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## *Polygala sibirica* L. (Polygalaceae): Component Composition and Possibilities of Using

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### Abstract

This review combines and clarifies data from studies which have examined the chemical composition and pharmacological properties of *Polygala sibirica* L. Detailed information on molecular diversity is presented, including selected structural formulas. These include: xanthones, triterpene saponins, new flavonol glycoside compounds, acetophenones, phenolcarboxylic acid derivatives, and other secondary metabolite groups. Data from studies examining the antioxidant, antibacterial, and other types of biological activity of extracts, their fractions, or individual components are also presented. The overall data confirm the possibility of using *P. sibirica* as an additional source of medicinal raw materials.

**Keywords:** *Polygala sibirica* L., xanthone, triterpenoid saponins, chemical constituents, biological activities

### INTRODUCTION

As the largest genus in the Polygalaceae family, *Polygala* L., includes from 470 to 720 species according to various estimates [1]. *Polygala* L. species are common in different areas of the Old and New World, with the exception of New Zealand, but they are unevenly distributed within the general area: more than 400 species grow in America, 206 in Africa, 70 in Asia, 32 in Europe, and 12 in Australia [2]. More than 10 species grow in Russia [3–5]. Species of this genus are perennial grasses, shrubs, and semi-shrubs. They are widespread in forests (tropical, mixed, coniferous), steppes, deserts and semi-deserts, rising in mountainous areas to alpine meadows.

Several species of the genus *Polygala* are used in folk and traditional medicine in Asia and Africa. These include, in particular: *P. senega* L.,

*P. tenuifolia* Willd., and *P. japonica* Houtt. Recently, *P. sibirica* L. has been actively studied chemically and pharmacologically.

*P. sibirica* L. is a perennial plant featuring: top-branched straight woody roots; straight or slightly-branched shortly-appressed hairy stems; up to 20 cm tall; and elliptical, ovate-lanceolate, or lanceolate leaves. Flowers are grouped in thin, one-sided brushes. Bracts are small, green, wings (inner sepals) are large, long or equal to the boat, slightly asymmetric, green along the main vein, whitish to the edge. Corolla are bluish or bluish-violet, lateral petals are shorter than the lower one, thinly and long-fringed boat petal. The fruit is a round, reverse-heart-shaped capsule with narrow-winged edges and a slight notch. It grows on dry limestone rocks, meadows with sandy-stony soil, and clay outcrops. In Russia, *P. sibirica* is found in the European, Caucasus, southern Si-

beria, and Far East regions growing on dry limestone rocks, meadows with sandy-stony soil, or clay outcrops. Outside Russia, this species is distributed in: Europe, the Caucasus and Asia (Western, South and Eastern) [6].

The species closely related to *P. sibirica* are *P. tenuifolia* Willd. and *P. japonica* Houtt. *P. tenuifolia* is distinguished by narrow-linear leaves and bare stems. It grows on dry meadow slopes and river terraces, and it is common in Siberia, the Far East, as well as in China, Mongolia and Korea [7].

*P. japonica*, in contrast to *P. sibirica*, features short inflorescences, no longer than the stems, and slightly leathery, shiny leaves. It is distributed from the south of the Russian Far East and Japan to Malaysia and New Guinea [8]. *P. japonica* is sometimes considered a synonym for *P. sibirica* [9], but many authors consider it an independent species [3, 10–15].

The roots of *P. sibirica*, along with *P. tenuifolia*, are included in the Chinese Pharmacopoeia (2005) sub name Polygalae Radix, that has been used for insomnia, coordination disorders, coughing, and breast tumors [16]. The modern data on pharmacological activity of Polygalae Radix is given in the review by X. Zhao *et al.* [17]. It was shown that Polygalae Radix exhibits an extensive range of pharmacological effects, particularly neuroprotective [18], antidepressant [19], enhancing cognitive function [20], antiarrhythmic [21], preventing cough and eliminating phlegm [22, 23], and other. However, potential toxicities and gastrointestinal side effects of Polygala Radix limit its application [17, 24, 25].

#### COMPONENT COMPOSITION OF POLYGALA SIBIRICA L.

As shown by composition analysis studies, *P. sibirica* accumulates a rich complex of terpenoid and phenolic substances (flavonoids, phenol-carboxylic acid derivatives, and other classes or groups). Among them, xanthenes are the most specific and structurally diverse components of *P. sibirica*. To date, more than 40 established xanthone structures have been found (Table 1).

Thus, new compounds found in *P. sibirica* roots, sibiricaxanthenes A **34** and B **35**, were new glycosides of 1,3,7-trihydroxyxanthone **2** [33]. Later, Y. H. Zhou *et al.* isolated five more compounds: sibiricaxanthenes C–G **38–42** [32]. In specific sibiricaxanthenes (C, D, F, G), glycosylation occurs at the C-6 position; in sibiricaxanthone E **40**, it occurs at the C-7 position. It should be

noted that sibiricaxanthone E **40** has methylenedioxy groups (rare for *P. sibirica* xanthenes) at the C-2 and C-3 positions. The same group is found only in two compounds: 1,6-dihydroxy-2,3-methylenedioxy-7,8-dimethoxyxanthone **12** and 1,7-dihydroxy-2,3-methylenedioxyxanthone **5** [26].

Some *P. sibirica* xanthenes have turned out to be biologically active substances. For example, 1,5-dihydroxy-6,7-dimethoxyxanthone **37** and 1,7-dihydroxyxanthone **1** showed antioxidant and antibacterial activity ( $IC_{50} = 12$  mg/L and  $IC_{50} = 13$  mg/L, respectively). Activity against *Staphylococcus aureus* has been noted for 1,7-dihydroxy-5,6-dimethoxyxanthone **6** (MIC = 217  $\mu$ M/L) [27].

A number of flavonoids have been isolated from the aerial portions of *P. sibirica*: kaempferol, rhamnetin, amentoflavone, linarin, ermanine, ombuin and rhamnocitrin. The latter three are found in extracts both in free and glycosylated (at the C-3 position) form [34, 35]. The main carbohydrate fragments of flavonoid aglycones are  $\beta$ -D-glucose and  $\beta$ -D-galactose. In the roots of *P. sibirica*, two flavonoid glycosides have been found: 5,3'-dihydroxy-7,4'-dimethoxyflavone-3-O- $\beta$ -D-glucopyranoside and rhamnetin-3-O- $\beta$ -D-glucopyranoside [28].

Six flavonoid glycosides have been found in ethanol extracts of aerial part of *P. sibirica*: polygalin A **43**, and polygalins C–G **45–49** [35]. Polygalins B–D **44–46** were present in ethanol extract of *P. sibirica* var. *megalopha* [36]. This variety differs from typical examples slightly leathery leaves, clear lateral veins rising from the axis, and relatively large appendages. *P. sibirica* var. *megalopha* is endemic to the Sichuan and Yunnan provinces in China; it grows on grassy slopes, hills, and in rare forests at an altitude of 1800–2600 m h. m. [13]. Polygalins as a group of compounds were found for the first time in *P. japonica* Houtt. [37]; they are flavones with hydroxyl and methyl groups at the 3' and 4' positions. They also differ in carbohydrate moiety structure, which is present at the 3rd carbon atom. The carbohydrate fragments of polygalins are represented by glucose, apiose, and galactose in various combinations (Fig. 1).

Later, from ethanol extracts of *P. sibirica* var. *megalopha*, two new flavonol glycosides were isolated: polygalin H **50**, and polygalin I **51** [38]. Both compounds have a hydroxymethyl group at the C-6 position, described for the first time in flavonoids of this type. Based on biosynthetic

TABLE 1

Xanthenes from *P. sibirica*.

Compound	Name	Structure	Part of plant	Reference
1	*1,7-Dihydroxyxanthone	$R_1 = R_2 = R_3 = R_4 = H$	Roots, aerial part	[26, 27]
2	*1,3,7-Trihydroxyxanthone	$R_1 = R_3 = R_4 = H$ $R_2 = OH$	Roots	[27]
3	1,3,7-Trihydroxy-2-methoxyxanthone	$R_1 = CH_3$ $R_2 = OH$ $R_3 = R_4 = H$	Roots, aerial part	[28, 29]
4	*1,7-Dihydroxy-2,3-dimethoxyxanthone	$R_1 = R_2 = CH_3$ $R_3 = R_4 = H$	Roots, aerial part	[26, 27, 29]
5	1,7-Dihydroxy-2,3-methylenedioxyxanthone	$R_1 = R_2 = CH_2OH$ $R_3 = R_4 = H$	Aerial part	[29]
6	*1,7-Dihydroxy-5,6-dimethoxyxanthone	$R_1 = R_2 = H$ $R_3 = R_4 = CH_3$	Roots, aerial part	[26, 27]
7	*1,3,6-Trihydroxy-2,7-dimethoxyxanthone (onjixanthone II)	$R_1 = R_4 = CH_3$ $R_2 = OH$ $R_3 = R_5 = H$	Roots, aerial part	[26–28]
8	*1,3,6-Trihydroxy-2,7,8-trimethoxyxanthone	$R_1 = R_4 = R_5 = CH_3$ $R_2 = OH$ $R_3 = H$	Aerial part	[26]
9	1,6,7-Trihydroxy-2,3-dimethoxyxanthone	$R_1 = R_2 = CH_3$ $R_3 = R_5 = H$ $R_4 = OH$	Aerial part	[29]
10	*1,6-Dihydroxy-5,7-dimethoxyxanthone	$R_1 = R_2 = R_5 = H$ $R_3 = R_4 = CH_3$	Roots	[27]
11	*1,6-Dihydroxy-3,5,7,8-tetramethoxyxanthone	$R_1 = H$ $R_2 = R_3 = R_4 = R_5 = CH_3$	Roots	[27]
12	*1,6-Dihydroxy-2,3-methylenedioxy-7,8-dimethoxyxanthone	$R_1 = R_2 = CH_2OH$ $R_3 = H$ $R_4 = R_5 = CH_3$	Roots	[27]
13	*3-Hydroxy-1,2,8-trimethoxyxanthone	$R_1 = R_2 = H$ $R_3 = CH_3$	Roots	[27]
14	*3-Hydroxy-1,2,7-trimethoxyxanthone	$R_1 = R_3 = H$ $R_2 = CH_3$	Aerial part	[30]
15	*3,6-Dihydroxy-1,2,7,8-tetramethoxyxanthone	$R_1 = OH$ $R_2 = R_3 = CH_3$	Roots	[27]

Table 1 (Continuation)

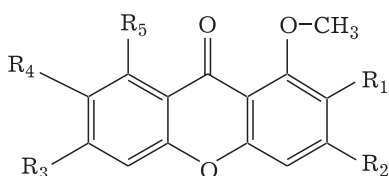
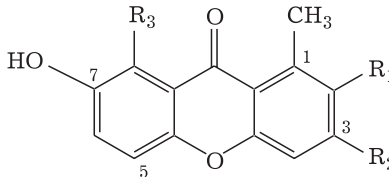
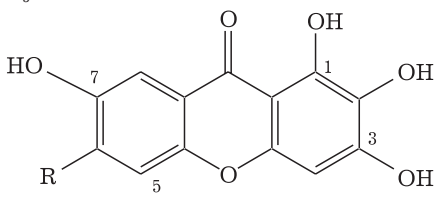
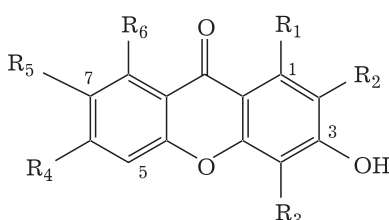
Compound	Name	Structure	Part of plant	Reference
16	*3-Hydroxy-1,2,6,7,8-pentamethoxyxanthone	$R_1 = R_2 = R_3 = \text{CH}_3$ 	Aerial part	[26]
17	*6-Hydroxy-1,7-dimethoxyxanthone	$R_1 = R_2 = R_5 = \text{H}$ $R_3 = \text{OH}$ $R_4 = \text{CH}_3$	Roots, aerial part	[26, 27]
18	6-Hydroxy-1,2,3,7-tetramethoxyxanthone	$R_1 = R_2 = R_4 = \text{CH}_3$ $R_3 = \text{OH}$ $R_5 = \text{H}$	Roots, aerial part	[28, 29, 31]
19	*6,8-Dihydroxy-1,2,3-trimethoxyxanthone	$R_1 = R_2 = \text{CH}_3$ $R_3 = R_4 = \text{H}$ $R_5 = \text{OH}$	Roots, aerial part	[26, 27]
20	*6-O-β-D-Glucopyranosyl-1,7-dimethoxyxanthone	$R_1 = R_2 = R_5 = \text{H}$ $R_3 = \text{O-Glc}$ $R_4 = \text{O-CH}_3$ 	Aerial part	[26]
21	*7-Hydroxy-1-methoxyxanthone	$R_1 = R_2 = R_3 = \text{H}$	Roots	[27]
22	*3,7-Dihydroxy-1,2-dimethoxyxanthone	$R_1 = \text{CH}_3$ $R_2 = \text{OH}$ $R_3 = \text{H}$	Roots	[27]
23	*3,7-Dihydroxy-1,2,8-trimethoxyxanthone	$R_1 = R_3 = \text{CH}_3$ $R_2 = \text{OH}$	Roots	[27]
24	7-Hydroxy-1,2,3-trimethoxyxanthone	$R_1 = R_2 = \text{CH}_3$ $R_3 = \text{H}$ 	Roots	[31]
25	*1,2,3,7-Tetramethoxyxanthone	$R = \text{H}$	Roots, aerial part	[26, 27]
26	1,2,3,6,7-Pentamethoxyxanthone	$R = \text{OH}$	Roots, aerial part	[28, 29]
27	6-(β-D-Glucopyranosyl)-1,2,3,7-tetramethoxyxanthone (polygalaxanthone VI)	$R = \text{Glc}$	Roots	[32]
28	*3,8-Dihydroxy-1,2,4-trimethoxyxanthone	$R_1 = R_2 = R_3 = \text{CH}_3$ $R_4 = R_5 = \text{H}$ $R_6 = \text{OH}$ 	Roots, aerial part	[26, 27]

Table 1 (Continuation)

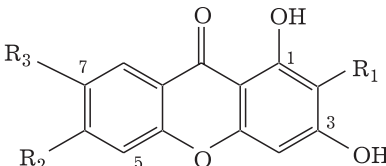
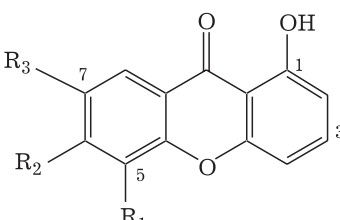
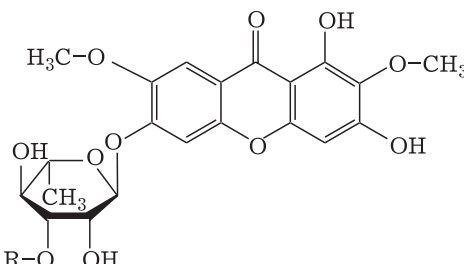
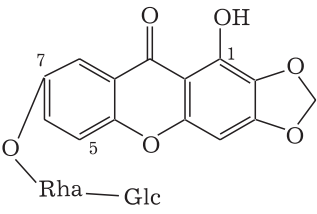
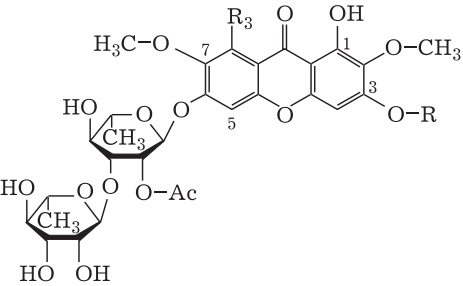
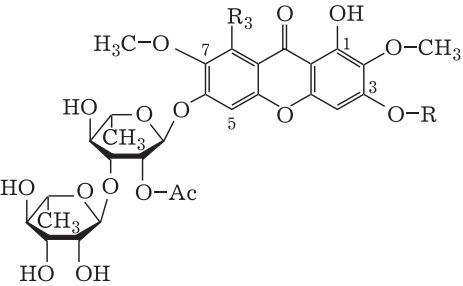
Compound	Name	Structure	Part of plant	Reference
29	4-O- $\beta$ -D-Glucopyranosyl-1,3,7-trihydroxyxanthone (lancerin)	R <sub>1</sub> = R <sub>5</sub> = OH R <sub>2</sub> = R <sub>4</sub> = R <sub>6</sub> = H R <sub>3</sub> = O-Glc	Roots	[28, 33]
30	4-O- $\beta$ -D-Glucopyranosyl-1,3,6-trihydroxy-7-methoxyxanthone	R <sub>1</sub> = R <sub>4</sub> = OH R <sub>2</sub> = R <sub>6</sub> = H R <sub>3</sub> = O-Glc R <sub>5</sub> = CH <sub>3</sub>	Roots	[32]
31	4-C-[ $\beta$ -D-Apiofuranosyl-(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranosyl]-1,3,6-trihydroxy-7-methoxyxanthone (polygalaxanthone III)	R <sub>1</sub> = R <sub>4</sub> = OH R <sub>2</sub> = R <sub>6</sub> = H R <sub>3</sub> = Api-Glc R <sub>5</sub> = CH <sub>3</sub>	Roots	[32, 33]
				
32	2- $\beta$ -D-Glucopyranosyl-1,3,6,7-tetrahydroxyxanthone (mangiferin)	R <sub>1</sub> = Glc R <sub>2</sub> = R <sub>3</sub> = OH	Roots	[32]
33	7-O-Methylmangiferin	R <sub>1</sub> = Glc R <sub>2</sub> = OH R <sub>3</sub> = CH <sub>3</sub>	Roots	[32]
34	2-C-[ $\beta$ -D-Apiofuranosyl-(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranosyl]-1,3,7-trihydroxyxanthone (sibircaxanthone A)	R <sub>1</sub> = Api-Glc R <sub>2</sub> = H R <sub>3</sub> = OH	Roots	[33]
35	2-C-[ $\beta$ -D-Apiofuranosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranosyl]-1,3,7-trihydroxyxanthone (sibircaxanthone B)	R <sub>1</sub> = Api-Glc R <sub>2</sub> = H R <sub>3</sub> = OH	Roots	[32, 33]
				
36	*7-O- $\beta$ -D-Glucopyranosyl-1-hydroxyxanthone	R <sub>1</sub> = R <sub>2</sub> = H R <sub>3</sub> = O-Glc	Aerial part	[26]
37	*1,5-Dihydroxy-6,7-dimethoxyxanthone	R <sub>1</sub> = OH R <sub>2</sub> = R <sub>3</sub> = O-CH <sub>3</sub>	Roots, aerial part	[26, 27]
				
38	6-O-[ $\alpha$ -L-Rhamnopyranosyl-1,3-dihydroxy-2,7-dimethoxyxanthone (sibircaxanthone C)	R = H	Roots	[32]
39	6-O-[ $\alpha$ -L-Rhamnopyranosyl-(1 $\rightarrow$ 3)- $\alpha$ -L-rhamnopyranosyl]-1,3-dihydroxy-2,7-dimethoxyxanthone (sibircaxanthone D)	R = Rha	Roots	[32]

Table 1 (Ending)

Compound	Name	Structure	Part of plant	Reference
40	7-O-[ $\alpha$ -L-Rhamnopyranosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranosyl]-1-hydroxy-2,3-methylenedioxyxanthone (sibiricaxanthone E)		Roots	[32]
41	6-O-[ $\alpha$ -L-Rhamnopyranosyl-(1 $\rightarrow$ 3)-2-O-acetyl- $\alpha$ -L-rhamnopyranosyl]-1,7-dihydroxy-2,7-dimethoxyxanthone (sibiricaxanthone F)	R = H 	Roots, aerial part	[32, 34]
42	3-O- $\beta$ -D-Glucopyranosyl-6-O-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 3)-2-O-acetyl- $\alpha$ -L-rhamnopyranosyl]-1-hydroxy-2,7-dimethoxyxanthone (sibiricaxanthone G)	R = Glc 	Roots	[32]

\* Information is applied to *P. sibirica* var. *megalopha* Fr.

pathways, it has been hypothesized that polygalin H **50** is derived from polygalin C **45**, previously found in extracts of *P. sibirica* var. *megalopha* [38].

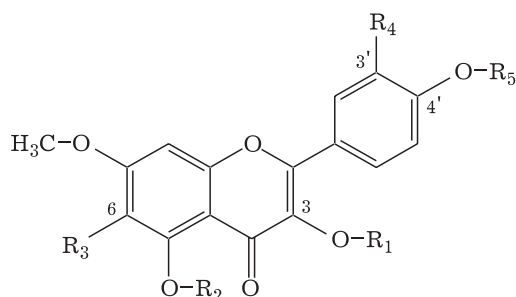
Polygalins D **46**, H **50**, and I **51** showed high inhibitory activity against xanthine oxidase ( $IC_{50} = 16.00 \mu\text{M}$ ,  $IC_{50} = 9.48 \mu\text{M}$ ,  $IC_{50} = 8.31 \mu\text{M}$ , respectively) [38].

In a recent study of *P. sibirica* var. *megalopha*, isolation of 4-hydroxy-3,5-dimethoxyacetophenone was reported [39]. Earlier, acetophenones were found in methanol extracts of the roots of *P. sibirica*: acetophenone glycoside (4'-O-[ $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranosyl]-aceto-

phenone). This turned out to be a new compound and was named sibiricaphenone [33].

Another new compound, first isolated from the roots of *P. sibirica*, is a benzophenone glucoside named sibiriphenone A, the structure of which was established as 2,4,6,4'-tetrahydroxy-3'-methoxybenzophenone-6-O- $\beta$ -D-glucopyranoside [28]. Later, another benzophenone glucoside from the aerial part of *P. sibirica* var. *megalopha* was isolated subname 2,6-dimethoxybenzophenone-4-O- $\beta$ -D-apiofuranosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranoside [40].

The group of phenolcarboxylic acid derivatives found in *P. sibirica* currently includes more



- 43 Polygalin A:  $R_1 = \text{Gal}$ ;  $R_2 = R_3 = R_4 = \text{H}$ ;  $R_5 = \text{CH}_3$   
 44 Polygalin B:  $R_1 = \text{Api-Gal}$ ;  $R_2 = R_3 = R_4 = \text{H}$ ;  $R_5 = \text{CH}_3$   
 45 Polygalin C:  $R_1 = \text{Gal-Api}$ ;  $R_2 = R_3 = \text{H}$ ;  $R_4 = \text{OH}$ ;  $R_5 = \text{CH}_3$   
 46 Polygalin D:  $R_1 = \text{Glc-Api}$ ;  $R_2 = R_3 = \text{H}$ ;  $R_4 = \text{OH}$ ;  $R_5 = \text{CH}_3$   
 47 Polygalin E:  $R_1 = \text{Glc-Api}$ ;  $R_2 = R_3 = R_5 = \text{H}$ ;  $R_4 = \text{OH}$   
 48 Polygalin F:  $R_1 = \text{Gal-Api}$ ;  $R_2 = R_3 = R_5 = \text{H}$ ;  $R_4 = \text{OH}$   
 49 Polygalin G:  $R_1 = \text{Gal}$ ;  $R_2 = R_3 = R_5 = \text{H}$ ;  $R_4 = \text{OH}$   
 50 Polygalin H:  $R_1 = \text{Api-Gal}$ ;  $R_2 = \text{CH}_3$ ;  $R_3 = \text{CH}_2\text{OH}$ ;  $R_4 = \text{OH}$ ;  $R_5 = \text{CH}_3$   
 51 Polygalin I:  $R_1 = \text{Api-Gal}$ ;  $R_2 = \text{CH}_3$ ;  $R_3 = \text{CH}_2\text{OH}$ ;  $R_4 = \text{H}$ ;  $R_5 = \text{CH}_3$

Fig. 1. Structures of polygalins A-I from *Polygala sibirica* L.

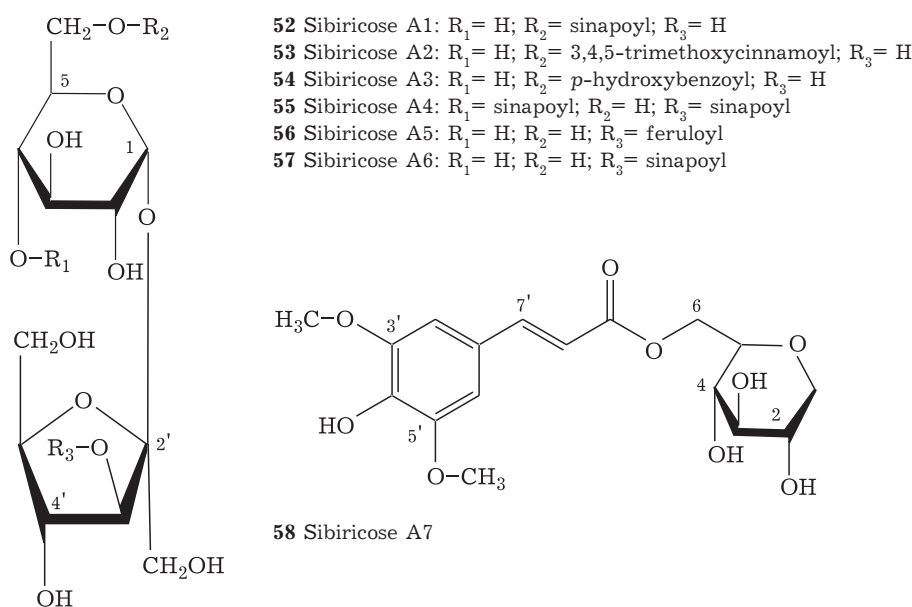
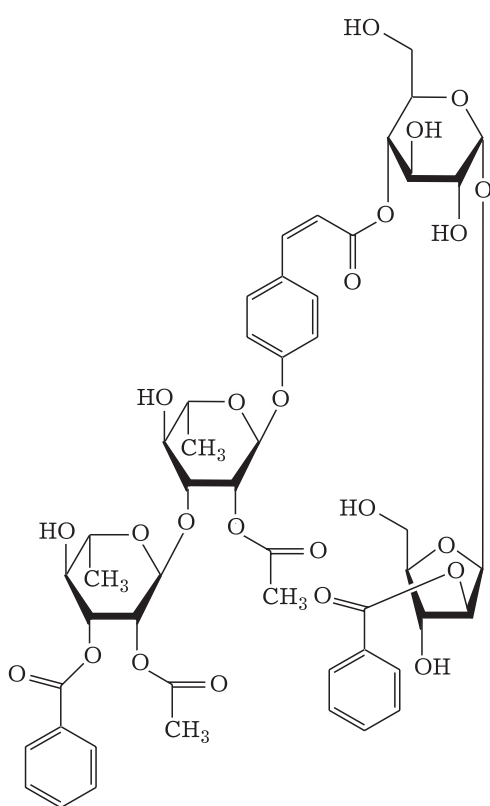


Fig. 2. Structures of sibiricoses A1–A7 from *Polygala sibirica*.



**59** Polygalasibiricoside I

Fig. 3. Polygalasibiricoside I from *Polygala sibirica*.

than 20 compounds, some of which have not been previously characterized. Seven new compounds were isolated from *P. sibirica* roots, which were named sibiricoside A1–A7 **52–58** (Fig. 2) [28, 33].

Other known compounds include: 3,6'-synapoyl sucrose, 6,3'-synapoyl sucrose, glomeratose A, cantoside A, 1-O-L-arabinopyranosyl-O-(6→1)-β-D-glucopyranosyl salicylate, and 3'-O-3,4,5-trimethoxycinnamoyl-6-O-4-methoxybenzoyl sucrose [30, 34].

*P. sibirica* roots contain 6-O-benzoyl-polygalathosyl-(2→1)-α-galactose, 4-O-benzoyl-polygalathosyl-(2→1)-α-galactose, and 4-O-β-apiosyl-(1→2)-glucoside of sinapoyl alcohol. These are termed polygalatenoside A, C, and E, respectively [28, 30]. The presence of tenuifolisides A, B, and C in the roots of *P. sibirica* has also been confirmed [28, 31, 34, 41]. It should be noted that tenuifoliside A, in addition to roots, was also found in the aerial part of *P. sibirica* and *P. sibirica* L. var. *megalopha* [34, 40]. In 2012, Y. L. Song *et al.* published a number of articles presenting findings from analysis of aerial part of *P. sibirica*. The authors isolated and characterized polygalasibiricoside I **59** (Fig. 3), as well as 2,4,4-trimethyl-3-formyl-6-hydroxy-2,5-cyclohexadien-1-one and 2-hydroxy-4,4,6-trimethylcyclohexa-2,5-dien-1-one, better known as lanierone [34, 42].

The chemical composition of aerial part *P. sibirica* L. var. *megalopha* has been studied in detail, with isolation of a number of compounds: 3,6'-disapoylsucrose; 3'-*E*-3,4,5-trimethoxycinnamoyl-6-benzoylsucrose, 3'-*E*-3,4,5-trimethoxycinnamoyl-4-benzoylsucrose, evofoline A, 3,4,5-trimethoxycinnamic acid and its methyl ester, salicylic acid and *trans*-sinapic acid methyl ester, sinapyl alcohol 4-O-β-D-apiofuranosyl-(1→2)-β-D-glucopyrano-

side and syringaldehyde [40, 41], as well as the flavonoid 5-hydroxy-4',6,7-trimethoxyflavone [39, 40].

Triterpene saponins are another important group of secondary metabolites among the species of the genus *Polygala*. Among these, more than 100 triterpene saponins alone have been isolated [43].

Study of triterpene saponins specifically from *P. sibirica* began relatively recently, as numerous earlier studies (on chemical composition and biological activity) used *Polygala radix*, a generic

name for raw material combining *P. sibirica* and *P. tenuifolia* [44]. It was found that triterpene saponins are synthesized in cells of the parenchyma of vegetative organs, and the secondary phloem and phelloderm of the root are their main depositories. The quantitative composition of triterpene saponins varies, depending on developmental stage, and their highest content has been recorded from April to May [45, 46]. Triterpene saponins isolated from *P. sibirica* are presented in Table 2.

TABLE 2

Triterpenoid saponins from *P. sibirica*.

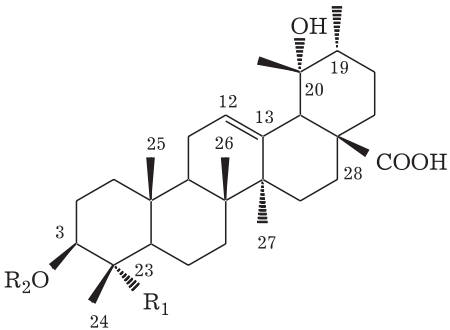
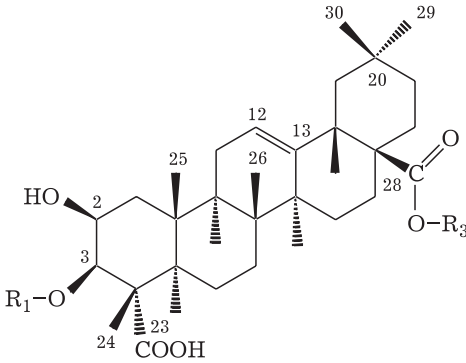
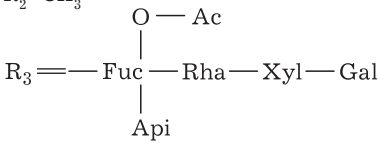
Compound	Name	Structure	Reference
			
60	3β,19α-Dihydroxyurso-12-ene-23,28-dioic acid 3-O-β-D-glucopyranoside (sibiricasaponin A)	R <sub>1</sub> = COOH R <sub>2</sub> = Glc	[47]
61	Pomolic acid 3-O-(3-O-sulfo)-α-L-arabinopyranoside (sibiricasaponin B)	R <sub>1</sub> = H R <sub>2</sub> = (3-O-sulfo)-Ara	[47]
62	Pomolic acid 3-O-(4-O-sulfo)-β-D-xylopyranoside (sibiricasaponin C)	R <sub>1</sub> = H R <sub>2</sub> = (4-O-sulfo)-Xyl	[47]
63	Pomolic acid 3-O-(2-O-acetyl-3-O-sulfo)-α-L-arabinopyranoside (sibiricasaponin D)	R <sub>1</sub> = H R <sub>2</sub> = (2-O-acetyl-3-O-sulfo)-Ara	[47]
			
64	27-Hydroxy-2,3-isopropylidenedioxy-olean-12-ene-23,28-dioic acid (presenegenin)	R <sub>1</sub> = H R <sub>2</sub> = CH <sub>2</sub> OH R <sub>3</sub> = H	[28]
65	(2β,3β)-3-(β-D-Glucopyranosyloxy)-2,27-dihydroxyolean-12-ene-23,28-dioic acid (tenuifolin)	R <sub>1</sub> = Glc R <sub>2</sub> = CH <sub>2</sub> OH R <sub>3</sub> = H	[28, 47]
66	3-O-β-D-Glucopyranosyl-medicagenic acid 28-O-β-D-galactopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)-(4-O-acetyl)-[β-D-apiofuranosyl-(1→3)]-β-D-fucopyranosyl ester (sibiricasaponin E)	R <sub>1</sub> = Glc R <sub>2</sub> = CH <sub>3</sub> R <sub>3</sub> = 	[47]



Table 2 (Ending)

Compound	Name	Structure	Reference
67	3-O-β-D-Glucopyranosyl-presenegenin-28-O-α-L-rhamnopyranosyl-(1→2)-β-D-fucopyranosyl ester (polygalasaponin XLVIII)	R <sub>1</sub> = Glc R <sub>2</sub> = CH <sub>2</sub> OH R <sub>3</sub> = Rha-Fuc	[47]
68	3-O-β-D-Glucopyranosyl-presenegenin-28-O-β-D-xylopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)-β-D-fucopyranosyl ester (polygalasaponin XXVIII)	R <sub>1</sub> = Glc R <sub>2</sub> = CH <sub>2</sub> OH R <sub>3</sub> = Xyl-Rha-Fuc	[31, 47]
69	3-O-β-D-Glucopyranosyl-presenegenin-28-O-β-D-xylopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)-(4-O-acetyl)-β-D-fucopyranosyl ester (polygalasaponin XXXIII)	R <sub>1</sub> = R <sub>3</sub> = R <sub>5</sub> = H R <sub>2</sub> = Ac R <sub>4</sub> = OH	[47]
70	3-O-β-D-Glucopyranosyl-presenegenin-28-O-β-D-galactopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)-(3,4-di-O-acetyl)-β-D-fucopyranosyl ester (polygalasaponin XXXV)	R <sub>1</sub> = R <sub>2</sub> = Ac R <sub>3</sub> = H R <sub>4</sub> = OH R <sub>5</sub> = Gal	[47]
71	3-O-β-D-Glucopyranosyl-presenegenin-28-O-β-D-galactopyranosyl-(1→4)-β-D-xylopyranosyl-(1→4)-[5-O-acetyl]-β-D-apiofuranosyl-(1→3)]-α-L-rhamnopyranosyl-(1→2)-(3,4-di-O-acetyl)-β-D-fucopyranosyl ester (polygalasaponin XXXVI)	R <sub>1</sub> = R <sub>2</sub> = Ac R <sub>3</sub> = Api-Ac R <sub>4</sub> = OH R <sub>5</sub> = Gal	[47]
72	3-O-β-D-glucopyranosyl-presenegenin-28-O-β-D-xylopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)-(3,4-di-O-acetyl)-β-D-fucopyranosyl ester (arilloside A)	R <sub>1</sub> = R <sub>2</sub> = Ac R <sub>3</sub> = R <sub>5</sub> = H R <sub>4</sub> = OH	[47]
73	3-O-β-D-Glucopyranosyl-presenegenin-28-O-β-D-xylopyranosyl-(1→3)-β-D-xylopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)-β-D-fucopyranoside (arilloside B)	R <sub>1</sub> = R <sub>2</sub> = R <sub>5</sub> = H R <sub>3</sub> = OH R <sub>4</sub> = Xyl	[31]
74	12-(Chloromethyl)-2,3-dihydroxy-27-norolean-13-ene-23,28-dioic acid (senegenin, tenuigenin)		[47]

Aglycones of *P. sibirica* saponins are diverse, but they are frequently represented by presenegenin **64** and medicagenic acid, which are characteristic almost of other *Polygala* species. The main carbohydrates are  $\beta$ -D-glucose,  $\alpha$ -L-arabinose,  $\beta$ -D-xylose,  $\beta$ -D-apiose,  $\beta$ -D-fucose, etc., in various combinations. Glycosidic residues are most often located at the 3rd and 28th carbon atoms.

Presenegenin **64** and its 3-glucoside tenuifolin **65**, found both in the roots and in the aerial part of *P. sibirica*, are chemotaxonomic markers and major components of saponins in the genus *Polygala* [48]. For example, tenuifolin **65** content in *P. tenuifolia* root is at least 2 % of dry weight [49]. In 2013, Y. L. Song *et al.* published results of preliminary testing of *P. sibirica* triterpene saponins on PC12 cells (rat pheochromocytoma): only tenuifolin showed an anti-ischemic effect, while other triterpene saponins did not show even moderate activity [35].

Of interest is also senegenin (tenuigenin) **74**, which contains a chlorine atom [50]. Senegenin is known for: ability to suppress hypoxia-induced apoptosis of neurons [51]; therapeutic potential against sepsis [52], as well as neurotrophic, neuroprotective, and neurogenerative effects [53, 54].

The group of compounds designated sibiricasaponin A–E **60–63, 66** was first isolated from ethanol extracts of aerial part *P. sibirica* [47]. Glycosides quite rare for *Polygala* aglycones are: 3 $\beta$ ,19 $\alpha$ -dihydroxyurso-12-ene-23,28-dione and pomolic acid. A notable feature is also sulfation in the C-3 position of arabinose, featured in sibiricasaponins B–D **60–62**. So far, sibiricasaponins have only been found in *P. sibirica*. Of the previously known saponins with pomolic acid as an aglycone, zigu-glycosides I and II were found in extracts of the aerial part and roots of *P. sibirica* [31, 34].

Several known lignans have been isolated from *P. sibirica* var. *megalopha*, namely: syringaresinol, (+)-medioresinol and pinioresinol [39]. The presence of squalene was identified among terpenoids by column chromatography of (aerial) *P. sibirica* extracts [29]. In *P. sibirica* var. *megalopha*, a new megastigmane glycoside was characterized as (6R,7E,9R)-9,13-dihydroxy-4,7-megastigmadiene-3-one-9-O- $[\beta$ -D-apiofuranosyl-(1 $\rightarrow$ 6)]- $\beta$ -D-glucopyranoside which inhibits the activity of xanthine oxidase ( $IC_{50} = 6.48 \mu M$ ) [40].

Steroids of *P. sibirica* are mainly represented by compounds widespread in the plant world:  $\alpha$ -spinasterol and its 3-O- $\beta$ -D-glucoside and  $\beta$ -sitosterol [29, 31]. In 2012, however, Y. L. Song *et al.* isolated a new steroid (polygalasterol A)

from a methanol extract of aerial part *P. sibirica*, namely: (24R)-24-sulfo-5 $\alpha$ -cholestan-3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ ,24-tetrol [42].

Among nitrogen-containing compounds in *P. sibirica*, a well-known nitrogen-containing glycolipid of aralium cerebroside was found: 1-O- $\beta$ -D-glucopyranosyl-(2S,3S,4R,8E)-2-[(2'R-2'-hydroxypalmitoylamino]-8-octadecene-1,3,4-triol [35].

## CONCLUSION

Thus, *P. sibirica* can be classified as a species with a diverse set of low molecular weight substances, many of which may have valuable therapeutic properties. In this regard, *P. sibirica* merits further pharmacological and chemical research, analogous to the detailed studies of *P. tenuifolia* and *P. japonica*, as an additional source of medicinal raw materials.

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