Phytochemical and pharmacological progress on the genus Syringa

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Abstract

Genus Syringa, belonging to the Oleaceae family, consists of more than 40 plant species worldwide, of which 22 species, including 18 endemic species, are found in China. Most Syringa plants are used in making ornaments and traditional medicines, whereas some are employed for construction or economic use. Previous studies have shown that extracts of Syringa plants mainly contain iridoids, lignans, and phenylethanoids that have antitumor, antihypertensive, anti-oxidant, and anti-inflammatory activities. This study reviews phytochemical and pharmacological progress on Syringa in the recent 20 years and discusses the future research prospects to provide a reference in further promotion and application of the genus.

Keywords: Syringa, Oleaceae, Iridoid, Lignan, Phenylethanoid, Bioactivities, Review

Introduction

Plants belonging to the family Oleaceae, which consists of 27 genera and 400 species worldwide, have important applications in the daily life of people living in developing countries. Plants of many well-known genera, including Forsythia, Syringa, and Osmanthus, have been widely used for medicinal and industrial purposes. For instance, the stems and roots of S. pinnatifolia var. alashanensis is the major composition of a traditional formula ‘Ba wei chenxiang’ powder that is used for treatment of asthma, cardiopalmus, and angina [1].

Most Syringa plants are deciduous shrubs and arbors and include more than 40 species distributed around Europe and Asia [2]. At present, 22 species are found in China, of which 18 are endemic species that are mainly distributed in the southwestern part of Sichuan, Yunnan, Tibet, and other Northwestern regions. Many Syringa species, such as S. chinensis, S. meyeri, and S. pekinensis, are used for making ornaments. Flowers of S. oblata and S. reticulata var. mandshurica are an ideal source of aroma oils or nectar. Some Syringa plants are also used for construction purposes or for manufacturing furniture [1].

Previous phytochemical studies on Syringa species have revealed the presence of more than 140 secondary metabolites, including iridoids, lignans, phenylethanoids, their glycosides, minor organic acids, and essential oils [3,4]. Modern pharmacological studies have shown the bioactivities of these metabolites, such as antitumor, antihypertensive, anti-oxidant, anti-inflammatory activities, and so on [5]. However, a systematic review of these studies has not been performed to date. This review summarizes the phytochemical and pharmacological progress on Syringa to date by focusing on its chemical classification, structural features, and biological and pharmacological applications to provide information for further research on this genus.

Chemical constituents

Previous studies have reported that extracts of Syringa plants contain iridoids (1–46), lignans (47–80), phenylpropanoids (81–105), phenylethanoids (106–121), and other compounds (122–142). The structures of these compounds are shown in Figures 1, 2, and 3 and related information are listed in Tables 1, 2, and 3.

Iridoids

Iridoids are one of the most important natural compounds that are widely distributed in various plant families such as Plantaginaceae, Rubiaceae, and Scrophulariaceae [6]. Iridoids are extensively present in almost all Syringa species and have antitumor, antihypertensive, anti-inflammatory, anti-oxidant, and antifungal activities. In addition, iridoids
play an important role in defense mechanism of ants [7]. Among all the iridoids reported in this genus, secoiridoids are the most abundant and have been shown to have anti-tumor activity. To date, 46 iridoids (1–46) have been described, including secoiridoids (1–30) and 40–44), eight typical iridoids (32–39), and three minor dimers (31, 45, and 46). Most iridoids exist as glycosides and are mainly produced by the glycosylation of glucose and galactose. *Syringa* iridoids are generally substituted by various acid fragments and phenolic moieties such as 1-O-cinnamoyl-β-D-glucopyranosyl, p-hydroxyphenethyl, 3, 4-dihydroxy-phenethyl, and caffeic acid, which contribute to their low polarity. *Syringa* iridoids have antitumor (33 and 40) [8,9], antihypertensive (4), and anti-oxidant (4 and 31) activities [10].

**Lignans**

Lignans are another major compounds in this genus, particularly in *S. komarowii* [27], *S. pubescens* [3], *S. reticulata* [10], *S. velutina* [28], *S. patula* [5], *S. vulgaris* [29], *S. pinnatifolia* var. alashanensis [30,31], and *S. reticulata* var. mandshurica [32]. *Syringa* species have 34 lignans and their glycosides (47–80), including monoepoxylignans (47–60, 62) and their dimers (63 and 64), neolignans (61, 73–74), cyclolignans (65 and 66), simple lignans (67–72), and bisepoxylignans (75–80). Lignans also exhibit many bioactivities. For example, compound 50 has anti-oxidant activity [10]; compounds 57 and 58 have antifungal activities [32]; and compound 75 has significant cytotoxic, antihypertensive, anti-inflammatory, and anti-oxidant activities [5].

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**Figure 1** The structures of iridoids from the genus *Syringa*.
Other compounds
Phenylethanoids (81–105), phenylpropanoids and their analogues (106–121), flavonoids (122–128), sesquiterpenes (129 and 130), and other minor compounds have been described in Syringa plants. Of these, phenylethanoids are predominant, particularly in *S. reticulata* [10,12,35], *S. vulgaris* [29], *S. pubescens* [3], *S. oblata* var. *alba* [36], *S. reticulata* var. *mandshurica* [35], *S. afghanica* [13], and *S. komarowii* [27]. Sesquiterpenes (129 and 130) are present in the stems of *S. pinnatifolia* var. *alashanensis* [37]. These miscellaneous compounds have cytotoxic, anti-inflammatory, antihypertensive, anti-oxidant, and antifungal properties.

Besides the abovementioned compounds, *Syringa* plants contain essential oils that form the most important constituents not only because of their economic utility but also because of their potential medicinal value as antimicrobial, antipyretic, and antiviral agents. Multiple analytical techniques such as headspace solid-phase microextraction, gas chromatography–mass spectrometry (GC–MS), GC–MS coupled with heuristic evolving latent projections, moving subwindow searching, nuclear magnetic resonance spectroscopy, and X-ray single-crystal diffraction analysis have been used to identify essential oils from fresh flowers of *S. oblata* var. *alba*. For instance, 39 volatile oil constituents were identified, including four characteristic isomers of lilac alcohols (lilac alcohols A–D) and lilac aldehydes A–D [38]. Ninety-five components, including 15 terpenes, 14 oxygenated terpenes, 10 aromatic compounds, and 13 n-alkanes were quantitatively analyzed from *S. oblata* buds [39]. Forty-nine components were described from essential oil of *S. pubescens* flowers, most of which are monoterpenes and sesquiterpenes [40]. Thirty-four volatile oil components, accounting for around 64.7% (zerumbone) of the oil, were identified from roots and barks of *S. pinnatifolia* var. *alashanensis* [4]. These data imply that *Syringa* plants could be considerably different from each other in terms of their essential oil components.

**Pharmacological activities**
Various crude extracts and isolated compounds from *Syringa* plants have shown significant antitumor, antihypertensive, anti-inflammatory, anti-oxidant, and antifungal activities.
Figure 3 The structures of other type of compounds from the genus Syringa.
| No | Compound                  | Part of plants                                      | Source                          | Reference       |
|----|---------------------------|------------------------------------------------------|---------------------------------|-----------------|
| 1  | Isoliguistroside          | leaves                                               | S. vulgaris                     | [11]            |
| 2  | Isooleuropein             | leaves                                               | S. vulgaris                     | [11]            |
| 3  | Oleoside 11-methyl ester | flowers, leaves and floral buds                      | S. pubescens                    | [3,5]           |
|    |                           |                                                     | S. patula                       |                 |
| 4  | Oleuropein                | flowers, leaves, barks and floral buds               | S. pubescens                    | [3,5,8,10,12-14]|
|    |                           |                                                     | S. reticulata, S. dilatata, S. velutina, S. afghanica, S. oblata var. alba, S. patula |                 |
| 5  | Neooleuropein             | leaves                                               | S. vulgaris                     | [15]            |
| 6  | 8(E)-Ligstroside          | flowers, leaves and barks                            | S. pubescens, S. reticulata, S. dilatata, S. afghanica | [3,8,10,13]    |
| 7  | 8(E)-Nüzhenide            | leaves                                               | S. reticulata                   | [16]            |
| 8  | Safghanoside A            | leaves                                               | S. afghanica                    | [13]            |
| 9  | Safghanoside B            | leaves                                               | S. afghanica                    | [13]            |
| 10 | Safghanoside C            | leaves                                               | S. afghanica                    | [13]            |
| 11 | Safghanoside D            | leaves                                               | S. afghanica                    | [13]            |
| 12 | Safghanoside E            | leaves                                               | S. afghanica                    | [13]            |
| 13 | Safghanoside F            | leaves                                               | S. afghanica                    | [13]            |
| 14 | Formoside                 | leaves                                               | S. afghanica                    | [13]            |
| 15 | Fraxiformoside            | leaves                                               | S. afghanica                    | [13]            |
| 16 | 2''-epi-frameroside       | leaves                                               | S. afghanica                    | [13]            |
| 17 | 1'''-O-β-D-glucosylformoside | leaves                                       | S. afghanica                    | [13]            |
| 18 | 1'''-O-β-D-glucosylfraxiformoside | leaves                   | S. afghanica                    | [13]            |
| 19 | Lilacoside                | barks and leaves                                     | S. vulgaris                     | [17,18]         |
| 20 | Fliederoside              | barks and leaves                                     | S. vulgaris                     | [17,18]         |
| 21 | 8(E)-Ligstroside          | leaves                                               | S. reticulata                   | [16]            |
| 22 | 8(E)-Nüzhenide            | leaves                                               | S. reticulata                   | [16]            |
| 23 | Oleoside dimethyl ester   | leaves                                               | S. afghanica                    | [13]            |
| 24 | 10-Hydroxyoleuropein      | flowers and leaves                                   | S. pubescens                    | [3]             |
| 25 | 10-Hydroxyoleoside dimethyl ester | flowers and leaves                                               | S. pubescens                    | [3]             |
| 26 | Secologanoside 7-methyl est | leaves                                         | S. reticulata                   | [19]            |
| 27 | Grandifloroside 11-methyl est | leaves                                           | S. pubescens                    | [3]             |
| 28 | 8-Epikingside             | barks                                                | S. vulgaris                     | [20]            |
| 29 | Syrveoside A              | leaves                                               | S. velutina                     | [21]            |
| 30 | Syrveoside B              | leaves                                               | S. velutina                     | [21]            |
| 31 | Jaspolyside               | barks                                                | S. reticulata                   | [10]            |
| 32 | Syringopicroside           | leaves                                               | S. dilatata, S. vulgaris, S. oblata, S. reticulata | [8,16,19,22,23]|
| 33 | Syringopicroside B         | leaves                                               | S. vulgaris                     | [9]             |
| 34 | 3'-O-β-D-glucopyranosylsyring-opicroside | leaves                                           | S. reticulata                   | [16]            |
| 35 | 4'-O-β-D-glucopyranosylsyring-opicroside | leaves                                           | S. reticulata                   | [16]            |
| 36 | 6'-O-α-D-glucopyranosylsyring-opicroside | leaves                                           | S. reticulata                   | [16]            |
| 37 | 6'-O-α-D-galactopyranosylsyring-opicroside | leaves                                           | S. reticulata                   | [19]            |
| 38 | Syringopicrogenin C        | seeds                                                | S. oblata                       | [24]            |
| 39 | Syringopicrogenin A        | seeds and crust                                      | S. oblata                       | [24,25]         |
Antitumor activity
Cytotoxic activities of crude extracts and chemicals obtained from *Syringa* plants have been extensively evaluated against various tumor cell lines. Aqueous extracts from the flowers and leaves of *S. pubescens* inhibited the growth of L2215 (hepatitis B virus) cells, with a 50% inhibitory concentration (IC₅₀) value of 78 µg/mL [51]. Hydrolysis of isoligustroside (1) and isooeuropin (2) were assayed using a disease-oriented panel of 39 human cancer cell lines. The results showed that the hydrolysis product of compound 2 had moderate cytotoxic activity against lung cancer cell lines DMS273 [log GI₅₀ = 5.19 (6.4 µM)] and DMS114 [log GI₅₀ = 5.06 (8.7 µM)]. Preliminary analysis of structure–activity relationship suggested that C-5′-OH plays an important role in this cytotoxic activity [11]. Isooleacteoside (40) showed weak cytotoxicity against LOX-IMVI melanoma cell line, with GI₅₀ value of 16 µM, and syringopicroside B (33) showed weak cytotoxic activity against NCI-H522 lung cancer cell line, with GI₅₀ value of 13 µM [9]. MTT assay used to assess the cytotoxicities of syringaresinol (78) and oleoside 11-methyl ester (3) showed that compound 78 had a strong dose-dependent effect on HepG2 cell line, with an IC₅₀ value of 94.6 µM, and compound 3 has a dose–response curve of low slope, with a high IC₅₀ value of 186.5 µM, compared with positive controls dexamethasone (IC₅₀ 14.2 µM) and paclitaxel (IC₅₀ 700 nM). However, compound 78 was cytotoxic even at the lowest concentration of 29.9 µM. β-Amyrin acetate (139) showed weak cytotoxicity against A2780 human ovarian cancer and HepG2 cell lines [5]. Oleuropein (4) and 2-(3, 4-dihydroxy)-phenylethyl-β-D-glucopyranoside (83) showed evident cytotoxicities against P-388, L-1210, SNU-5, and HL-60 cell lines, with IC₅₀ values varying from 8.5 to 139.8 µM [12]. Verbasoside (86) showed moderate cytotoxic activity against SNB-75 (brain cancer) and SNB-78 cell lines, with GI₅₀ values of 7.4 and 7.7 µM, respectively [9]. A pharmacokinetic study showed that compound 86 interacted with the catalytic domain of PKC and acted as a competitive inhibitor of adenosine triphosphate (Kᵢ = 22 µM) and non-competitive inhibitor of phosphate acceptor (histone III). Because 83 is one part of 86 in its molecular structure, the cytotoxic effect could be attributed to 3, 4-dihydroxyphenylethoxy moiety, which may act as a competitive inhibitor to the catalytic domain of PKC. Therefore, 83 is a potentially essential skeleton of most cytotoxic phenylethanoid glycosides [12].

Hypotensive activity
Syringin (110) and kaempferol-3-O-rutinoside (125) showed antihypertensive activity. Intravenous injection of 10 mg/kg of compound 86 significantly decreased systolic, diastolic, and mean arterial blood pressure in Pentothal-anesthetized rats. Moreover, the depressor effect of compound 86 was independent of muscarinic and histaminergic receptors because it did not block the effect of atropine (an antimuscarinic agent) and chlorpheniramine/cimetidine (antihistaminergic agents) [36]. *In vitro* studies showed that oleuropein (4) significantly lowered blood pressure. It is interesting to note that antihypertensive effect of compound 4 (33% at 30 mg/kg dose) on the blood pressure of anesthetized rats was similar to that of compound 86 (39.04% ± 2.38% at 10 mg/kg dose) [14,36], which is probably because of the similarity in their structures, with both possessing the same aromatic fragment having two hydroxy groups.

Anti-inflammatory activity
Iridoid glycosides (IGs) exerted obvious anti-inflammatory effects on ulcerative colitis *in vivo* by inhibiting relative proinflammatory cytokines [53]. IGs significantly ameliorated macroscopic damages and histological changes, reduced the activity of myeloperoxidase, and strongly inhibited epithelial cell apoptosis. Moreover, IGs markedly decreased the levels of tumor necrosis factor-α, interleukin-8, cyclooxygenase-2, and transforming growth factor-β1 in colonic tissues in a dose-dependent manner. Moreover, effects of IGs (160 and 240 mg/kg) were superior to those of positive control salicylsulfaipyridine (150 mg/kg). Furthermore, IGs significantly blocked NF-κB signaling by inhibiting inflammatory bowel phosphorylation/degradation and inhibitor kappa B kinase β activity; downregulated protein and mRNA expressions of Fas/Fasl, Bax, and caspase-3; and activated Bcl-2 in intestinal epithelial cells.

### Table 1 Iridoids from the genus *Syringa* (Continued)

| 40 | Isooleacteoside | leaves | S. vulgaris | [9] |
| 41 | Oleacteoside | leaves | S. reticulata | [9,26] |
| 42 | Oleoechinacoside | leaves | S. reticulata | [9,26] |
| 43 | Reticuloside | barks | S. reticulata | [10] |
| 44 | Jasinoside | whole plant | S. komarowii | [27] |
| 45 | Safghanoside H | leaves | S. afghanica | [13] |
| 46 | Safghanoside G | leaves | S. afghanica | [13] |
β-Amyrin acetate (139) and syringaresinol (78) at a dose of 20 μg/mL evidently inhibited lipopolysaccharide-induced nitric oxide (NO) production, with inhibition rates of 49.97% and 33.21%, respectively [5].

**Liver-protective and cholagogic effects**

Crude extract of *Syringa* species, interferon (IFN), and an injection of “Gan-Yan-Ling” were compared to evaluate their liver-protective effects on the survival rates of HepG2.215 cells and secretion of hepatitis B surface antigen (HBsAg) and HBeAg. The results indicated that all the three assayed drugs may suppress the secretion of HBsAg and HBeAg from HepG2.215 cells in a dose-dependent manner, with the effect of crude extract of *Syringa* being intermediate those of IFN and Gan-Yan-Ling. Therefore, extracts of *Syringa* plant

### Table 2 Lignans from the genus *Syringa*

| No | Name | Part of plant | Source | Reference |
|----|------|---------------|--------|-----------|
| 47 | (--)-Olivil | whole plant | *S. komarovii* | [27] |
| 48 | Olivil 4-O-β-D-glucopyranoside | barks | *S. reticulata, S. patula* | [10] |
| 49 | Olivil 4''-O-β-D-glucopyranoside | barks | *S. reticulata* | [27] |
| 50 | Armandiside | barks | *S. reticulata* | [10] |
| 51 | Syripinnalignan A | roots and stems | *S. pinnatifolia var. alashanensis* | [31] |
| 52 | Syripinnalignan B | roots and stems | *S. pinnatifolia var. alashanensis* | [31] |
| 53 | (8R, 8'R, 9R)-4''-dihydroxy-3, 3', 9-trimethoxy-9''-epoxyxiligan | roots and stems | *S. pinnatifolia var. alashanensis* | [30] |
| 54 | (8R, 8'R, 9R)-4''-dihydroxy-3, 3', 9-trimethoxy-9''-epoxyxiligan | roots and stems | *S. pinnatifolia var. alashanensis* | [30] |
| 55 | (8S, 8'S, 9R)-4''-dihydroxy-3, 3', 9-trimethoxy-9''-epoxyxiligan | roots and stems | *S. pinnatifolia var. alashanensis* | [30] |
| 56 | (8S, 8'S, 9R)-4''-dihydroxy-3, 3', 9-trimethoxy-9''-epoxyxiligan | roots and stems | *S. pinnatifolia var. alashanensis* | [30] |
| 57 | Mandshuricol A | leaves | *S. reticulata var. mandshurica* | [32] |
| 58 | Mandshuricol B | leaves | *S. reticulata var. mandshurica* | [32] |
| 59 | (+) -Lariciresinol | seeds crust | *S. oblata* | [25] |
| 60 | (++)-Lariciresinol 4-O-β-D-glucopyranoside | barks | *S. vulgans* | [29] |
| 61 | Balanopholin | roots and stems | *S. pinnatifolia var. alashanensis* | [30] |
| 62 | (++)-Lariciresinol 4''-O-β-D-glucopyranoside | leaves | *S. reticulata* | [19] |
| 63 | Syripinnalignin A | roots and stems | *S. pinnatifolia var. alashanensis* | [33] |
| 64 | Syripinnalignin B | roots and stems | *S. pinnatifolia var. alashanensis* | [33] |
| 65 | Cycloolivil 6-O-β-D-glucoside | barks | *S. reticulata* | [10] |
| 66 | (+)-Cycloolivil | whole plant | *S. komarovii* | [27] |
| 67 | (--) -Secoisolariciresinol | stems | *S. pinnatifolia var. alashanensis* | [30,31] |
| 68 | PiperphilipininVI | roots and stems | *S. pinnatifolia* | [30] |
| 69 | Dihydrocubebin | roots and stems | *S. pinnatifolia var. alashanensis* | [30] |
| 70 | Syripinnalignin C | roots and stems | *S. pinnatifolia var. alashanensis* | [34] |
| 71 | Syripinnalignin D | roots and stems | *S. pinnatifolia var. alashanensis* | [34] |
| 72 | Syripinnalignin E | roots and stems | *S. pinnatifolia var. alashanensis* | [34] |
| 73 | (7S, 8R)-Guaiacylglycerol-8-O-4''-sinapyl ether 9''-O-β-D-glucopyranoside | leaves | *S. velutina* | [28] |
| 74 | (7S, 8R)-Syringylglycerol-8-O-4''-sinapyl ether 9''-O-β-D-glucopyranoside | leaves | *S. velutina* | [28] |
| 75 | Pinoresinol-4-O-β-monoglycoside | barks | *S. reticulata* | [10] |
| 76 | Syringaresinol-4-O-bis-β-D-monoglucoside | barks | *S. reticulata* | [10] |
| 77 | Syringaresinol-4, 4''-O-bis-β-D-glucoside | barks | *S. reticulata* | [10] |
| 78 | Syringaresinol | floral buds, flowers and leaves | *S. patula, S. pubescens* | [3,5] |
| 79 | (+)-Medioresinol-4-O-glucoside | floral buds | *S. patula* | [5] |
| 80 | (--) -Pinoresinol | roots and stems | *S. pinnatifolia var. alashanensis* | [30] |
Table 3 Other type of compounds from the genus *Syringa*

| No | Name                                      | Part of plant               | Source                  | Reference               |
|----|-------------------------------------------|----------------------------|-------------------------|-------------------------|
| 81 | Isosyringalide                            | leaves                     | *S. reticulata*         | [41]                    |
| 82 | Forsythiaside                             | barks                      | *S. vulgaris*           | [29]                    |
| 83 | 2-(3, 4-dihydroxy)-phenylethyl-β-D-glucopyranoside | barks                      | *S. reticulata*         | [10,12]                 |
| 84 | cis-Echinacoside                          | leaves                     | *S. reticulata*         | [35]                    |
| 85 | Isoverbascoside                           | leaves                     | *S. pubescens*          | [3]                     |
| 86 | Verbascoside                              | leaves                     | *S. pubescens, S. oblata var. alba, S. vulgaris* | [3,9,29,14,36] |
| 87 | Echinacoside                              | barks, leaves and flowers  | *S. pubescens, S. reticulata* | [3,9,42] |
| 88 | Forsythoside B                            | leaves                     | *S. reticulata var. mandshurica* | [35] |
| 89 | Salidrose                                 | barks                      | *S. reticulata*         | [10]                    |
| 90 | 3′O-β-D-glucopyranosylsalidroside         | leaves                     | *S. reticulata var. mandshurica* | [35] |
| 91 | 2-(3, 4-dihydroxyphenyl) ethanol          | leaves                     | *S. pubescens*          | [3]                     |
| 92 | Osmanthuside F                            | leaves                     | *S. reticulata*         | [35]                    |
| 93 | (S)-(−)-2-(3, 4-dihydroxyphenyl)-2-ethoxylethanol | leaves                     | *S. reticulata var. mandshurica* | [43] |
| 94 | (S)-(−)-2-(3, 4-dihydroxyphenyl)-2-acetoxyethanol | leaves                     | *S. reticulata var. mandshurica* | [43] |
| 95 | Decaffeoylacteoside                       | leaves                     | *S. reticulata*         | [35]                    |
| 96 | Syringalide B                             | leaves                     | *S. reticulata*         | [41]                    |
| 97 | Poliumoside                               | leaves                     | *S. afghanica*          | [13]                    |
| 98 | 2-(4-hydroxyphenyl)-ethyl behenate        | whole plant                | *S. komarowii*          | [27]                    |
| 99 | 2-(4-hydroxyphenyl)-ethyl tricosanate     | whole plant                | *S. komarowii*          | [27]                    |
| 100| 2-(4-hydroxyphenyl)-ethyl lignocerate     | whole plant                | *S. komarowii*          | [27]                    |
| 101| 2-(4-hydroxyphenyl)-ethyl pentacosanate   | whole plant                | *S. komarowii*          | [27]                    |
| 102| 2-(4-hydroxyphenyl)-ethyl hexacosanate    | whole plant                | *S. komarowii*          | [27]                    |
| 103| Bongardol                                 | whole plant                | *S. komarowii*          | [27]                    |
| 104| 2-(4-hydroxyphenyl)-ethyl 1-dodecyloctadecanoate | whole plant                | *S. komarowii*          | [27]                    |
| 105| 2-(4-hydroxyphenyl)-ethyl dotriacontanoate | whole plant                | *S. komarowii*          | [27]                    |
| 106| Coniferin                                 | barks                      | *S. vulgaris*           | [29]                    |
| 107| Coniferylaldehyde                         | roots and stems            | *S. pinnatifolia var. alashanensis* | [44] |
| 108| Coniferylaldehyde glucoside               | barks                      | *S. reticulata*         | [10]                    |
| 109| Sinapaldehyde glucoside                   | barks                      | *S. reticulata*         | [10]                    |
| 110| Syringin                                  | barks                      | *S. vulgaris, S. reticulata* | [10,45,46] |
| 111| Isosyringinoside                          | barks                      | *S. reticulata*         | [10]                    |
| 112| Eugenol                                   | floral buds                | *S. patula*             | [5]                     |
| 113| Lirinaphthanoe                            | roots and stems            | *S. pinnatifolia var. alashanensis* | [30] |
| 114| Cinnamic acid                             | leaves, roots and stems    | *S. afghanica, S. pinnatifolia var. alashanensis, S. reticulata* | [44,47] |
| 115| Caffeic acid                              | roots and stems            | *S. pinnatifolia var. alashanensis* | [44] |
| 116| Ferulic acid                              | roots and stems            | *S. pinnatifolia var. alashanensis* | [44] |
| 117| 7-Methoxycoumarin                         | roots and stems            | *S. pinnatifolia var. alashanensis* | [44] |
| 118| Esculetine                                | roots and stems            | *S. pinnatifolia var. alashanensis* | [44] |
| 119| Umbelliferone                             | roots and stems            | *S. pinnatifolia var. alashanensis* | [44] |
| 120| O-β-D-xilopyranosyl (1→6) β-D-glucopyranosyl-7-hydroxycoumarin | roots and stems            | *S. pinnatifolia var. alashanensis* | [44] |
| 121| Syringafghanoside                         | leaves                     | *S. afghanica*          | [13]                    |
| 122| Astragalin                                | bark                       | *S. vulgaris*           | [48]                    |
Table 3 Other type of compounds from the genus Syringa (Continued)

| Compound | Plant Part | Species | Source |
|----------|------------|---------|--------|
| 123 | Kaempferol-3, 7-α-L-dirhamnoside | flowers and leaves | S. pubescens |
| 124 | Kaempferol-3-β-D-glucoside-7-α-L-dirhamnoside | flowers and leaves | S. pubescens |
| 125 | Kaempferol-3-O-rutinoside | flowers | S. vulgaris |
| 126 | Luteolin | leaves | S. afghanica |
| 127 | Rutin | leaves | S. vulgaris |
| 128 | Rhoifolin | leaves | S. afghanica |
| 129 | Guai-9-en-4β-ol | roots and stems | S. pinnatifolia var. alashanensis |
| 130 | 14, 15-dinorguai-1, 11-dien-9, 10-dione | roots and stems | S. pinnatifolia var. alashanensis |
| 131 | Mormorcerebroside I | whole plant | S. komarowii |
| 132 | Phytolacca cerebroside | whole plant | S. komarowii |
| 133 | Pubescenside A | flowers and leaves | S. pubescens |
| 134 | Stigmastane-3β, 6α-diol 3-O-tetradecanoate | whole plant | S. komarowii |
| 135 | Stigmastane-3β, 6α-diol 3-O-palmitate | whole plant | S. komarowii |
| 136 | Stigmastane-3β, 6α-diol 3-O-stearate | whole plant | S. komarowii |
| 137 | β-sitosterol | foral buds and whole plant | S. patula, S. komarowii |
| 138 | Daucosterol | whole plant | S. komarowii |
| 139 | β-Amyrin acetate | foral buds | S. patula |
| 140 | Jasminidin | leaves | S. vulgaris |
| 141 | Jasminin | leaves | S. vulgaris |
| 142 | Nortropin | foral buds | S. patula |

could be used to develop effective and less toxic anti-hepatitis B medicines [55].

Aqueous extracts of S. reticulata var. mandshurica significantly decreased the levels of alanine transaminase and aspartate transaminase and the concentration of malondialdehyde in the serum but increased the activity of superoxide dismutase (SOD) in the liver. These extracts showed protective effects on acute liver injury induced by CCl4 in mice [56]. In addition, the essential oils of Syringa exerted protective effects on the liver and cholecyst [39].

Antifungal activity

Phenylpropanoids such as verbascoside (86) and forsythiaside (82) exhibit significant antimicrobial activity [29]. Compounds 93 and 94 at 1- mM concentration inhibited the radial growth of Phytophthora capsici after 6 days of incubation, with inhibition rates 59.1% and 72.5%, respectively [43]. Two sesquiterpenes, guai-9-en-4β-ol (129) and 4, 15-dinorguai-1, 11-dien-9, 10-dione (130), have antibacterial and antifungal properties. Compound 129 was active against Bacillus coagulans [inhibition zone (IZ) = 15.34 mm] and Aspergillus niger (IZ = 13.20 mm) while compound 130 significantly inhibited Escherichia coli (IZ = 15.34 mm) and Fusarium oxysporum (IZ = 15.32 mm) [37].

Compound 3 showed effective antimicrobial activity against Lactobacillus pentosus (IZ = 1 mm), and compound 139 inhibited the growth of Candida species at concentrations of 30–250 μg/mL [5].

Antioxidant activity

A 70% EtOH extract of S. reticulata barks showed potent superoxide anion and DPPH free radical scavenging activities, with EC50 values of 5.88 and 38.10 μg/mL, respectively [10].

Among the compounds isolated from the bark of S. reticulata, six (4, 31, 50, 77, 83, and 111) showed significant superoxide anion scavenging activity, with EC50 values of 2.57, 4.97, 10.64, 15.98, 4.97, and 14.14 μg/mL, respectively. Compound 4 also interacted with the stable free radical DPPH, with an IC50 value of 40.4 μM [8,10]. These different anti-oxidant activities are closely related to their structural features. Presence of 2-(3, 4-dihydroxyphenyl)-ethoxy moiety might be important for a higher activity because the most potent compounds (EC50 = 2.57–4.97 μM), including the two secoiridoid glycosides (31 and 4) and a phenylethanol glycoside (83), possess the same structural features. Comparison of the structures of compounds 4 and 83 with those of 8(Z)-ligstrose (21) and salidroside (89) showed that presence of ortho-coupling hydroxyl group at C-2 might be responsible for their different activities. It has been previously reported that 1, 2-dihydroxybenzene moiety is crucial to its DPPH scavenging activity [10].
Syringaresinol (78) showed a strong scavenging activity against DPPH, with EC$_{50}$ value as low as 12.5 µg/mL, which might be responsible for its strong inhibition of NO production [5].

Eugenol (112) inhibited the catalytic activity of H$_2$O$_2$/Ca$^{2+}$ human erythrocyte membrane lipid peroxidation at a concentration of 200 µmol/L, with an inhibition rate of 62%, and completely suppressed the catalytic activity of dibenzoyl peroxide/Ca$^{2+}$ human erythrocyte membrane lipid peroxidation at a concentration of 100 µmol/L. Compound 112 exerted its effect in a non-competitive manner by reacting with Ca$^{2+}$ and inhibiting the formation of hydroxyl radicals, thus, protecting the cell membrane lipid from oxidation [2].

Inhibition of platelet aggregation

Aqueous extract of S. aramaticum significantly inhibited adenosine diphosphate (ADP) and collagen-induced platelet aggregation, with inhibition rates of 37.4% and 69.7%, respectively [57]. Mandshuricols A (57) and B (58) showed antagonistic activities at platelet-activating factor (PAF) in [3H]PAF receptor binding assay, with IC$_{50}$ values of 4.8 × 10$^{-5}$ and 3.5 × 10$^{-6}$ M, respectively [32].

Others

Essential oils from the stems and roots of S. pinnatifolia var. alashanensis (SPEO) reduced the deviation of ST of leaf extract of S. vulgaris, S. pubescens, S. afghanica, S. reticulata, and S. velutina and barks of S. vulgaris and S. reticulata and low concentrations present in the flowers (S. pubescens), seeds, and seeds crust (S. oblatata). This difference may be associated with their ecological roles, because iridoids are produced mainly to fight predators and/or microbes. Moreover, high concentrations of lignans in the stems and roots can be attributed to the rigidity of these plants. This may be the reason for the absence of iridoids in S. pinnatifolia var. alashanensis because materials used for chemical investigation included peeled stems and roots. Anti-inflammatory effects of extracts from these plants are mainly responsible for their applications in traditional medicine. However, only preliminary work has been performed on most isolated compounds, such as in vitro cytotoxicity screening (1, 2, 78, and 139). Limited studies have been performed on the in vivo effects of these compounds; thus, providing opportunities for further detailed research. It is particularly worthy to mention that China has an abundant resource of Syringa, with many endemic species. For instance, S. pinnatifolia var. alashanensis is a well-known Mongolian medicine traditionally used for myocardial ischemia in clinical practice. However, no substantial evidence is available on its bioactive ingredients and mechanisms of action underlying this effect.

Therefore, it deserves further phytochemical and pharmacological studies.

Review and conclusions

This review describes phytochemical and pharmacological progress on the genus Syringa in the recent 20 years and discusses the future research prospects.

Syringa plants are used not only as traditional medicines to treat rheumatoid arthritis, asthma, cardiopalmus, and angina pectoris by natives in China but also for making ornaments, volatile oils, food additives, and bactericides worldwide, particularly in developing countries. Previous phytochemical studies on crude extracts from various species of this genus have identified iridoids, lignans, phenylpropanoids, and phenylethanoids having antitumor, anti-hypertensive, anti-oxidant, and anti-inflammatory activities. Iridoids, lignans, and phenylethanoids are the most predominant compounds in Syringa plants that probably contribute independently or synergistically to their main biological activities.

To the best of our knowledge, 46 iridoid representatives have been reported in Syringa plants, with high concentrations present in the leaves of S. vulgaris, S. pubescens, S. afghanica, S. reticulata, and S. velutina and barks of S. vulgaris and S. reticulata and low concentrations present in the flowers (S. pubescens), seeds, and seeds crust (S. oblatata). This difference may be associated with their ecological roles, because iridoids are produced mainly to fight predators and/or microbes. Moreover, high concentrations of lignans in the stems and roots can be attributed to the rigidity of these plants. This may be the reason for the absence of iridoids in S. pinnatifolia var. alashanensis because materials used for chemical investigation included peeled stems and roots. Anti-inflammatory effects of extracts from these plants are mainly responsible for their applications in traditional medicine. However, only preliminary work has been performed on most isolated compounds, such as in vitro cytotoxicity screening (1, 2, 78, and 139). Limited studies have been performed on the in vivo effects of these compounds; thus, providing opportunities for further detailed research. It is particularly worthy to mention that China has an abundant resource of Syringa, with many endemic species. For instance, S. pinnatifolia var. alashanensis is a well-known Mongolian medicine traditionally used for myocardial ischemia in clinical practice. However, no substantial evidence is available on its bioactive ingredients and mechanisms of action underlying this effect. Therefore, it deserves further phytochemical and pharmacological studies.
Competing interests
The authors declare that they have no competing interests.

Authors' contributions
SG, CY, LC, GX, and YX have all been involved in preparing this review. SG, TP and CX are responsible for writing, checking and revising the manuscript. All authors read, discussed and approved final version of the manuscript.

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