloleoside	Seeds	Zhang, Guo, Han, Zhao, & Wang, 2011

macroporous resin, HPLC, and GC coupled with multiple spectroscopic analyses, such as ultraviolet, nuclear magnetic resonance, and mass spectra. Results revealed the presence of iridoids, iridoid glycosides, lignans, triterpenoids, phenylpropanoids, phenylethanoids, flavonoids, and others (Jilin Provincial Drug Standards, 1997; Yu, Wang, & Wu, 2016; Ma et al., 2020; Li et al., 2018a,b; Gao, Jiao, Ma, Liu, & Chai, 2020). Pharmacological investigations revealed the antimicrobial, antioxidant, antiproliferative, and hepatoprotective activities of extracts from *S. oblata* leaves and flower buds. In the current paper, the phytochemical and pharmacological research of *S. oblata* were summarized, providing an up-to-date review, a scientific rationale for the medicinal uses of *S. oblata*, and a beneficial reference for future studies on the quality control, clinical uses, and utilization of Mongolian medicinal products.

2. Chemical constituents of *S. oblata*

Previous studies showed that phytochemicals present in the leaves, barks, seed coats, stems, twigs, flowers, and flower buds of *S. oblata* are iridoids, lignans, triterpenoids, phenylpropanoids, phenylethanoids, phenolic acids, flavonoids, and others. Those compounds reported from *S. oblata* include 22 iridoids, 14 lignans, 19 triterpenoids, 25 phenols, seven flavonoids, and 10 others.

2.1. Iridoids

Iridoids are monoterpenoids derived from iridodial, in the general form of cyclopentanopyranl. They are a group of medicinally valuable metabolites that are found in a wide variety of plants, especially in dicotyledons (Wu, Zhao, & Qin, 2002; Wu, 2005). Since 1958 when the basic core of iridoids was firstly identified, numerous researchers had focused on it. Up to now, over 1000 iridoids have been reported and the number is still increasing. Notably, many of them were found to have potent bioactivities, such as protecting the cardiovascular system, regulating the immune system, and antitumor, antivirus, hepatoprotective, choleretic, antidiabetic, antihyperlipidemic, anti-inflammatory, anticoagulant, antioxidant, antispasmodic, laxative, and neuroprotective effects (Ma, Tian, Zhang, & Xu, 2008; Xing et al., 2009; Wang et al., 2019; Kong, Vencent, Hu, & Dong, 2021).

The presence of iridoids in *S. oblata* was firstly reported in 1982, isolating and identifying syringopicroside (**4**) (Wang et al., 1982). It was reported that there were two dominant conformations, and the coupling constant of H-1 and H-9 (J < 3 Hz or J = 7–10 Hz) was corresponding to the dihedral angle of H-1 and H-9 (60° or 180°, respectively). (8*E*)-gstroside (**16**), which was previously reported from *S. vulgaris* L. and *S. pubescens* subsp. *patula* (Palib.) M. C. Chang & X. L. Chen, was isolated from the EtOAc fraction of EtOH extract of *S.oblata* barks for the first time (Zhang, Zhang, & Wang, 2006). Wang et al. (2010) conducted a phytochemical study on the EtOAc extract of *S.oblata* seed coats. Syringopicrogenin A (**6**), along with syringopicrogenin B (**1**), syringopicroside (**4**), oleuropein (**15**), and (8*E*)-ligstroside (**14**) were isolated and identified, indicating that compounds **4** and **15** also existed in seed coats. Syringopicrogenin B (**1**) was also found in the EtOAc extract of *S. oblata* flower buds (Dong, Wang, Zhao, & Zhang, 2011). In continuous phytochemical studies on the EtOH extract of *S. oblata* leaves, syringopicrogenin C (**7**) and 7β-D-glucopyranosyl-11-methyloleo side (**22**) were reported from the *n*-BuOH portion (Zhang, Chen, Li, & Yang, 2011). A new iridoid syringopicrogenin F (**10**) was reported from the EtOAc portion (Zhang, Li, Li, Wang, & Zhao, 2014). Then, another four iridoids from *S.oblata* leaves were found for the first time in 2018, including syringopicroside B (**2**), (8*E*)-ligstroside B (**11**), (8*E*)-ligstroside A (**12**), and fliederoside B (**3**) (Zhang et al., 2018). Other iridoids reported from *S. oblata* leaves are **5** (Li, Xu, Hao, Yang, & Li, 2009), **8** and **9** (Zhao et al., 2016),

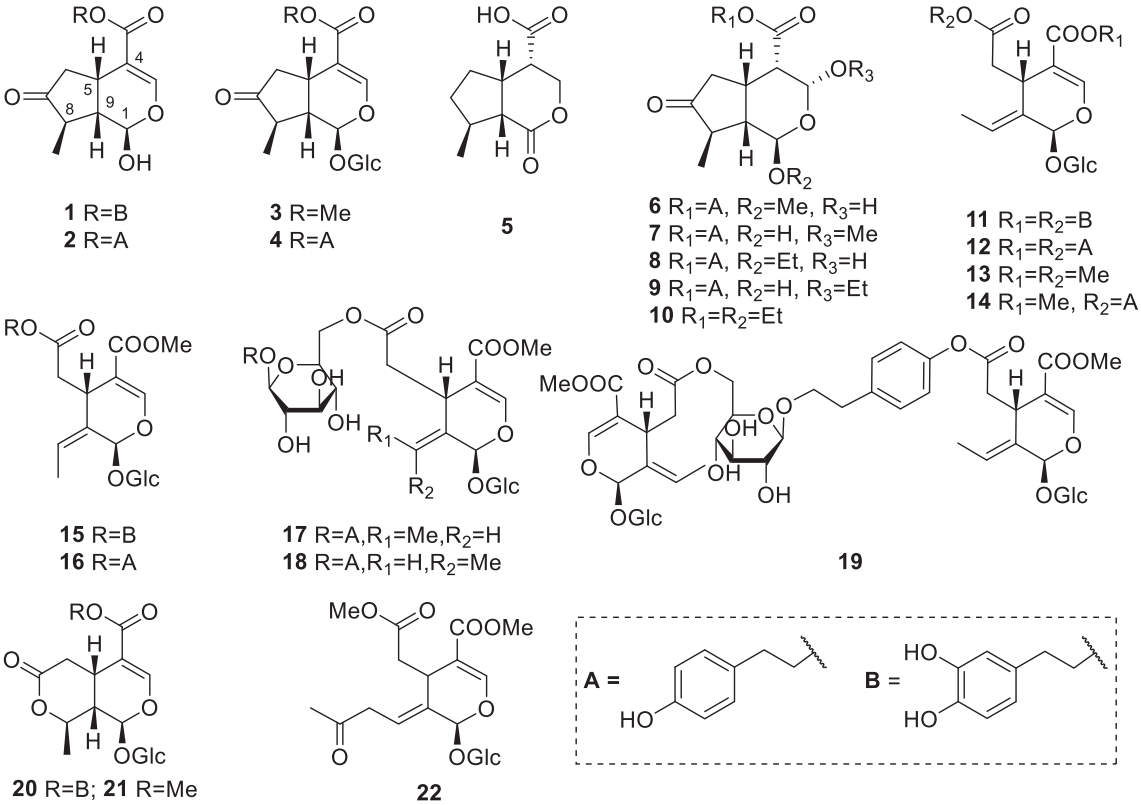

Fig. 1. Structures of iridoids in *S. oblata* (**1**–**22**).

Table 2
Lignans isolated from *S. oblata* (**23**–**36**).

No.	Compounds	Plant parts	References
23	Syringa oblata ligninoside B	Leaves	Wei, 2004
24	Syringa oblata ligninoside A	Leaves	Wei, 2004
25	7*R*,8*S*-4,9,9′-Trihydroxyl-3,3′-dimethoxyl-7,8-dihydrobenzofuran-1′-propylneolignan	Leaves	Zhao et al., 2016
26	3,4:3′,4′-bis(Methylene-dioxy)-9′-hydroxyl-lignane-9-methyl-*O*-*β*-D-glucopyranoside	Leaves	Zhou, 2005
27	(+)-Pinoresinol	Twigs	Zhao, Han, Lv, & Zhang, 2012
28	(+)-Pinoresinol-4″-*O*-*β*-D-glucopyranoside	Leaves	Tian, Li, Lv, Zhang, & Liu, 2013
29	4,4′-Dihydroxyl-3,3′,5-trimethyoxyl bisepoxy lignan	Twigs	Zhao, Han, Lv, & Zhang, 2012
30	(+)-Syringaresinol	Twigs, seed coats	Wang, Zhang, Dong, Zhao, & Zhang, 2010; Zhao, Han, Lv, & Zhang, 2012
31	(9*R*)-9-*O*-Methylcubebin	Twigs	Zhao, Han, Lv, & Zhang, 2012
32	(9*S*)-9-*O*-Methylcubebin	Twigs	Zhao, Han, Lv, & Zhang, 2012
33	Lariciresinol	Twigs, leaves	Zhao, Han, Lv, & Zhang, 2012; Zhang et al., 2018
34	Lariciresinol-4-*O*-*β*-D-glucopyranoside	Leaves	Tian, Li, Lv, Zhang, & Liu, 2013
35	4,4′,8,9-Tatrahydroxyl-3,3′-dimethyoxyl-7,9′-monoepoxylignin	Twigs	Zhao, Han, Lv, & Zhang, 2012
36	Lariciresinol acetate	Leaves	Zhang, Li, Li, Wang, & Zhao, 2014

13 (Zhang et al., 2018), **20** (Wang, 2008), and **21** (Tian, Li, Lv, Zhang, & Liu, 2013). Compound **5** has a chiral center at C-4 and does not possess the carbonyl group at C-7, which is different from other typical iridoids in *S. oblata*. Detailed information on these isolates was listed in Table 1 and Fig. 1.

Iridoids are a group of major components of *S. oblata* leaves. Among them, three iridoids syringopicroside (32.63 mg/g), oleuropein (28.43 mg/g), and ligstroside (15.83 mg/g) from the 75% ethanol extract of *S. oblata* leaves were characterized as the major compounds by an HPLC-MS-based quantitative analysis, and the structures of these major compounds were further confirmed by NMR data (Zhu et al., 2021). An HPLC-MS-based chemical profiling of *S. oblata* var. *alba* leaves also revealed the major compounds including syringopicroside, oleuropein, and ligstroside (Nenadis, Vervoort, Boeren, & Tsimidou, 2007).

2.2. Lignans

Lignans are another major group of chemical constituents from *S. oblata*. Lignans are derived from two monolignols, which possess a C6-C3 core. And the coupling of the monolignols usually occurs at C-8 (Wu, 2010). The name derives from the Latin word for "wood". They are widely found in roots, rhizomes, stems, leaves, flowers, fruits, heartwoods, and resins of plants, especially rich in heartwood and resins (Feng, 2007). Due to the high structural diversity of lignans, they showed multiple biological activities including antivirus, antitumor, antioxidant, anticoagulant, antidiabetic, and anti-inflammatory effects (Zhang, Li, Lin, & Wang, 2007; Wu et al., 2021).

Syringa oblata ligninosides A and B (**23**, **24**) are two macrophyllin-type bicyclo[3.2.1]octanoid neolignans reported from aqueous extract of *S. oblata* leaves, which belong to a group of bioactive compounds showing platelet-activating factor antagonistic activities (Wei, 2004). A dihydrobenzofuran lignan named (7*R*,8*S*)-4,9,9′-trihydroxyl-3,3′-dimethoxyl-7,8-dihydrobenzofuran-1′-propylneolignan (**25**), a lignan glycoside 3,4:3′,4′-bis(methylene-dioxy)-9-hydroxyl-lignane-9-methyl-*O*-*β*-D-glucopyranoside (**26**), and lariciresinol-4-*O*-*β*-D-glucopyranoside (**34**) were also isolated from *S. oblata* leaves (Zhao et al., 2016; Zhou, 2005; Tian, Li, Lv, Zhang, & Liu, 2013). The EtOAc extracts of *S. oblata* seed coats and twigs were studied in 2010, leading to the isolation of (+)-syringaresinol (**30**) (Wang, Zhang, Dong, Zhao, & Zhang, 2010; Zhao, Han, Lv, & Zhang, 2012). Another four typical C-8–C-8′ connected lignans, (9*R*)-9-*O*-methylcubebin (**31**), (9*S*)-9-*O*-methylcubebin (**32**), 4,4′,8,9-tatrahydroxyl-3,3′-dimethyoxyl-7,9′-monoepoxylignin (**35**), and lari-

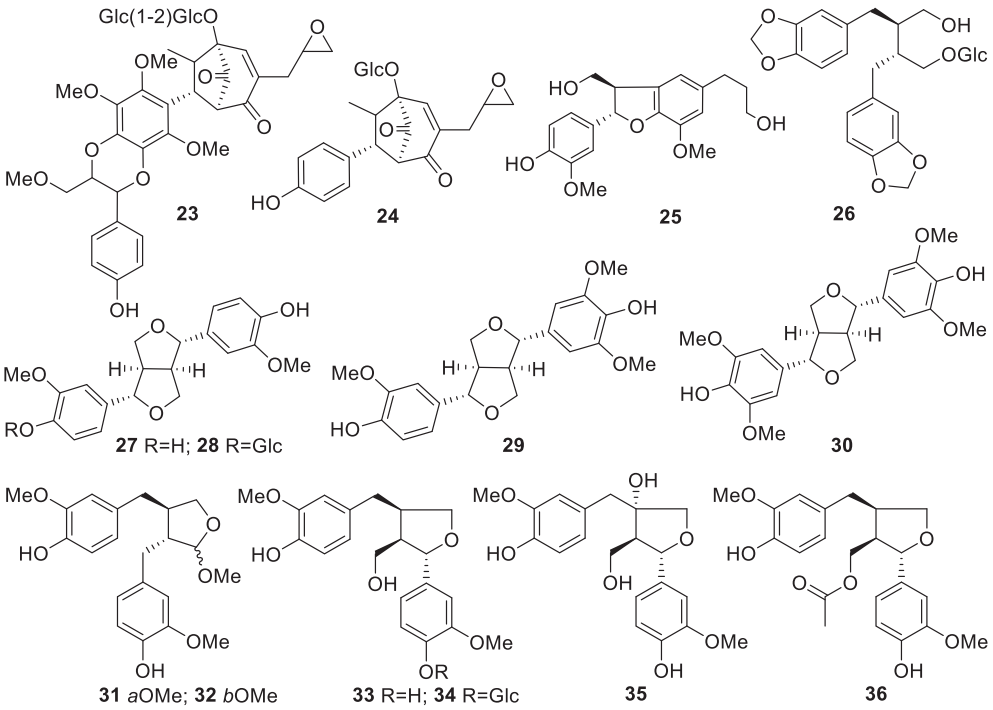

Fig. 2. Structures of lignans in *S. oblata* (**23**–**36**).

ciresinol acetate (**36**), and a neolignan 4,4′-dihydroxyl-3,3′,5-trimethyoxyl bisepoxylignan (**29**) were found from the EtOAc and *n*-BuOH fractions of EtOH extract of *S. oblata* twigs (Zhao, Han, Lv, & Zhang, 2012). Detailed information about lignans in *S. oblata* was described in Table 2 and Fig. 2.

According to the previous phytochemical studies on *S. oblata* and other *Syringa* species, lignans are the major group of compounds from *Syringa* plants, especially the leaves, roots, and stems (Zhu et al., 2021). However, the stems and roots of *S. oblata*, which are used as medicinal parts in Mongolian medicine, have rarely been studied. Phytochemical research on lignans from this Mongolian medicine is necessary for revealing its therapeutic constituents.

2.3. Triterpenoids

Obaculactone (**37**), also known as limonoic acid di-delta-lactone, is the first triterpenoid found in the aqueous extract of *S. oblata* leaves (Lu, Li, & Li, 2003). It is a member of furanolactones with a bitter flavor and a broad spectrum of bioactivities. Then, a series of triterpenoids were found from different plant parts of *S. oblata*. Three compounds, lupanic acid (**39**), oleandic acid (**42**), and daucosterol (**54**), were firstly reported from the EtOH extract of *S. oblata* barks in 2006 (Zhang, Zhang, & Wang, 2006). From the EtOAc extract of *S. oblata* flower buds, four triterpenoids including oleandic acid (**42**), ursolic acid (**51**), lupanic acid (**39**), and luprol (**41**) were isolated and identified (Dong, Wang, Zhao, & Zhang, 2011). In continuous phytochemical studies on *S. oblata* leaves, from the dichloromethane and EtOAc fractions of EtOH extract, 19α-hydroxyl ursolic acid (**52**) was found for the first time in 2009 (Li, Xu, Hao, Yang, & Li, 2009); from the EtOAc extract, 21α-hydroxy-serrat-14-en-3β-yl-dihydrocaffeate (**53**) was found in the *n*-BuOH fraction (Zhang, Chen, Li, & Yang, 2011). These above-mentioned compounds were shown in Table 3 and Fig. 3.

Most of the triterpenoids found in *S. oblata* are pentacyclic triterpenoids. Many of them including compounds **40**, **51**, and **54** were reported to have antitumor, antiviral, and anti-inflammatory activities. However, they may not be the unique bioactive compounds in *S. oblata*, because they are widely distributed in the barks of many plant species. Those triterpenoids substituted by coumaroyls may need to be deeply studied for explaining if they contribute to the pharmacological effects of *S. oblata*.

Table 3
Triterpenoids isolated from *S. oblata* (**37**–**55**).

No.	Compounds	Plant parts	References
37	Obaculactone	Leaves	Lu, Li, & Li, 2003
38	Lup-20(29)-en-3-one	Leaves	Wei, 2004
39	Lupanic acid	Barks, flower buds	Zhang, Zhang, & Wang, 2006; Zhang, Chen, Li, & Yang, 2011
40	Betulinic acid	Leaves	Li, Xu, Hao, Yang, & Li, 2009; Zhang et al., 2018
41	Luprol	Flower buds	Dong, Wang, Zhao, & Zhang, 2011
42	Oleandic acid	Barks, leaves, flower buds	Zhang, Zhang, & Wang, 2006; Dong, Wang, Zhao, & Zhang, 2011; Cao, 2017; Zhang et al., 2018; Li, Yan, & Liu, 2019
43	Maslinic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
44	3-*O*-*trans*-*p*-Coumaroyl maslinic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
45	3β-*O*-*cis*-*p*-Coumaroyl maslinic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
46	2α-Hydroxy ursolic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
47	3β-*O*-*trans*-*p*-Coumaroyloxy-2α-hydroxyurs-12-en-28-oic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
48	3β-*O*-*cis*-*p*-Coumaroyloxy-2α-hydroxyurs-12-en-28-oic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
49	3β-*O*-*trans*-*p*-Coumaroyl tormentic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
50	3β-*O*-*cis*-*p*-Coumaroyl tormentic acid	Leaves	Zhang, Chen, Li, & Yang, 2011
51	Ursolic acid	Leaves, flower buds	Li, Xu, Hao, Yang, & Li, 2009; Zhang, Chen, Li, & Yang, 2011; Han, 2012; Zhang et al., 2018; Li, Yan, & Liu, 2019
52	19α-Hydroxy ursolic acid	Leaves	Li, Xu, Hao, Yang, & Li, 2009
53	21α-Hydroxy-serrat-14-en-3β-yl-dihydrocaffeate	Seeds	Zhang, Guo, Han, Zhao, & Wang, 2011
54	Daucosterol	Barks, leaves, Twigs	Zhang, Zhang, & Wang, 2006; Li, Xu, Hao, Yang, & Li, 2009; Zhao, Han, Lv, & Zhang, 2012
55	β-Sitosterol	Leaves, flower buds	Zhou, 2005; Wang, 2008; Dong, Wang, Zhao, & Zhang, 2011

2.4. Simple phenols

Simple phenolic compounds include phenylpropanoids, phenylethanoids, coumarins, and other phenolics with only one benzene ring. They are a group of precursors contributing to the structural diversity of iridoids, lignans, and triterpenoids in *S. oblata*. Five compounds including three phenylpropanoids (**61**, **68**, **69**) and two simple phenolic derivates (**79** and **80**) were found in twigs of *S. oblata* (Zhao, Han, Lv, & Zhang, 2012). A phytochemical study on the EtOH extract of *S. oblata* barks resulted in the isolation and identification of two phenylethanoids, 3,4-dihydroxy phenylethano1 (**60**) and 2-(3,4-dihydroxy)phenyl ethyl acetate (**62**) (Zhang, Zhang, & Wang, 2006). In another study on the EtOAc extract of *S. oblata* barks, compounds **60**, 3,4-dihydroxylphenyletha nolglucoside (**82**), and hydroxylphenylethanolglucoside (**58**) were found (Zhang, Jiao, Wang, & Zhang, 2007). From the EtOAc extract of *S. oblata* seed coats, compounds **58**, **60**, and *p*-hydroxyphenyl ethyl acetate (**59**) were reported (Wang, Zhang, Dong, Zhao, & Zhang, 2010). From the aqueous extract of *S. oblata* leaves, **59** and 3,4-dihydroxybenzene-styrene glycol (**63**) were isolated and identified (Han, 2012; Tian, Li, Lv, Zhang, & Liu, 2013). Verbascoside (**56**) is a caffeoyl phenylethanoid glycoside, in which the phenylpropanoid caffeic acid and the phenylethanoid hydroxytyrosol form an ester and an ether bond respectively, to the rhamnose part of a disaccharide (Andary, Wylde, Laffite, Privat, & Winternitz, 1982). Several studies on the *S. oblata* leaves revealed the presence of **56** and other 12 phenolic constituents (Zhang et al., 2018; Wang et al., 1982; Zhou, 2005; Li, Xu, Hao, Yang, & Li, 2009). Simple phenolics reported from *S. oblata* were described in Table 4 and Fig. 4.

2.5. Flavonoids

Phytochemicals in the aqueous extract of *S. oblata* leaves were studied by (Lu, Li, & Li, 2003), leading to the isolation of a flavonoid named formonometin (**81**). Another study on the dichloromethane and EtOAc fractions from EtOH extract of *S. oblata* leaves reported the presence of 5,7,4′-trihydroxyl flavanone (**82**), which was also found in *S. oblata* twigs (Li, Xu, Hao, Yang, & Li, 2009; Zhao, Han, Lv, & Zhang, 2012). Five flavonoids, kaempferol-3-*O*-α-L-rhamnosyl-(1 → 6)-β-D-glucoside (**83**), quercetin (**84**), rutin (**85**), quercetin-3-*O*-β-D-glucoside (**86**), and naringenin (**87**) were iso-

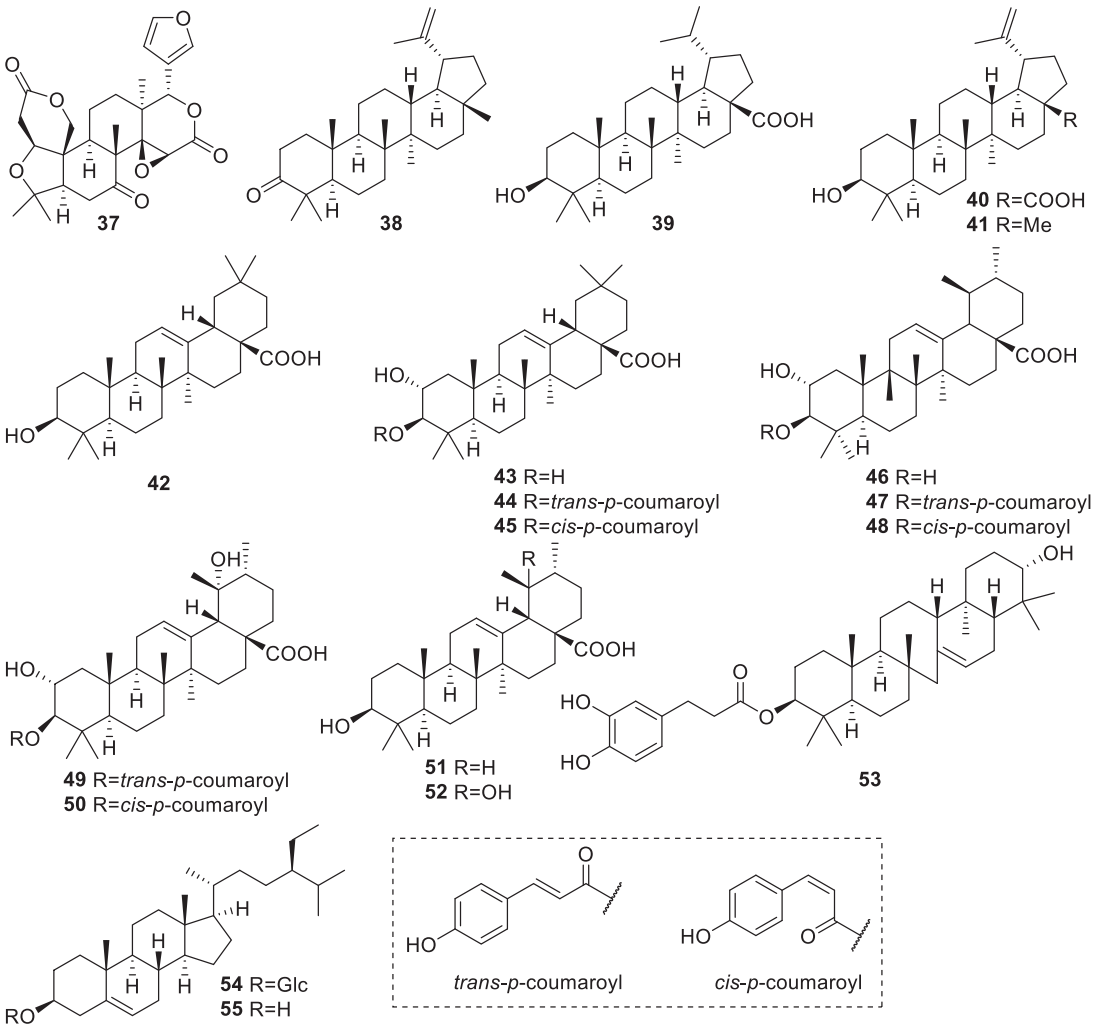

Fig. 3. Structures of triterpenoids in *S. oblata* (**37**–**55**).

lated and identified from the *S. oblata* leaves (Bai, Kong, Lin, & Zhang, 2016; Cao, 2017). Detailed information on the flavonoids was shown in Table 5 and Fig. 5.

Different from the iridoids, triterpenoids, and lignans which were mainly found in *S. oblata* leaves, these flavonoids were mostly isolated from flowers. However, rutin was characterized as a bioactive compound with antimicrobial effects in *S. oblata* leaves, with a concentration ranging from 0.175 to 0.216 mg/mL (Liu et al., 2018). It deserves a further phytochemical study on the flavonoids from *S. oblata* leaves, barks, and other medicinal parts.

2.6. Other compounds

Except for the abovementioned five groups of phytochemicals, several other types of compounds were reported from *S. oblata*, including fatty acids and polyhydric alcohols. A phytochemical study on the EtOAc and *n*-BuOH fractions from the aqueous extract of *S. oblata* leaves resulted in the isolation and identification of D-mannitol (**88**) (Wang et al., 1982). In another study on the aqueous extract of *S. oblata* leaves, (Lu, Li, & Li, 2003) found succinic acid (**89**). Also, from the aqueous extract of *S. oblata* leaves, cyclohexanehexol (**90**) was reported in the genus *Syringa* (Zhou, 2005). Another two compounds, 3(*Z*)-enol glucoside (**91**) and grasshopper ketone (**92**) were first isolated from *S. oblata* leaves (Zhang et al., 2018). From the EtOAc and *n*-BuOH fractions of EtOH extract of *S. oblata* barks, palmitic acid (**97**) and lauric acid (**95**) were isolated, resulting in the first report of **97** in the genus *Syringa* (Cao, 2017). Other classes of compounds from *S. oblata* were described in Table 6 and Fig. 6.

Essential oils from the leaves, flowers, and stems of *S. oblata* were chemically profiled by several researchers, using GC–MS-based metabolomics. In the essential oil of *S. oblata* leaves, eugenol (40.43%) was found to be the dominant component. Eugenol acetate (28.78%) was the second major component, followed by *β*-caryophyllene (21.99%) and *α*-caryophyllene (3.46%) (Jing et al., 2018). Terpenes and oxygenated terpenes, aromatic compounds, a series of alkanes, and heterocyclic compounds were characterized as the main components of *S. oblata* flowers and buds (Zhao, Liang, Fang, & Li, 2005). In another GC–MS-based study, the variation of volatile compounds emitted from *S. oblata* var. *alba* flowers in different florescence stages was investigated (Li, Lee, & Shen, 2006). Results revealed that lilac aldehydes A–D, lilac alcohols A–D, *α*-pinene, sabinene, *β*-pinene, myrcene, D-limonene, eucalyptol, *cis*-ocimene, benzaldehyde, terpinolene, linalool, benzene acetaldehyde, *α*-terpineol, *p*-methoxyanisole, *p*-anisaldehyde, (*Z*, *E*)-*α*-farnesene and (*E*,*E*)-*α*-farnesene were the most abundant volatiles released from fresh flowers and may contribute to the scent of fresh flowers. In our previous study on essential oils from *S. oblata* stems, 46 chemical components were identified by GC–MS (Gegen et al., 2022). *α*-Cadinol (15.65%), T-cadinol (11. 68%), and

Table 4
Phenolic constituents isolated from *S. oblata* (**56**–**80**).

No.	Compounds	Plant parts	References
56	Verbascoside	Leaves	Zhang et al., 2018
57	*p*-Hydroxyphenylethyl alcohol	Leaves	Wang et al., 1982; Zhou, 2005
58	*p*-Hydroxylphenylethanolglucoside	Seed coats, barks	Wang, Zhang, Dong, Zhao, & Zhang, 2010; Zhang, Jiao, Wang, & Zhang, 2007
59	*p*-Hydroxyphenyl ethyl acetate	Seed coats, leaves	Wang, Zhang, Dong, Zhao, & Zhang, 2010; Han, 2012
60	3,4-Dihydroxyl benzene ethyl alcohol	Leaves, barks, seed coats, flowers	Wang et al., 1982; Zhang, Zhang, & Wang, 2006; Wang, Zhang, Dong, Zhao, & Zhang, 2010; Zhang et al., 2018; Zhang, Jiao, Wang, & Zhang, 2007
61	2-(3,4-Dihydroxy)phenyl ethyl acetate	Barks, leaves, twigs	Zhang, Zhang, & Wang, 2006; Han, 2012; Zhao, Han, Lv, & Zhang, 2012
62	3,4-Dihydroxylphenylethanolglucoside	Barks	Zhang, Jiao, Wang, & Zhang, 2007
63	3,4-Dihydroxybenzene-styrene glycol	Leaves	Tian, Li, Lv, Zhang, & Liu, 2013
64	*p*-Hydroxyphenylethyl propyl ester	Seeds	Zhang, Guo, Han, Zhao, & Wang, 2011
65	Esculetin	Barks	Zhang, Zhang, & Wang, 2006
66	7-Hydroxy-6-methoxy-2*H*-chromen-2-one	Leaves	Li, Xu, Hao, Yang, & Li, 2009
67	1,3-Benzodioxole-5-propanol	Leaves	Zhang et al., 2018
68	Syringin	Twigs	Zhao, Han, Lv, & Zhang, 2012
69	3,5-Dimethyoxyl-4-hydroxyl cinnamaldehyde	Twigs	Zhao, Han, Lv, & Zhang, 2012
70	*p*-Hydroxy benzene propyl alcohol	Flower buds, leaves	Dong, Wang, Zhao, & Zhang, 2011; Zhang et al., 2018
71	*trans*-*p*-Hydroxycinnamic acid	Leaves	Wang et al., 1982
72	6-*O*-(*E*)-feruloyl-(α)-glucopyranoside	Leaves	Tian, Li, Lv, Zhang, & Liu, 2013
73	6-*O*-(*E*)-feruloyl-(β)-glucopyranoside	Leaves	Tian, Li, Lv, Zhang, & Liu, 2013
74	Caffeic acid	Flowers	Cao, 2017
75	Dictamnoside A	Flowers	Cao, 2017
76	3,4-Dihyroxybenzoic acid	Leaves	Wang et al., 1982; Zhou, 2005
77	2-Furancarboxylic acid	Leaves	Zhou, 2005; Lu, Li, & Li, 2003
78	4-Hydroxy-3-methoxybenzoic acid	Leaves	Li, Xu, Hao, Yang, & Li, 2009
79	Sesamol	Twigs	Zhao, Han, Lv, & Zhang, 2012
80	3,5-Dimethoxy-4-hydroxybenzaldehyde	Twigs	Zhao, Han, Lv, & Zhang, 2012

isocalamenediol (7.11%) were the top three major compounds. The major compounds from essential oils of leaves, flowers, and stems of *S. oblata* are significantly different. It may help to explain the different medicinal uses of these plant parts. Moreover, *S. pinnatifolia*, a famous Mongolian medicine and a botanical relative of *S. oblata*, has been well studied on its stems. Sesquiterpenoids are a specific group of compounds in *S. pinnatifolia* that were confirmed to be bioactive compounds contributing to its cardiac protective effects (Li et al., 2022). However, these compounds have not been studied in *S. oblata*. A further study on the volatile components and sesquiterpenoids from *S. oblata* stems may help to reveal scientific evidence of its traditional use in Mongolian medicine.

3. Pharmacological effects of *S. oblata*

S. oblata has shown potent medicinal properties including antimicrobial, antioxidant, antitumor, hepatoprotective, and choleretic activities, drawing the interest of many researchers.

3.1. Antimicrobial activities

The antibacterial activities of dichloromethane, EtOAc, and *n*-BuOH fractions of the EtOH-aqueous extract of *S. oblata* leaves were evaluated. Results showed that the EtOAc fraction had the strongest activity. A further bioactivity-guided fractionated afforded five compounds possessing inhibitory effects against *Staphylococcus aureus*, *Shigella flexneri*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Among them, 3,4-dihydroxy phenylethano1 was significantly active, with a minimum bacteriostatic concentration of 6.25 μg/mL (Wang et al., 1982). Another antibacterial assay conducted by (Hu et al., 1993) showed that *S. oblata* could inhibit *Staphylococcus aureus*, *S. epidermidis*, and *Proteus*. Eugenol, a major volatile metabolite in the flower buds of *S. oblata*, showed potential antimicrobial activity against *Alternaria alternata*, *Phytophthora parasitica* var. *nicotianae*, and *Ralstonia solanacearum*. It exhibited the best antimicrobial effect on *A. alternata*, with a minimum bacteriostatic concentration of 150 μg/mL and a minimum bactericidal concentration of 250 μg/mL (Jing, Gou, Han, Wu, & Zhang, 2017; Jing et al., 2018). Another study showed that eugenol dose-dependently inhibited catalase and succinate dehydrogenase in *Pseudomonas solanacearum* at concentrations ranging from 0.1 to 0.3 mg/mL (Bai, Kong, Lin, & Zhang, 2016). The aqueous extract of *S. oblata* showed an antibiofilm effect against *Streptococcus suis* by inhibiting the synthetase in the bacteria (Liu et al., 2018). A further study revealed that rutin was the bioactive compound, showing an antibiofilm activity by targeting the chloramphenicol acetyltransferase. The total flavonoids extracted from *S. oblata* leaves showed a potential inhibitory effect against *E. coli* K 87 and K99, indicating that the extract could be a promising antidiarrhea agent for pigs (Wang, 2013). The antibacterial effects of essential oils from *S. oblata* flower buds and extract of *S. oblata* leaves were evaluated by *in vivo* experiments on mice infected by *S. aureus*, results showed that both the essential oil and leaves extract showed inhibitory effects against *E. coli* (Wang, 2008; Zhang et al., 2020; Yang, 2016).

3.2. Antioxidant activities

A phenolics extract from *S. oblata* leaves was evaluated for its inhibitory effect against the oxidization of low-density lipoprotein (LDL) by detecting the concentration of malondialdehyde and lipofuscin in the oxidized LDL. At concentrations ranging from 50 μg/mL to 400 μg/mL, the extract of *S. oblata* leaves showed inhibitory rates of 10.0%–71.9% against malondialdehyde and 29.2%–56.2% against lipofuscin. At the concentration of 100, 200, and 400 μg/mL, the extract inhibited the relative electrophoretic mobility of oxidized LDL, with initiatory rates of 17.5%, 22.4%, and 31.2%, respectively. Besides, the extract of *S. oblata* leaves also showed potent antioxidant activity in inhibiting the oxidization of cooking oil (Wang & Zhao, 2006, 2007; Tóth et al., 2016). A bioactivity-guided fractionation of phenolics from *S. oblata* showed that nonpolar constituents had the strongest antioxidant activity (Zhao, Lv, Zhu, Zhang, & Guo, 2015). At the concentration of 70 μg/mL, the DPPH free radical scavenging capacity was 79.44%. Furthermore, the nonpolar constituents were found to exhibit a stronger antioxidant activity when they were treated with simulated gastric fluid, but to show a lower antioxidant activity when treated with simulated intestinal fluids. Wu (2015) found that a higher relative

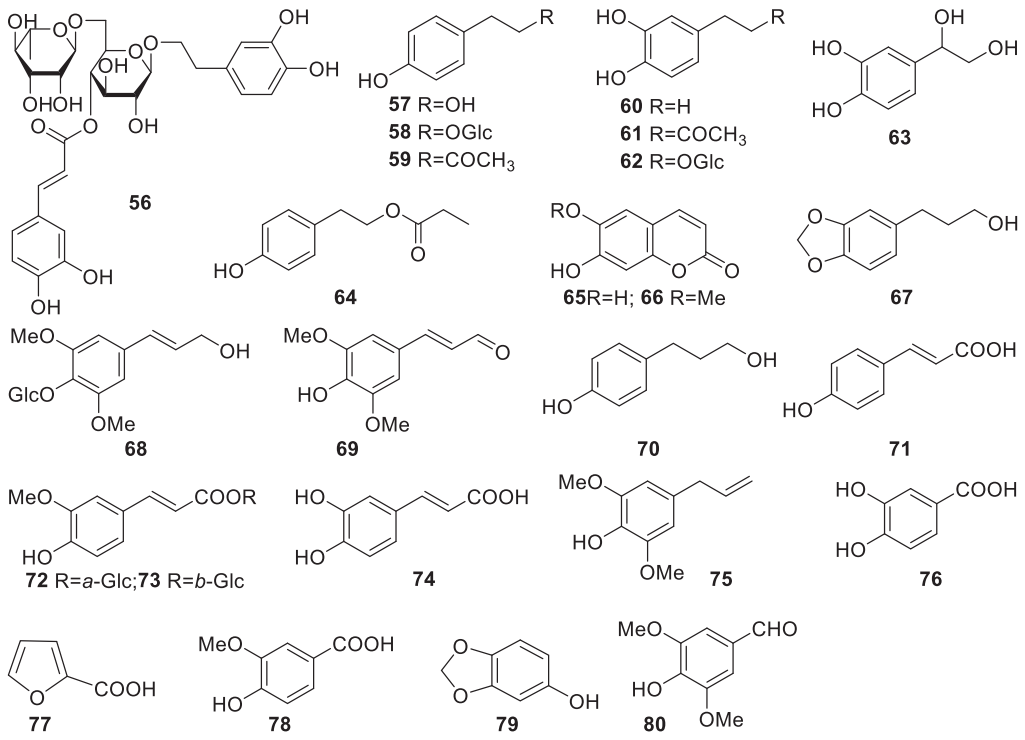

Fig. 4. Structures of phenols in *S. oblata* (**56**–**80**).

Table 5
Flavonoids isolated from *S. oblata* (**81**–**87**).

No.	Compounds	Plant parts	References
81	Formonometin	Leaves	Zhou, 2005; Lu, Li, & Li, 2003
82	5,7,4′-Trihydroxyl flavanone	Leaves, twigs	Li, Xu, Hao, Yang, & Li, 2009; Zhao, Han, Lv, & Zhang, 2012
83	Kaempferol-3-*O*-α-L-rhamnosyl-(1 → 6)-β-D-glucoside	Flowers	Bai, Kong, Lin, & Zhang, 2016; Cao, 2017; Cui et al., 2019
84	Quercetin	Flowers	Cao, 2017; Cui et al., 2019
85	Rutin	Flowers	Cao, 2017; Cui et al., 2019
86	Quercetin-3-*O*-β-D-glucoside	Flowers	Cao, 2017; Cui et al., 2019
87	Naringenin	Flowers	Cao, 2017; Cui et al., 2019

content of phenolic acids in the extract of *S. oblata* leaves resulted in a stronger antioxidant effect within the concentration from 8 to 16 mg/mL in DPPH assays, indicating that the antioxidant activity may be associated with phenolic acids in *S. oblata*.

3.3. Antiproliferative activities

The antiproliferative activities of syringin against HepG2 human liver cancer cells (IC_{50} = 40.13 μg/mL) and PC-3 human prostate cancer cells (IC_{50} = 88.08 μg/mL) were evaluated (Qin & Zhu, 2018). Results showed that syringin inhibited the viabilities of these two tumor cell lines by accelerating their apoptosis in a dose-dependent manner at 10–160 μg/mL. Hu, Li, Tie, and Jin (2019) found that the essential oil of *S. oblata* flowers could dose-dependently accelerate the apoptosis of several human gas-

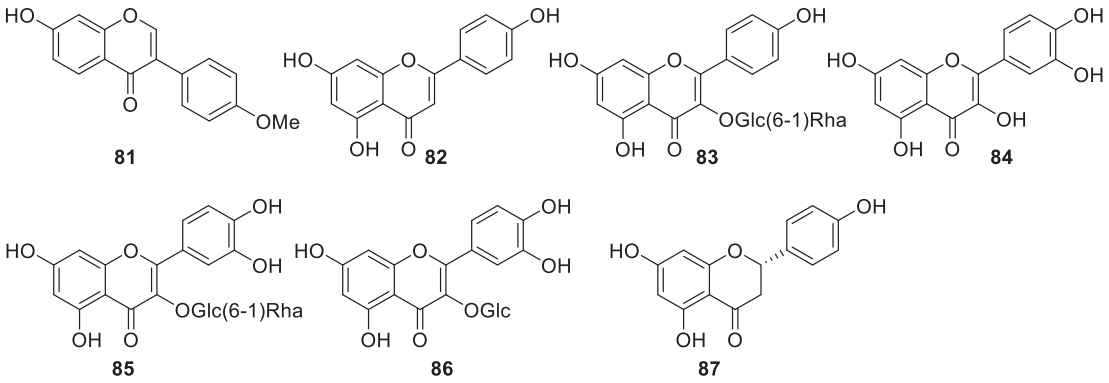

Fig. 5. Flavonoids from *S. oblata* (**81**–**87**).

Table 6
Other classes of compounds reported from *S. oblata* (**88**–**97**).

No.	Compounds	Plant parts	References
88	D-Mannitol	Leaves	Wang et al., 1982; Zhou, 2005; Lu, Li, & Li, 2003
89	Succinic acid	Leaves	Zhou, 2005; Lu, Li, & Li, 2003
90	Cyclohexanehexol	Leaves	Zhou, 2005
91	3(*Z*)-Enol glucoside	Leaves	Zhang et al., 2018
92	Grasshopper ketone	Leaves	Zhang et al., 2018
93	Nonacosane	Leaves	Wei, 2004
94	4-Methyl-12-tricosanol	Leaves	Wei, 2004
95	Lauric acid	Flowers	Cao, 2017; Cui et al., 2019
96	4,19-Dimethyl-12,13-dihydroxy-docosane	Leaves	Wei, 2004
97	Palmitic acid	Flowers	Cao, 2017; Cui et al., 2019

tric cancer cell lines using the TUNEL method. The strongest antiproliferative activity was found in HGC-27 cells, indicating that the essential oil of *S. oblata* flowers may be a potential antitumor agent against HGC-27 cells. A phenylethanoid hydroxytyrosol and a glycosylated seco-iridoid oleuropein both showed inhibitory activity against the H_2O_2-induced oxidative stress in LLC-PK_1 (Liu, 2013). And hydroxytyrosol exhibited a stronger inhibition than oleuropein.

3.4. Hepatoprotective and choleretic activities

S. oblata has been traditionally used to treat hepatitis in folk, and this usage is recorded in *Medicinal Plants of Changbai Mountain*. Some modern pharmacological studies also validated the hepatoprotective effect of *S. oblata* (Wang et al., 2000; Gao et al., 2003a). The extract of *S. oblata* leaves was made into clinical medicines to treat acute icteric hepatitis, resulting in that 93.7% of patients being cured (Department of Infectious Diseases, 1978). An *in vitro* study showed that the extract of *S. oblata* leaves inhibited hepatitis B viral proteins HBeAg and HBsAg, indicating the inhibitory activity against the hepatitis B virus (Bai, Kong, Lin, & Zhang, 2016; Gao et al., 2003a). As previously reported, *S. oblata* leaves extract could also relieve the liver damage induced by chemical drugs (Hao, 2008), and the hepatoprotection may be associated with triterpenoid glycosides (Bai, Kong, Lin, & Zhang, 2016; Gao et al., 2003b). Another *in vivo* study showed that the extract of *S. oblata* leaves protected mice from the CCl_4-induced liver injury at an effective concentration of 200 mg/kg (Li et al., 2018a,b). The extract (100 and 200 mg/kg) significantly reversed CCl_4-induced changes in serum and liver biochemical parameters and showed antioxidant activities both *in vitro* and *in vivo*, significantly depressing the supernatant and serum levels of ALT, AST, and GSTA1 as well as the cell and tissue level of MDA. Besides *S. oblata* leaves were reported to possess a choleretic activity. Wang et al. (1982) conducted a phytopharmacological study on *S. oblata* leaves, revealing that syringopicroside was the bioactive compound contributing to the choleretic activity.

3.5. Other pharmacological activities

As previously reported, the extract of *S. oblata* leaves sometimes was used to treat epilepsy and acute icteric hepatitis (Department of Microbiology and Pharmacy, Heilongjiang College of Traditional Chinese Medicine, 1978; Department of Infectious Diseases, 1978). Due to the folk use of *S. oblata* leaves for treating Pink Eye, some researchers conducted pharmacological studies to evaluate the efficiency of treating keratitis and conjunctivitis (Yang & Xing, 1990; Xing, 1992; Xing & Li, 1996). The medicine made from *S. oblata* leaves could treat herpes simplex virus keratitis by changing the pH of tears and regulating the level of IgA, IgG, and IgM. It showed a potential efficiency in treating epidemic hemorrhagic conjunctivitis as well. Besides, iridoids from *S. oblata* inhibited ulcerative colitis in rats by inhibiting the oxidization of immunoglobulins (Liu & Wang, 2011). Oleuropein was reported to protect from kidney damage by inhibiting the H_2O_2-induced oxidative stress on LLC-PK_1 (Liu, 2013). Terpenoids from *S. oblata* could inhibit the production of NO, TNF-α, and IL-6 in LPS-induced BV-2 murine microglial cells, indicating the potential anti-inflammatory effect of *S. oblata* (Jing et al., 2018; Liu et al., 2018; Yang, 2016). Moreover, the aqueous extract of *S. oblata* flowers and lauric acid showed *in vitro* coagulation activities by shortening the activated partial thromboplastin time, prothrombin time, and thrombin time in the plasma of rabbits (Cui et al., 2019).

4. Conclusion and discussion

S. oblata has been traditionally used in Chinese medicine. And its leaves, barks, seed coats, twigs, flowers, and flower buds have been systematically investigated in phytochemistry and pharmacology. Phytochemicals from *S. oblata*, including iridoids, phenylpropanoids, triterpenoids, phenylethanoids, and flavonoids, have been well studied in their biological activities. Iridoid glycosides showed potent anti-inflammatory activity. The antimicrobial activities of syringopicroside and flavonoids were examined. Antiproliferative effects of syringin were found in several cancer cell lines. And the total saponins extract of *S. oblata* exhibited a hepatoprotective effect. Unique chemical constituents and pharmacological effects have been found in *S. oblata*. It merits further studies on

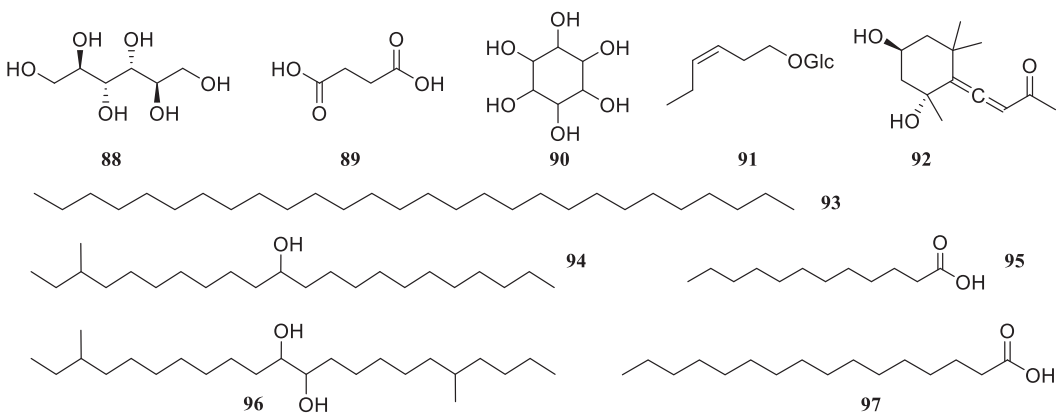

Fig. 6. Structures of other compounds in *S. oblata* (**88**–**97**).

the chemical composition as well as systematic evaluation and mechanisms of the pharmacological effects.

The medicinal parts and applications of *S. oblata* in Mongolian medicine are different from those in traditional Chinese medicine. *S. oblata* and its botanical relative *S. pinnatifolia* are similarly used as Mongolian medicines in Alashan, Inner Mongolia. The medicinal part of *S. oblata* in Mongolian medicine is the heartwood, and the traditional use is to treat heart diseases caused by *Heyi*. The traditional medicinal uses of *S. oblata* documented in the legal drug standards of Mongolian medicines are also similar to *S. pinnatifolia*. It is documented in *Mongolian Medicine Standards of Inner Mongolia* (supplemental edition in 2015). Recently, the anti-myocardial ischemia, antimicrobial, antitumor, antidiabetic, hepatoprotective, pain-relieving, and sedative effects of *S. pinnatifolia* have been well studied by many researchers (Ma et al., 2020; Su et al., 2015a). Although there are several studies on *S. oblata* in Chinese medicine, it lacks a systematic study on the heartwood of *S. oblata* in Mongolian medicine. Especially, modern research in the ethnopharmacology of *S. oblata* in Mongolian medicine has rarely been reported.

Moreover, in *Newly Revised Jingzhu Bencao*, it is recorded that the stems of *S. oblata* and its botanical relatives in the genus *Syringa* could be used as substitutes for sandalwood in Tibet medicine, the substitutes were called Huang-Tan-Xiang (Luo, 2004). The abovementioned traditional uses and modern pythopharmacological studies both supported that *S. oblata* is a medicinally important plant. However, there is a gap in the systematic study of *S. oblata* heartwoods. Are there any sesquiterpenoids that are characteristic compounds in the genus *Syringa* (Ma et al., 2020)? Are there lignans which may have synergy with sesquiterpenoids (Li et al., 2019; Su et al., 2015b)? It deserves further phytochemical and pharmacological studies in this Mongolian medicine. An integrated study on the system biology and phytopharmacology of *S. oblata* may help to uncover the multiple targets and signaling pathways involved in its protection of the cardiovascular system, to provide scientific evidence for clinic uses, and to give references to the utilization of Mongolian medicinal products made from *S. oblata*.

Last but not least, all ethnomedicines containing *S. oblata* deserve a deep thought about their pharmacologically active components, botanical source verification, and resource survey.

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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