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Bistorta Scop. Genus (Polygonaceae): Chemical Composition and Biological Activity

M. S. VORONKOVA and G. I. VYSOCHINA

Central Siberian Botanical Garden, Siberian Branch of the Russian Academy of Sciences, Ul. Zolotodolinskaya 101, Novosibirsk 630090 (Russia)

E-mail: bmc_87@mail.ru

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Abstract

A review of the data on the chemical composition and biological activity of species of the genus *Bistorta* Scop. of the world flora was carried out. It was shown that species of the genus *Bistorta* were of interest as the source of raw materials containing valuable biologically active compounds – phenolcarbonic acids, flavonoids, triterpenoids, and steroids.

Key words: *Bistorta* Scop., phenolcarbonic acids, flavonoids, triterpenoids, steroids, biological activity

INTRODUCTION

The genus *Bistorta* Scop. (Bistort) is represented by perennial meadow and meadow-swamp plants with a thick snake-like-curved rhizome. It includes around 50 kinds in countries of the Northern Hemisphere, mainly in mountain areas [1]. On the territory of Russia and neighbouring countries, 12 species of the genus *Bistorta* grow, six in Siberia, two of them are *Bistrorta officinalis* Delarbre and *Bistorts vivipara* (L.) Delarbre are widely spread in the Northern Hemisphere [2, 3]. They are used as decorative, nutritive, fodder and melliferous plants [4].

The goal of the present work is the review of published materials on the composition and biological activity of secondary metabolites of species of the genus *Bistorta* Scop. of the world flora.

COMPONENT COMPOSITION AND BIOLOGICAL ACTIVITY

BISTORTA OFFICINALIS

The chemical composition of species of this genus sort is poorly studied, along with that, most of the studies is devoted to the two species mentioned. A short review on photochemistry and pharmacology of *Polygonum bistorta* L. was published [5].

Scientific medicine recognizes the only species of the genus, viz, *B. officinalis* Delabre (=*Bistorta major* S. F. Gray, *Polygonum bistorta* L.), snakeweed medicinal, snakeweed big, serpent grass, bistort. This is a perennial herbaceous plant with a spicate inflorescence of the height up to 100 cm. Perianth is pale or bright pink. Lower leaves oblong-ovate or broadly lanceolate, decurrent to petiole at the base, acuminate to the apex. A rhizome is thick, ligneous, curved. *B. officinalis* is a typically mesophilic plant. It occurs on forest, flooded and a watershed meadow, forest edges and thickets, is raised into the subalpine zone. It has extensive area, covering almost the entire territory of Eurasia [6].

Rhizomes of *B. officinalis* are used as an astringent for intestinal disorders, inflammation of the mucous membranes, dysentery. This is a good substituent of a root of tropical rhatany [7]. From the underground part of plants the tannin-containing Bistalbin preparation was

obtained [8]. It is the underground part of plants that is most thoroughly researched. The content of tannin (hydrolysable) substances in the rhizomes varies from 8.3 to 36 % [9]. Catechins of rhizomes are represented by (+)-catechin, (−)-catechin, (−)-epicatechin, (+)-catechin 7-O-β-*D*-glucopyranoside, (+)-catechin 5-O-β-*D*-glucopyranoside, (−)-epicatechin 5-O-β-*D*-glucopyranoside [10−12]. Out of 10 kg of dried roots of *P. bistort*a 15 mg of phenylpropanoid-substituted catechin is isolated; its structure is proven by NMR spectroscopy [13].

There are data in the literature regarding the composition and content of phenolcarbonic acids and their derivatives in various parts of *P. bistorta.* A rhizome contains caffeic, protocatechuic, gallic, ellagic, 2,6-dihydroxybenzoic, 3,4-dihydroxybenzoic, chlorogenic acids, 6-galloyl glucose and 3,6-digalloyl glucose, in leaves, there are protocatechuic, caffeic, chlorogenic, sinapic acids; for plants, as a whole, caffeic and ferrulic acids [11, 12, 14−20] were indicated. In chloroform extract of *P. bistorta* and plants of some other species of the genus *Polygonum* L., by the chromatographic-mass spectrometric method, 4-hydroxybenzoic, 4-hydroxy-3-methoxybenzoic, 4-hydroxy-3-methoxycinamic, 4-hydroxycinamic, 3,4-dihydroxycinamic acids and their methyl esters [17] were found. According to [18], in the overground part of *P. bistorta*, there are 53.3 μg/g of acids, in a rhizome, 14.1 μg/g; ferrulic acid (21.0 μg/g) prevails. Out of organic acids, succinic acid [21] was found.

A new compound, named bistortaside A (4-O-β-*D*-(6′-O-3″-3-methylgalloyl)-glucopyranoside-3-methylgallic acid), related to tannin and the known compound 3-O-β-*D*- glucopyranoside quercetin were isolated from rhizomes of *Polygonum bistorta* L. [22] (Fig. 1).

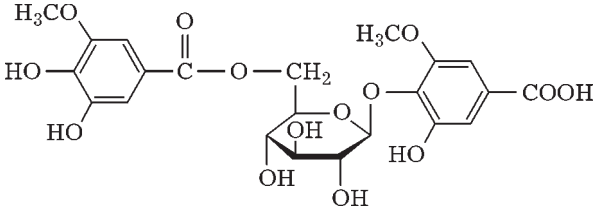


Fig. 1. Bistortaside A − 4-O-β-*D*-(6′-O-3″-methylgalloyl)-glucopyranoside-3-methylgallic acid).

The author of [23] identified in the rhizome of *P. bistorta* flavonol glycosides: rutin, hyperine, isoquercitrin, luteolin-7-O-glucoside, luteoline-8-C-glucoside (orientin), apigenine-6-C-glucoside (isovitexin). From rhizomes of China plants of this species, two previously unknown flavonols, viz, 2,3′,4′,4,6-pentahydroxyflanone and 2,5,6-trhydroxy-4,2′-dimethoxyflanone that possess the coagulant action, were isolated. In this regard, the underground part of plants can be used in medicine and pharmacy as a nontoxic natural source of coagulants [24].

Besides, in a rhizome, triterpenoids of cycloartan series were found: 24(*E*)-ethylidenecycloartanone and 24(*E*)-ethylidenecycloartan-3-α-ol and previously known cycloartane-3,2,4-dione, 24-methylenecycloartanone, frideline, 3-β-fridelinol, fridelane, as well as steroids: 5-glutinene-3-one, γ-citosterine, β-citosterine and stigmast-5-ene-3-one. Frideline and stigmast-5-ene-3-one are identified for *P. bistorta* for the first time [25, 26]. From the underground organs, seven compounds including triterpenoids, coumarin and steroid [27], as well as per stilbene (3,5-methoxy-2-hydroxy-*E*-stilben [28] were isolated.

Coumarins were found in the underground organs and aboveground part of plants: umbelliferone in all organs, scopoletin, in rhizome only [29−31].

Flavonoids are one the major groups of compounds of the complex of phenol compounds of the overground part of *P. bistorta.* They are mainly represented by flavonols. During mass flowering, the peak of the accumulation of flavonols is observed, herewith, their content varies in the limits of 1.1−5.6 % (in the flowers) and 0.7−5.1 % (in leaves). Plants growing in Gorny Altai under conditions of the elevated insolation on the height of 1500−2000 m above the sea level and higher contain flavonoids in a greater amount than plants of meadow communities of the plains [32]. According to the data of authors of [29], the content of flavonoids in leaves of *P. bistorta* in the early period of the fruit-formation of plants is 7.8 %, in the stem 6.5 %, in inflorescences 14.1 % (per the mass of the absolutely dry raw materials).

Aglycons include flavonols, quercetin and kaempferol [33, 34]. It was established by methods of high performance liquid chromatography (HPLC) that these flavonols were also contained in hydrolysates of aqueous-alcoholic extracts from the above overground part, herewith; the major aglycon was quercetin [32]. In addition to these components, the author of [35] discovered in the overground part of *P. bistorta* free aglycons: taxifolin, luteolin, quercetin-3-methyl ester and rhamnetin. It was noted in the work [35] that quercetin prevailed among aglycons.

Out of ten glycosides of *B. officinalis* found by chromatography on paper, quercimeritrin, avicularin and quercetin 5-O-β-*D*-glucopyranozide were isolated [16, 21, and 34]. In the work [23], seven flavonoglycosides were identified in the aboveground part by the method of HPLC: rutin, hyperine, quercitrin, isoquercitrin, miquelianin (quercetin 3-O-β-glucuronide), spirozide (quercetin 1′-O-β-glucoside) and astragaline. In the flowers, the following anthocyanins were detected: cyanidin, delphinidin and unknown anthocyanidin [36, 37].

The content of tannins in leaves of plants was varied from 5.0 to 17.5 % [9].

Compounds possessing the antitumor activity, including phenolic: gallic, protocatechuic, *para*-oxybenzoic, chlorogenic, vanillic, syringic acids, pyrogallol, hydroquinone, catechol, 2,6-dimethoxyphenol, 4-methylcatechol and fatty acids, viz, myristic, palmitic, linoleic, were isolated using preparative HPLC from rhizomes of *P. bistorta* and identified [40].

Anti-inflammatory, antitumor, and antibacterial properties of rhizomes of *P. bistorta* were described in the literature [25, 38–40]. They are used in China in folk medicine to treat dysentery with bloody diarrhea, diarrhea at acute gastroenteritis, acute respiratory infection with cough, carbuncle, and aphthous ulcers, nasal and hemorrhoidal bleeding; bites of poisonous snakes, *etc.* [22]. In folk medicine of Russia, this plant is used as a astringent and styptic at bleeding, hemoptysis, indigestion, cholera, dysentery, cystitis, cholecystitis, colpitis, vaginitis, inflammatory diseases of the skin and mucous membranes, scurvy, and also for burns and bites of rabid animals [9]. In the composition of biologically active substances with antibacterial and antitumor properties, gallic and chlorogenic acids, catechin were noted; the content of gallic acid in rhizomes is, in average, 0.50 %, of chlorogenic acid, 0.86 %, of catechin, 0.77 %. Astringent, hemostatic, sedative, diuretic and antipyretic actions of *P. bistorta* were reported [13]. It was shown based on experiments on animals that the extract of rhizomes *P. bistorta* possessed a powerful hepatoprotective action for the protection and can be used for the protection and treatment of toxicological damages to the liver and kidneys as a mean of non-traditional medicine [41, 42]. It is proven that the anti-inflammatory action of rhizomes of *P. bistorta* is provided by two active compounds, *viz.*, 5-glutinen-3-one and friedelanol [25]. An alcoholic extract of rhizomes exhibits the interferon-like activity [43].

The overground part of plants was studied to a lesser extent. Active components of extract of *P. Bistorta* possessing the anti-inflammatory effect were revealed. It was also established that the extract itself exerted an analogous action in the treatment of swelling paw of the rat caused by carragheenin [16]. The fraction of phenol compounds of the extract from the overground part shows immunomodulatory effects at the antibody-formation [44]. It was found that *P. bistorta* suppressed the mutagenicity Trp-P-1 [26]. Chloroform and hexane fractions from *P. bistorta* were tested on the cytotoxic activity on cancer cells of the lines P338 (Marine lymphocytic leukaemia), HepG2 (Hepatocellular carcinoma), J82 (Bladder transitional carcinoma), HL60 (Human leukaemia), MCF7 (Human breast cancer) and LL2 (Lewis lung carcinoma). Some fractions showed a medium and very high activity [45]. It was noted that a bistort could be used for the prevention and therapy of intoxications caused by the cumulation of strontium cations [46].

CHEMICAL COMPOSITION AND BIOLOGICAL ACTIVITY OF *BISTORTA VIVIPARA*

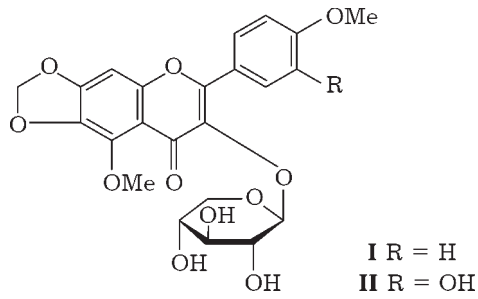
The second species of the genus *Bistorta*, *viz.*, *Bistorta vivipara* (L.) Delarbre (=*Polygonum viviparum* L.) is widely spread in the Northern Hemisphere. This is a perennial herbaceous plant of the height up to 50 cm with tuberiform thickened rhizome and a rosette of

long-petiolate oblong leathery leaves. The flowers are of the white, pink or red colour, assembled in a cylindrical spike; the lower flowers are usually replaced by bulbils. It blooms from June until autumn. The reproduction is seed and vegetative. The fruit is three-edged. The number of chromosomes: $2n$ = 80, 100 [3].

For rhizomes of *B. vivipara*, a high content of tannins [8–19 %] is typical, while for the overground part, vitamin C, carotene [9]. Two components out of the class of steroids have been isolated: β-citosterine [47] and daucosterin (from the fruit) [48]. In the overground part of plants *B. vivipara* phenolcarboxylic acids: ferulic [47], caffeic and chlorogenic [14], gallic (in the fruits) [48].

Researchers paid a great attention to flavonoids *B. vivipara*. The author of [48] established that 2.9–7.5 % flavonoids were contained in plants from mountain regions of Kazakhstan. Plants from regions of Siberia accumulate more than 5.0 % of flavonoids; moreover, in the period of mass flowering plants, their content varies in the limits of 1.2–5.6 % (in the flowers), 1.7–5.0 % (in the leaves). To the end of flowering, it is reduced to 2.8 % (in the flowers) and 4.2 % (in leaves) [49]. The aglycone composition of flavonoids (flavonols) is represented by kaempferol, quercetin and myricetin [33, 36, and 50]. These three aglycons were also found in hydrolysates of aqueous-alcoholic extracts of organs of the overground part of *B. vivipara* by HELC methods. The major aglycone of *Bistorta vivipara* is quercetin (up to 5.8 % in the flowers, 6.8 % in leaves) [49].

From the aboveground part of plants *P. viviparum*, there were discovered: isorhamnetin, 5,8,2-trihydroxy-5-methoxyflavone, quercetin 3-O-2-*L*-rhamnoside, kaempferol 3-O-β-*D*-glucoside, quercetin 5-O-β-*D*-glucoside, apigenine 7-O-β-*D*-glucoside, 7-O-β-*D*-rutinoside-5-hydroxy-4-methoxyflavone. Their structure was proven by spectroscopic and chemical methods [46, 47]. Two flavone glycosides were also isolated: 5,4′-dimethoxy-6,7-methylenedioxyflavone 3-O-β-*D*-xylopyranoside (**I**, *viviparum* A) and 3-O-β-*D*-xylopyranoside of 3′-hydroxy-5,4′-dimethoxy-6,7-methylenedioxyflavone (**II**, *viviparum* B). The structure of compounds **I** and **II** was established using IR, UV, PMR, ^{13}C NMR and mass spectra [51].



I 5,4′-dimethoxy-6,7-methylenedioxyflavone 3-O-β-*D*-xylopyranoside (*viviparum* A);
II 3′-hydroxy-5,4′-dimethoxy-6,7-methylenedioxyflavone 3-O-β-*D*-xylopyranoside (*viviparum* B).

In the composition of volatile emissions, 58 compounds were found, among which terpene compounds (20.84 %) prevail. Ethers (9.43e%), heterocyclic compounds, aldehydes, alkenes and alkanes were also isolated [52].

B. vivipara is widely used in the folk medicine of the East. The spectrum of its application is almost identical to that of *B. officinalis*. In Transbaikalia, it is used in food in the raw and cooked kind, grinded into flour and cooked porridge, brewed and drank a decoction instead of tea. A tincture is used at a diarrhea and colic in a stomach [9]. A decoction of the rhizomes is used as a remedy for stomach and hemostatic, colds, diseases of the urogenital tract; decoction of is applied in diseases of the stomach [9, 53, 54]. In Mongolia, the rhizome of the *Bistorta vivipara* is used in the mixture Sorool-4 for the treatment of the respiratory diseases at bronchitis and pneumonia [55]. An extract from leaves possesses a powerful antioxidant effect [56]. Leaves contain a significant amount of quercetin (1–2 mg/g of the dry mass) in the form of glucoside, rhamnoside and rutinoside. Phenol compounds affect the synthesis of fatty acids in the organism; therefore, plants of *B. vivipara* can be used as a quercetin producer lowering the level of lipids in the blood plasma [57].

CHEMICAL COMPOSITION OF OTHER SPECIES OF THE GENUS *BISTORTA*

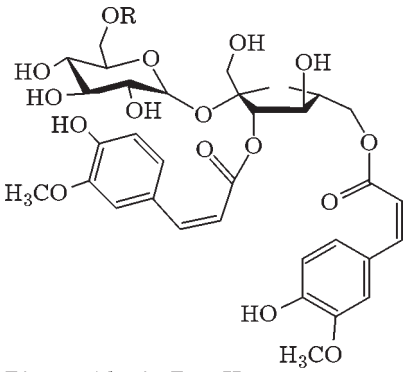
Major flavonoids of plants of Siberian and Far Eastern species: *B. abbreviata* Kom., *B. alopecuroides* (Turcz. ex Meissn.) Kom., *B. ellptica* (Willd. ex Speng.) Kom. (syn. *Polygonumat-*

tenuatum V. Petrov ex Kom.), *B. manshuriensis* Kom., *B. pacifica* (V. Petrov ex Kom.) Kom. and Caucasian specie *B. carnea* Kom. (*Polygonum bistorta* L. ssp. *carneum* (C. Koch) Coode & Cullen) are represented by flavonol glycosides based on kaempferol, quercetin and anthocyanin cyanidin [34, 36]. They are usually used in traditional medicine for the same purposes, as and widely spread species of *B. officinalis* and *B. vivipara.*

As noted in [58], plants of *Bistorta carnea* contain more than 5 % of flavonoids in vegetative and generative organs. As a part of flavonoids of its aboveground organs, quercetin 3-O-*D*-glucuronopyranoside, quercetin 3-O-*L*-rhamnopyranoside, quercetin 3-O-*D*-galactopyranoside, kaempferol 3-O-*L*-rhamnopyranoside and catechin were found [59]. In the ether oil extracted from the flowers of *Polygonum bistorta* L. ssp. *carneum* (C. Koch) Coode & Cullen, the major group of compounds is represented by carbohydrates (54.5 %), among them: triclosan (21.3 %), hexacosane (14.0 %), palmitic acid (13.3 %), heneicosane (7.7 %), lavandulol (6.1 %), terpenoids are contained in a smaller amount, *viz.*, 14 % [60].

Flavonols quercetin, isorhamnetin and flavonol C-glycosides: luteolin 6-C-β-*D*-glucopyranoside, luteolin 8-C-β-*D*-glucopyranoside, apigenin 6-C-β-*D*-glucopyranoside, apigenin 8-C-β-*D*-glucopyranoside and triacetin 8-C-β-*D*-glucopyranoside were extracted from leaves of *Bistorta affinis* (D. Don) Green (Syn. *Polygonum affine* D. Don, *Persicaria affinis* (D. Don) Ronse Decr.) [61].

Korean scientists [62] isolated cerebroside, soya-cerebroside, 5-hydroxypyrolidine-2-one, vanillic, protocatechuic, caffeic acids, caffeic, chlorogenic and 3,5-di-O-caffeoylquinic acids methyl esters, avicularine, quercetin, quercitrin, isoquercitrin, quercetin-3-O-β-*D*-glucoside, luteolin, afzelin from the above-ground part of plants *B. manshuriensis* used traditionally in Korea at a diarrhea. Later [63], two new substances, derivatives of ferulic acid and sacharose: bistoroside A and bistoroside B, as well as three known compounds, viz, helonioside A, helonioside B and smilaside were isolated. The structure of bistoroside A was proven as (3,6-di-O-Z-feruloyl)-β-*D*-fructofuranosyl-(1→2)-α-*D*-glucopyranoside, and bistoroside B, as (3,6-di-O-Z-feruloyl)-β-*D*-fructofuranosyl-(1→2)-(6′-O-acetyl)-α-*D*-glucopyranoside.



Bistoroside A: R = H
Bistoroside B: R = $COCH_3$

CONCLUSION

It has been shown that plants of the genus *Bistorta* contain a complex of biologically active substances and they are the reserve of medical remedies of a various directions of action. The preparation of medical preparations from above-ground and underground organs of plants and their testing may become the goal of their further study.

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