

Sanguinaria canadensis (Sanguinaria canadensis L.)  
Publication 1: botanical characterization, synonymy, chemical composition, use in dentistry, homeopathy and veterinary medicine, food use experience

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Blood root (Sanguinaria canadensis L.). Article 1: botanical characteristics, synonymic, chemical composition, use in Dentistry, Homeopathy and Veterinary and as a food supplement

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#### SUMMARY

An informational and analytical study of *Sanguinaria canadensis* L. in terms of botanical characteristics of the plant, problems of synonymy, as well as modern ideas about the chemical composition, nutritional use and use of this plant in dentistry, homeopathy and veterinary medicine has been carried out. It is shown that an erroneous automatic translation, including in the PubMed database of scientific publications, leads to terminological confusion in the definition of the botanical name and synonymy of Canadian *sanguinaria*.

Many years of experience in homeopathic use and the absence of toxicity for matrix tinctures and low dilutions of homeopathic medicines in therapeutic doses were revealed. The experience of food use, as well as the wide spectrum of action and the absence of toxicity established for *Sanguinaria canadensis* L. in veterinary medicine, allows us to consider the issue of the prospects of creating biologically active food additives (BAA) and specialized food products based on Canadian *sanguinaria*.

Key words: traditional medicine, homeopathy, *Sanguinaria Canadensis* L., *sanguinaria*, canadian *sanguinaria*, alkaloids, isoquinoline alkaloids, quaternary benzophenanthridine alkaloids, *sanguinarine*, *chelerythrine*, *protopine* alkaloids.

#### RESUME

Current review presents the analytical study of *Sanguinaria canadensis* L, with regards to its botanical characteristics, synonymic problems as well as its chemical composition, use as a food supplement and in dentistry, homeopathy and veterinary medicines. It is shown that the wrong translation of this plant, even in the PubMed database, results in likely terminological errors in the botanical identification and synonymic confusion of *Sanguinaria canadensis* L.

It was identified that blood root, *Sanguinaria canadensis* L, has a long-time use in homeopathy, no toxicity was observed in therapeutic doses and matrix solutions.

The established function of *Sanguinaria canadensis* L. as a food supplement, as well as in a wide spectrum of its usage without toxicity in veterinary medicines, allow scientists to consider its use in biologically active supplements and as a specialized food supplement.

Keywords: traditional medicine, Homeopathy, *Sanguinaria canadensis* L., bloodroot, alkaloids, isoquinoline alkaloids, quaternary benzophenanthridine alkaloids, *sanguinarine*, *chelerythrine*, *protopin* alkaloids.

#### INTRODUCTION

The growing interest in herbal antiviral, antimicrobial, antifungal and anticancer drugs is today a global trend in the medical and pharmaceutical industry. This is due, among other things, to the lack of effectiveness and safety of pharmacotherapy using synthetic drugs.

According to foreign studies (including ethnobotanical and ethnopharmacological), one of the promising herbal sources for obtaining medicinal preparations of the indicated spectrum of action is Canadian *sanguinaria* - *Sanguinaria canadensis* L. [32]. In our country, *sanguinaria* is not found in the wild, but it is successfully and rather widely cultivated as an ornamental plant or a source of rhizomes for the purpose of self-healing. *Sanguinaria canadensis* L. in the Russian Federation is not an officinal plant and is used so far only in homeopathy [1, 10].

The review, which consists of two consecutive publications, presents the results of biological and medico-pharmaceutical studies that allow evaluating the effectiveness of extracts from this plant in various diseases, including benign and malignant neoplastic processes.

The purpose of this information and analytical study is to objectify information about synonyms, the spectrum of biological activity (in comparison with the experience of traditional use), the chemical composition and the prospects for the use of Canadian *sanguinaria* as a source of modern domestic drugs and / or phytonutrients.

Publication 1 is devoted to botanical characteristics, problems of synonymy, modern ideas about the chemical composition *Sanguinaria canadensis* L., the use of this plant in homeopathy and veterinary medicine, as well as its experience food use.

#### MATERIALS AND METHODS

The objects of research were normative documents recommended for use in the prescribed manner, and bibliographic sources of a high degree of reliability, including monographs, scientific periodicals, reference publications, dissertations, dissertation abstracts, as well as electronic scientific and official databases.

data. We also took into account Internet resources with links to bibliographic sources of a high degree of reliability.

When performing the work, the following research methods were used: information-analytical, historical, content analysis, systematization.

### 1. Characteristics of the research object

Systematics. Canadian sanguinaria - *Sanguinaria canadensis* L. belongs to the Poppy family - Papaveraceae. Genus *Sanguinaria* L. in accordance with modern taxonomy includes the only species *Sanguinaria canadensis* L. described K. Linnaeus in 1753 [80] (Fig. 1-3).



Rice. 1. Canadian sanguinaria (*Sanguinaria canadensis*): © mbgarchives (source: [6])



Rice. 2. Canadian sanguinaria (*Sanguinaria canadensis*): © Eric Hunt (source: [6])



Rice. 3. Rhizome of *Sanguinaria*: © Bruno Bergeron (source: [6])

According to the United Plant Savers portal [25] and the official USDA Plants Database [81], the full Latin name of the only species of the genus *Sanguinaria* L. is *Sanguinaria canadensis* L. var. *rotundifolia* (Greene) Fedde.

According to [32], the first documented botanical description *S. canadensis* recorded in 1635 in the work *Historia Plantarum Canadensium Cornuti*, where the plant was named *Chelidonium americanum flore albo* [63]. Other names for the species were proposed by Parkinson in 1640 - *Rannunculus virginensis albus* [32, 66] and Plunket in 1696 - *Papaver corniculatum* [32, 70]. Modern botanical name *Sanguinaria*, derived from the Latin *sanguis* (blood) and *canadica* (plant range), suggested by the French florist Pierre Morin in 1651 [42].

Johann Jacob Dillenius, professor of botany at Oxford University, recognized for the first time that the plant is a unique genus [32, 34], while the definition of the genus is attributed to Linnaeus in his book "Species Plantarum", where he simply reduced several Dillenius species to one called *Sanguinaria canadensis* [32, 57]. Subsequently, Rafinesque identified several varieties: *Parviflora*, *Cespitosa*, *Reniformis*, *Repens*, *Multipetala* (double petals) and *Stenopetala* (narrow linear petals) [32, 71].

Synonyms. *Sanguinaria* [1, 7], *Sanguinaria* [79], bloody root, canadian bloodstream, blood root, canadian blood root, canadian highlander snake, snake root, ovary, bloodworm, plakun, canadian bloodstream, canadian bloodworm, bloodroot [1, 4, 10], canadian wolf foot [2], Bloodroot [80]. Confusion in the synonymy of Canadian sanguinaria on domestic sites appeared, apparently due to the use of automatic translation from English by some authors "Bloodroot" into Russian. In particular, an incorrect automatic translation of the botanical name (Bloodroot = cinquefoil) was noted by us in the Pubmed database [<https://www.ncbi.nlm.nih.gov/pubmed/>] when working with research articles *Sanguinaria canadensis*, in particular with the article [93], as well as on the portal [25].

According to the American PDR for Herbal Medicines [67] published by Thomson Reuters in 2007, as well as other specialized publications [25, 30, 86], sanguinaria (Bloodroot) has the following colloquial synonyms in English: Indian Paint - Indian paint, Tetterwort - Canadian wolf foot, Red Root - red root, Coon Root - raccoon root, Snakebite - snake bite, Sweet Slumber - sweet nap, sweet sleep, sweet oblivion [67], Indian Plant - Indian plant, Paucon - pukkon or pukkun [30, 86], Pauson - pauson [67]. On the professional portal United Plant Savers, the following names are presented: Bloodroot; Bloodword, Red Root, Red Puccoon [25].

Description. *Sanguinaria canadensis* L. - plant up to 40-60 cm, naked, with branching rhizomes. Leaves petiolate, glabrous, up to 15 cm long, lobes from rounded-reniform to heart-arrow-shaped,

predominantly palmate-5-lobed, up to 25 cm wide, jagged edges, the lower surface is glaucous (grayish-green) [80], reticulate with prominent orange veins, has gray pubescence, the upper surface is light green [32, 47]. The rosette may contain one or several leaves [80]. *Sanguinaria canadensis* in shape resembles the print of a wolf's paw, therefore in some sources this plant has the popular name "Canadian wolf foot" [2] (Fig. 4).



Rice. 4. *Sanguinaria canadensis* is shaped like a wolf's paw print:© Bruno Bergeron (source: [6])

The flower is usually the only one, occasionally 2-3 flowers are found on 1 stem. Bracts are absent. Flowers are located on stems up to 15 cm long. A cup of two sepals, about 1 cm in size. Petals are white, pinkish, unequal - from oblong to obverse lanceolate, 1.5-3.0 cm in size, number 6-12. Numerous stamens. It blooms in early spring [80]. After the flower has opened, the plant has a height of 15-30 cm, and the leaf reaches its full development and remains until August [32, 47]. By the middle of summer, the aerial parts of *S. canadensis* dies off. Dormant plants can tolerate temperatures down to -20 ° C and are considered hardy [43].

The fruit is a fusiform bivalve box from 3.5 to 6 cm long; unfolds from the base. Seeds are black to red-orange in color, indistinctly reticulate [80] (Fig. 5).



Rice. 5. Seeds of *Sanguinaria*:© Seig (source: [6])

Rhizome *S. canadensis* reddish brown (Fig. 3), 2.5-10 cm long and up to 4 cm in diameter. The rhizome is shortened and covered with orange-red roots [47]. When the rhizome is cut, a thick red sap (latex) is released, containing a number of alkaloids that protect the plant from microorganisms, insects and herbivores [3].

According to the information presented in the 30th volume of the Flora of North America [80], the leaves *Sanguinaria canadensis* pretty varied in shape and size, and the stems and petals vary considerably in length. In some individuals, the petals are clearly differentiated into sets of two different sizes, in others, the differentiation is barely noticeable. Extreme variations in these characters served as the basis for identifying several forms, varieties, and even individual species; however, intermediate links of the discovered forms were identified, and the variation was weakly correlated with geography or habitat. Therefore, botanists found it advisable to limit the formal recognition of *Sanguinaria canadensis* as one highly variable species in the genus *Sanguinaria* [80].

Habitat and ecology. *Sanguinaria* is native to eastern North America. Its range extends in different directions from Florida to Nova Scotia and west to the Rocky Mountains. [38] According to more modern data, the plant is widespread in the eastern regions of North America (Man., NB, NS, Ont., Que. ; Ala., Ark., Conn., Del., DC, Fla., Ga., Ill., Ind., Iowa, Kans., Ky., La., Maine, Md., Mass., Mich., Minn., Mo., Nebr., NH, NJ, NY, NC, N. Dak., Ohio, Okla., Pa., RI, SC, S. Dak., Tenn., Tex., Vt., Va., W.Va., Wis.). The discovery of representatives of this species was also reported from Mississippi, but no specimens for description in the Flora of North America were submitted [80].

According to the professional portal United Plant Savers [25] and the US Department of Agriculture [81], the geographic regions of distribution of *Sanguinaria* are territories from South Manitoba in Canada to southeastern Texas and from South Dakota to the Atlantic Ocean. It is found in all states of the United States except Alaska, Hawaii, California, Nevada, Washington, Oregon, Idaho, Montana, New Mexico, Colorado, Utah, and Wyoming. It is also found in the Canadian provinces of Manitoba, New Brunswick, Nova Scotia, Ontario and Quebec [25].

Bloody root grows best on light to medium well-drained soils and can tolerate a wide pH range with optimal growth in soils with a pH of 5–7 or higher [25, 58]. It can grow in the sun, but is more common in semi-shady, light forests with moist, acidic soil [25]. Prefers forests and thickets, but it can also be found along fences and tree felling [27], in river floodplains and along streams [25]. *S. canadensis* grows more successfully in soils with a low ratio of carbon to nitrogen (C: N), as evidenced by an increase in the number of leaves and flowers [27].

In Russia, *sanguinaria* is successfully cultivated as an ornamental plant [6].

There are conflicting reports on the influence of altitude above sea level on the growth of *sanguinaria* [27, 77]. According to official data, the plant is widespread in designated areas at an altitude of 0 to 1300 m - from humid to dry forests and thickets, often in floodplains and on the banks, near streams on slopes, less often in glades and meadows or on dunes, rarely - in areas with disturbed vegetation [4, 80].

It is one of the earliest plants to bloom in spring, covering forest areas with white flowers. Refers to milky latex plants. When the rhizome is cut, a blood-red sap appears, which is why *sanguinaria* got its name Bloodroot, or bloody root [32].

According to the professional portal United Plant Savers, the overall risk of extinction for the species is 47. *Sanguinaria canadensis* in the United States is considered a "vulnerable to exploitation" species in New York State and has a "special care" status in Rhode Island [25].

Possible impurities in the preparation of raw materials. Amateur pickers and poachers are often confused *S. canadensis* with *Jeffersonia diphylla* due to the visual similarity of flowers, leaves and roots. Differential diagnosis of species is based on the fact that in roots *J. diphylla* is missing dark red latex and alkaloids [25].

Reproduction. Due to the peculiarities of biology *S. canadensis*, dispersion of *sanguinaria* seeds (Fig. 5) depends mainly on ants, carrying on them for the purpose of eating a lipid membrane (eliosome). However, according to the data of professional biologists, non-native species of fire ants that have settled in the *sanguinaria* range damage the seeds when they eat the eliosome or leave the seeds in unsuitable conditions for further germination, which already threatens the reproduction of the species [25].

*Sanguinaria* seeds ripen in the United States in mid to late spring. When the oblong seed pods are fully ripe, the pods open and the seeds pop out to the ground. If they are not harvested on time, the seeds will sprout around the mother plant, usually as early as next spring. For artificial propagation, it is recommended to collect the seeds using gauze bags or fine nylon mesh (veil material) to pack the young seed pods before they open. The pouch should be placed over the unripe pod and tied loosely around the stem. When the seed tray is opened, the seeds are released but are collected in a pouch rather than scattered on the ground [25].

At present, the reproduction of *sanguinaria* in the USA, as a rule, is carried out not only by collecting and sowing seeds (Fig. 5), but also by dividing the rhizomes (Fig. 3) in spring or autumn [25].

According to the professional portal United Plant Savers [25], the sufficient volume of reproduction of *sanguinaria* is limited by the fact that the seeds of the bloody root are not always available in the required quantities, and the rhizomes are relatively expensive. To plant them, it is recommended to cut the whole rhizomes vertically approximately two inches long (1 inch = 2.54 cm), making sure that there is at least one bud on each segment (there can be up to 12 buds on the rhizome).

In a well-prepared hole 3 feet wide (1 foot = 30.48 cm), plant the rhizome pieces deep enough to cover them with one to two inches of soil (usually about 4 inches deep). When forming plantings six inches apart, it is advisable to ensure that each bud is pointing vertically upward when placing the rhizome chunks in the ground [25].

In the future, it is necessary to provide a sufficient amount of moisture during the growing season. Despite the fact that the bloody root does not grow well in waterlogged soil, during dry periods, sufficient watering of the plants must still be ensured. Raw materials will be ready for harvesting only 4–5 years after planting the rhizomes [25].

Cultivation and protection measures. According to the professional portal United Plant Savers, at present, even specialists do not quite understand how many rhizomes are harvested in the United States annually. Various sources claim that this amount is between 38 and 55 tons per year. A report prepared for the North Carolina Consortium on Natural Medicinal Products states that 135,000 lb (1 lb = 0.45359 kg) rhizomes were sold to various industries back in 2001, but since then, sales have grown steadily [25].

Therefore, today the cultivation of *sanguinaria* is becoming an urgent need for the conservation of the species. According to [25], industrial cultivation *S. canadensis* is strategically important also due to the constant increasing demand for rhizomes. Today, in the USA and Canada, the entire volume of *sanguinaria* products sold is made from wild-growing rhizomes, which causes irreparable damage to the natural thickets of this species.

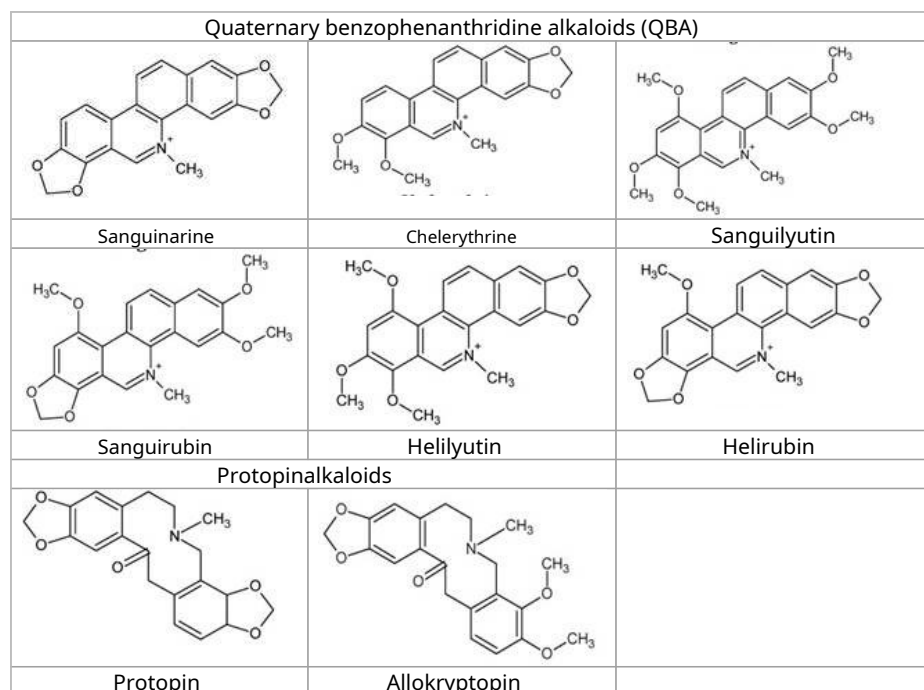
Bloody root can be successfully grown under 70-80% artificial shade or under natural forest canopy. In particular, in the forest, *sanguinaria* can be cultivated in raised flower beds, as well as in raised flower beds with an artificial shade structure. An introduction method is also used that mimics the growth in the wild ("wild imitated"). If an open field is used, it is recommended to create a wood or polypropylene structure seven feet or higher with two opposite ends exposed to the prevailing wind direction to provide the necessary degree of shading [25].

## 2. Chemical composition

According to the PDR for Herbal Medicines (2007), *sanguinaria canadensis* contains isoquinoline alkaloids of the benzophenanthridine type (4-7%), the main of which is sanguinarine. Other isoquinoline alkaloids of the benzophenanthridine type have also been found, in particular chelerythrine and oxysanguinarine. From isoquinoline

alkaloids of the protoberberine type identified berberine and coptisine; type of protopin - protopin, alpha- and beta-alcryptopin [67].

Later, works were published confirming the presence of these alkaloids, as well as other representatives of this class of biologically active substances (BAS). In particular, it is reported in the review [32] and experimental work [19] that *S. canadensis* contains eight isoquinoline alkaloids at biologically significant concentrations. Of these, six quaternary benzophenanthridine alkaloids (QBA): sanguinarine, chelerythrine, sangilyutin, chelilyutin, sanguirubin, chelirubin and two protopin alkaloids: protopin and allriprotin (Fig. 6).



Rice. 6. Biologically active isoquinoline alkaloids of Canadian sanguinaria (according to [32])

Pure chelerythrine was isolated for the first time in the world in 1893 [55], pure sanguinarine - in 1924 [44]. Minor quaternary benzophenanthridine alkaloids QBA (minor QBA) chelirubin and chelilyutin were first isolated from the herb of celandine *Chelidonium majus* (0.013% and 0.002% of the sum of its alkaloids, respectively) [32]. Later, they were also obtained from a number of species of the family *Papaveraceae*, including from *S. canadensis* rhizomes. Todayday it is this type of raw material that has the highest content of the indicated minor QBA - 0.04% and 0.229%, respectively [82, 83]. Sangilyutin and sanguirubin were isolated in 1960 also from *S. canadensis* [83]. Moreover, of the six species of QBA alkaloids, these minor alkaloids were found only in *S. canadensis* [87]. Thus, the alkaloid composition of sanguinaria rhizomes is unique.

The maximum content of sanguinarine was found in the rhizomes of plants, and less in the roots [29]. The minimum concentration of alkaloids is found in leaves and flowers. Distribution of other alkaloids in various morphological groups of raw materials *S. canadensis* has not yet been described [32]. Almost all authors who studied the variability of the alkaloids content depending on the influence of various external factors, as well as the stage of plant development, noted territorial and seasonal fluctuations in the content of sanvinarin and even minor alkaloids in all morphological groups of raw materials *S. canadensis* [20, 21, 32, 41, 46, 49, 73, 78].

A difference was also noted in the accumulation of alkaloids in the samples of raw materials harvested from wild and cultivated plants [32]. Cultivated rhizomes are often larger, but have a lower content of alkaloids than wild ones, possibly due to the low need of cultivated plants for chemical protection. Also, cultivated rhizomes do not have seasonal variations in the quantitative content of alkaloids, in contrast to wild-growing samples. The intensive effect of fertilizers significantly reduces the concentration of alkaloids [46].

Salmore AK and Hunter MD (2007) showed that the concentration of some alkaloids (especially most benzophenanthridine alkaloids) in sanguinaria raw material is highly dependent on clonal genetics, with the clone being attributed to a 10-fold concentration variance. However, this genetic influence is not universal, since the concentrations of helirubin and protopin alkaloids were found not to be associated with a clone [78].

The same researchers were able to establish that an increase in illumination increases the concentration of benzophenanthridine and protopin alkaloids in *S. canadensis* [78]. Since benzophenanthridine alkaloids are photoreactive toxins that can cause auto-toxic effects under high light conditions [18], when its intensity decreases, plants can reduce the concentration of alkaloids to reduce the risk of autotoxicity [18, 50].

In addition to alkaloids in various morphological groups of raw materials *S. canadensis* found long-chain alcohols (C<sub>26</sub>-C<sub>34</sub>), phyosterols, triterpenes [50], resins and starch [67].

Data on the spectrum of proven biological action and experience from traditional use as well as modern

indications for the use of extracts of *sanguinaria canadensis* will be presented in Publication 2.

### 3. Application in homeopathy

The bloody root is historically and still used in world homeopathic practice [67, 90, 91]. Currently, in homeopathy, using 60% ethanol, a matrix tincture is prepared from dried rhizomes with roots according to paragraph 4a of the Homeopathic Pharmacopoeia of Germany, as well as a homeopathic medicine in the first decimal dilution - D1 (1/10) [14].

#### 3.1. Homeopathic monotherapy

3.1.1. Modern integrated clinical homeopathy (according to [14]). In accordance with the ideas of modern integrated clinical homeopathy (according to [14]), the active substances of the matrix homeopathic tincture and dilution of D1 are sanguinarine, chelidonic acid, chelerythrine.

Directions of action: 1) arterial system, 2) liver. Leading symptoms: hyperemia in the head and chest, redness of the face, burning, dry mucous membranes, offensive, acrid secretions. Modalities: worse from any noise, from motion. Improvement: from a blow, in the dark [14].

By systems. Cardiovascular system: headaches and dizziness due to congestion of blood to the head, flushes of blood, agitated cardiac activity, pulse hard, fast. Respiratory organs: raw and burning sensation in the upper respiratory tract, corrosive coryza. Digestive organs: inflammatory diseases of the stomach. Genitourinary system: pronounced metrorrhagia, especially during menopause. Musculoskeletal system: rheumatic muscle pains and pains in the limbs, muscle stiffness (especially the deltoid muscle on the right), worse from cold. Better from warmth. Fever: burning heat in palms and soles (makes you get out of bed at night); alternating heat and chills, sweating [14].

Clinical indications. Nervous migraine in combination with diseases of the hypogastric region D4-D6. Acute laryngitis D4. Allergic rhinitis (climacteric) D4-D8. Right shoulder-arm syndrome. Menopause sweating and vascular activity (high blood pressure) D4-D12. Right-sided remedy with hot flashes (with menopause) with flushing of the head. Burning and dry mucous membranes. Worse morning and evening. [14]

3.1.2. According to S.R. Fataku [13]: *Sanguinaria* - right-sided remedy; affects the head, liver, chest organs cells, deltoid muscle. It is indicated for vasomotor disorders, when there is limited redness of the cheeks, abdomen, tongue, etc.; congestion - congestion of blood to the head, chest, abdomen, etc.; hot flashes and a sensation of pulsation throughout the body [13].

Sensation of burning heat and boiling of blood. The mucous membranes become dry. There is a burning sensation in the throat, behind the breastbone; in confined areas or in the form of burning stitches in the chest; burning in palms and soles. Sensation as if tongue were burnt. Symptoms intensify until vomiting of bile occurs, or cease with it [13].

Sore feeling inside. Acrid, blood-streaked, or offensive discharge. The patient lies on his back with his head elevated. Climacteric disorders. Diseases of the biliary tract. The pains increase and decrease in accordance with the movement of the sun over the horizon. Sudden cessation of airway catarrh followed by diarrhea. Polyps of the nose, uterus. Mushroom growths. Faintness and fainting from the smell of flowers. Pain in places where bones are least covered by soft tissues [13].

Modalities. Worse: periodically - in accordance with the movement of the sun; every week; every night, during menopause, from smells, from concussion, from light, from sweets, from movement, when looking up, from touch, when raising hands. Better: from sleeping, lying on the back, from vomiting, from cool air, when intestinal gases pass, from acidic foods, lying on the left side [13].

Information on the effect on individual systems of the body is presented in the publication [13, p. 750-752].

3.1.3. According to G. Storch [16]. According to the brief practical edition of G. Storch, the main indications for the use of *sanguinaria* drugs in homeopathy are: congestive headache, vasomotor migraine, climacteric migraine, catamenial migraine, neuralgia of the cervical, occipital, supraorbital nerves, brachial plexus. Vasomotor rhinitis, turbinate hypertrophy, chronic retronasal catarrh, laryngitis, bronchial asthma. Spasmodic urine. Vegetative lability. Menopause disorders, including rosacea and hyperhidrosis. An effect is possible in rheumatism of the jaw joints, polyps of the mucous membrane (nose, uterus) [16].

Detailing of indications: by means of various alkaloids, it acts mainly on the vasomotor nerves, especially the head, on the mucous membrane of the respiratory tract, stomach and intestines, as well as on the skin. Characterized by dryness of the mucous membranes with hyperemia, a tendency to bleeding. Burning pain that migrates to all organs. Burning of hands and feet. There are reports of a preference for the right half of the body [16]. Periodically recurring throbbing pain extending from the occiput through the vertex and fixing in the (right) supraorbital region. Nausea, vomiting of bile. During an attack, pulsation and swelling of the temporal arteries. The headache worsens with the rising of the sun and weakens again with its setting (cf. : *Spigelia*); hungry headache. Waking at night between 2 and 4 o'clock with unbearable occipital headache. Agonizing tickling cough in the evening after going to bed. Pletoric; sees everything in red. Gloomy, irritable, impatient, angry, anxious [16].

Modalities. Worse, heat, sun, radiation, motion, bending, touching, noise (even if someone is walking in the room), light, odors. Amelioration after vomiting, often after passing copious light urine, cold, rest, lying down, after sleep, in the dark and from eating [16].

3.1.4. According to V.I. Varshavsky [1]. In accordance with the practical guide V.I. Varshavsky [1], *sanguinaria* has a specific effect on the autonomic nervous system (vasomotor nerves), the mucous membranes of the respiratory tract.

Symptoms Periodic migraine starting in the morning from the occipital region and moving during the day to

right eye, resulting in vomiting. Hot flushes with redness of cheeks, burning in palms and soles. Tickling, pain, cough after hypothermia with bright hyperemia and dryness of the mucous membrane of the posterior pharyngeal wall. Pain in the right deltoid muscle, which does not allow raising the arm, more at night [1].

Modalities. Worse, at night, damp weather, on motion, cold. Amelioration: After sleep, in the dark, lying on left side. The predominant side of the defeat is the right. The frequency of symptoms is weekly. Divisions: 3, 6 [1].

3.1.5. According to E. Farington [11, 12]. Also in 1939 E. Farington in Homeopathic Clinical Pharmacology was it is noted that the seeds of *Sanguinaria* are somewhat narcotic [11]. The plant itself (as well as homeopathic remedies from its roots) is primarily an irritant, "whether it is applied through the mouth, whether it is applied to the skin, or when it is brought by blood to other tissues." "As the primary and most important action of this agent in the latter case, we have tissue irritation" [11, 12]. E. Farington gives the following description of this action of the *sanguinaria* in the form of a table (Table 1).

Table 1

Irritant effect *S. canadensis* (according to [11, 12])

Sanguinaria canadensis annos:	Brain	Anxiety, irritability
	Nose	Fainting from odors
	Ears	Sensitivity to sudden sounds
	Circulation	Headache. Dizziness. Bleeding. Climatic period. Fever. Menstruation. Galloping consumption. Local tides (local congestion)
	Mucous membranes	Feeling dry and / or raw. Cough. Croup. Ulceration. Polyps. Diarrhea. Inflammation of the lungs (pneumonia)
	Glands	Salivation
	Leather	Acne, ulcers
	Muscle	Rheumatism. Muscle pain (myalgia), weakness. Nausea, lightheadedness (fainting)

Particular attention is paid to "irregularities and disorders in the field of blood circulation." A more detailed description of *Sanguinaria* in comparison with other homeopathic remedies for various symptoms is presented in the publication [12, p. 212-218].

3.1.6. According to J. Charette [15]. In Practical Homeopathic Medicine by J. Charette, the physiological action characterized as follows. Large doses of tincture cause violent vomiting, burning in the stomach, fainting, dizziness, threatening loss of energy, even real cholera. In non-toxic doses, *sanguinaria* is a drug that irritates the mucous membranes and inhibits blood circulation [15].

Characteristic. 1) Extreme dryness of the mucous membranes with burning. 2) Particular sensitivity to odors, reaching the point of loss of consciousness. 3). Continuous change of symptoms: as soon as a new one appears, the previous one disappears. 4) Disorder of the vasomotor. 5) Urination is frequent, at night, profuse, urine as light as water. 6) Limited blush on the cheeks. 7) A burning sensation, as from hot water [15].

Chair. Constipation; unsuccessful urging to stool, with sensation of a large mass in the rectum. Diarrhea; stool is bilious, watery, flatulent, preceded by colic. Diarrhea following sudden disappearance of catarrh of the respiratory tract. Menses premature, profuse, clotted, and strong odor. Amenorrhea with hot flashes, palpitations, neuralgia in the right temple and abdominal pain as if menses were about to appear [15].

Main indications. Pharyngitis: acute, on the right side, dry, pharynx red, smooth and shiny, sensation of lack of saliva. Chronic pharyngitis, when there is a sensation of heat in the throat, pain, detachment of the mucous membrane, yellow, thick or muco-bloody discharge. Tuberculosis: A debilitating fever with limited flush on the cheeks; about 14-16 hours. Burning and fullness in the chest. The right lung is more affected than the left. Rheumatism: Rheumatic pains at the base of the neck, in the shoulders and arms; sharp stitching, wandering pains. *Sanguinaria* has the same affinity for the right deltoid muscle as *ferrum* for the left [15].

Eye diseases: Scleritis, recurrent inflammation of the iris and choroid associated with menstruation, is cured by *sanguinaria*. Headache: Migraine; pain manifests itself in the morning, intensifies and weakens with the sun, it starts from the back of the head, spreads forward and focuses on the right eye (above the left eye of the spigelia). Ameliorated by lying in the dark. Migraines appear every seven days [15].

Cough. Generally dry, intermittent, caused by tingling in the mucous membrane, mucus is coughing up with great difficulty, worse when lying down, easier when sitting. Coughing up scanty, slimy or rusty, or wet cough with purulent, stinking expectoration. Burning, sharp, stitching pains in the right side of the chest, with dyspnoea. *Sanguinaria* corresponds to the 2nd and 3rd stages of bronchitis and croupous pneumonia; it stands between phosphorus and sulfur. It will also be useful in cases of congestion and hardening of the lungs with localized foci. In case of inflammation in the lower lobe of the right lung with jaundice, one should think about *sanguinaria*, *chelidonium* and phosphorus [15].

Doses. Both very high and very low dilutions have been used with success [15].

Summary by J. Charette. *Sanguinaria* affects the mucous membranes, especially the respiratory tract. She calls numerous disorders in the vasomotor sphere, which indicate it in the climacteric period. Her headache is specific. Its affinity for the right side is a very characteristic feature [15].

3.1.7. Modern monopreparations based on *sanguinaria* rhizomes for wide nonprescription use [26].

The largest American retail chain Walmart Inc. (formerly Wal-Mart Stores Inc.) [92] offers an alcoholic extract of wild *Sanguinaria* rhizomes as a homeopathic remedy intended "for the health of the immune system" [26].

A 2008 study of the market for homeopathic remedies for the treatment of menopausal symptoms (438 patients) showed that homeopathic monopreparations *S. canadensis* ranks fifth out of 16 most effective remedies leading to relief of symptoms and / or improvement of the patient's condition [28]. However, according to objective assessments of academic clinicians, the type and design of the study does not yet allow us to reliably state the effectiveness of monotherapy *S. canadensis* during menopause [32].

### 3.2. Complex homeopathic preparations

The American trademark Hyland's offers a complex homeopathic medicine for the treatment of menopausal syndrome based on *S. canadensis*. As part of lactose-based granules: Amyl nitrosum 6X - 3 × (dilution 1: 1,000,000); *Sanguinaria canadensis* 3X - 3 × (dilution 1: 1000); *Lachesis mutus* 12X - 12 × (1:10 dilution) [51]. In the United States, this homeopathic remedy is marketed over the counter based on the positive results of more than 50 years of study [32, 52]. At the same time, a randomized study (involving 83 patients) was described with a Jadad score of 5. It was found that patients who used the antimenopausal drug Hyland's had higher symptom severity scores, as well as more frequent and more severe headaches compared with control groups using a single-component drug and even with a placebo, which indicated the lack of efficacy of the complex drug in menopause [32, 59].

The homeopathic remedy Zeel Comp has been shown to be effective in treating osteoarthritis in dogs. N (Zeel) derived from *Sanguinaria Canadensis* (Canadian *sanguinaria*), *Arnica Montana* (mountain arnica), *Solanum dulcamara* (nightshade bittersweet), *Rhus toxicodendron* (rus toxicodendron) and Sulfur (sulfur) [48].

A number of clinical studies have also been conducted on patients suffering from osteoarthritis. One (blind study) compared Zeel Injectable with intra-articular sodium hyaluronate. For five weeks, Zeel was injected twice a week, sodium hyaluronate - once a week [62]. Another double-blind, randomized study in 121 patients compared the efficacy of oral diclofenac (25 mg) with oral Zeel. Both pills were taken three times a day for 10 weeks [65]. The third large, open-label, prospective, multicenter, controlled cohort study comparing the efficacy of Zeel tablets and COX-2 inhibitors, enrolled 592 patients [22].

## 4. Application in veterinary medicine

Historically, high doses of *sanguinaria* were used by Native Americans to terminate pregnancy in horses [25].

Today, the bulk of commercially mined *sanguinaria* is exported to Europe as a natural feed additive for animals. It is also used in the form of veterinary dental products as part of antibacterial mixtures [25].

In 2006, the European Union ratified a document banning the use of antibiotics as additives for raising animals, due to the reliable development of antibiotic resistance [39]. This prohibition stimulated the interest of researchers in herbal feed additives, which could reduce the level of gastrointestinal pathogens, allowing animals to redistribute immune defense resources [75].

As a result of the research carried out, the substance Sangrovit (*Sangrovit*) obtained from *S. canadensis* rhizomes or aboveground parts *Macleaya cordata*, has been proposed as a natural feed additive for animals [23, 85].

Several studies have shown that Sangrovit increases weight gain in weaned piglets [53], broilers [89] and tilapia [72]. The use of Sangrovit significantly reduced the amount of *Salmonella enteritidis* in the caecum of broilers 7 days after the start of its introduction [69]. In the diets of pigs fed with 1.5 g of QBA alkaloids per 1000 kg of feed, a more effective reduction in the excretion of fecal *Salmonella* was observed than in pigs that received chlortetracycline, which is widely used as a feed antibiotic in the United States [74]. The increase in the mass of individuals caused by Sangrovite in fish was explained by the stimulation of appetite [72].

In connection with reports of the potential toxicity of *sanguinaria* alkaloids in high doses, 90-day experiments with *Sanguine* in rats and pigs were carried out in terms of feeding animals with quantities of alkaloids 50 times higher than the recommended doses. Experiments showed no genotoxic damage to lymphocytes or hepatocytes in rats [85], as well as histological and hematological toxicity or the formation of DNA adducts in pigs, despite the fact that the levels of sanguinarine and chelerythrine in plasma reached 0.11 and 0.2 µg / ml, respectively [56]. The results obtained allowed us to conclude that taking alkaloid-containing supplements from *S. canadensis* has nothing to do with their toxicity [32].

Currently sangrovite from rhizomes *S. canadensis* is officially recognized in the EU as a food additive, acting as an antibiotic and antiparasitic alternative to banned toxic pharmaceuticals for use in agriculture and aquaculture [25, 32]. The norm has been established for the content of Sanguinarine in Sangrovit - not more than 1.5% w / w [32].

As a veterinary remedy, *Sanguinaria* preparations have been used to treat equine sarcoidosis. Despite local invasiveness, these common equine tumors rarely metastasize but often recur after treatment [88]. In the USA, the following modern drugs based on *sanguinaria* are used in veterinary practice: XXTerra (Larson Labs, Fort Collins, CO, USA), ointment (Newmarket premixes, Catley Cross, Halstead, UK) and Animex (Nies, Las Vegas, NV, USA) ... As part of Newmarket, for example, the content of *sanguinaria* rhizomes is 40% w / w in an extract of 1: 3 (25% methyl alcohol / 75% water), 48% w / w in an ointment (emulsification with the participation of



10% zinc chloride and preservatives) [32].

Small pilot studies have shown that the rate of complete cure of sarcoidosis with sanguinaria alkaloids in horses was comparable to Imiquimod [64, 68]. According to the results of a retrospective survey, 98% of 57 horse owners reported complete cure in animals of small sarcomas less than 2 cm in diameter with the use of sanguinaria preparations [95].

Sanitary veterinary drugs such as Neoplasen are used in dogs (female golden retrievers) to treat tumors, developing fluctuating skin mass after intratumoral injection with subsequent postoperative complications [31].

When used at therapeutic doses, no studies have reported toxicity of sanguinaria-based products [32].

#### 5. The use of sanguinaria in dentistry to obtain an antibacterial effect

Broad spectrum of alkaloids activity *S. canadensis* in relation to microorganisms of the oral cavity caused the development of a number of methods for the treatment of gingivitis and the fight against dental plaque [32, 36]. As an alternative to chemical-based oral antiseptics, the Viadent mouthwash was proposed in the 1980s (Viadent) containing 0.3 mM sanguinarine chloride, and a toothpaste containing 0.7 mM sanguinarine chloride [54]. However, after some time - at the very end of the twentieth century - in the scientific community, the use of Viadent became associated with the development of leukoplakia (precancerous condition) of the vestibule of the maxillary bone [33].

Despite the fact that rinsing the mouth has a short-term effect (lasting only a few minutes), the vestibule of the upper jaw has a rather low rate of saliva turnover and, therefore, prolonged contact of the mucous membrane with residual amounts of rinse, according to some experts, was possible [94].

Therefore, the safety and clinical efficacy of oral care products based on *S. canadensis* were evaluated in a number of toxicological studies for animals and humans [61]. The food was found to be safe in the experiment, but none of these studies were longer than 6 months [32]. At the same time, 84% of the examined patients with an established diagnosis of "maxillary vestibule leukoplakia" used Viadent for a long time - on average, for 4.4 years [40]. Stopping the use of Viadent did not lead to regression of leukoplakia, which suggests the occurrence of persistent genetic changes in epithelial cells [17].

Clinically, Viadent did reduce plaque levels, but it was inferior to chlorhexidine in treating gingivitis and bleeding gums [37]. Viadent was withdrawn from the market in North America due to unwarranted concerns about its as yet unproven potential carcinogenic activity [32]. There has also been no evidence of the safety of the other ingredients in Viadent mouthwash to the scientific community.

There has been published evidence of low toxicity of products based on sanguinaria, including in terms of the effect on the development of glaucoma [36].

#### 6. History of food use of Canadian sanguinaria

In addition to medical purposes, indigenous people in America have traditionally used sanguinaria products as an aphrodisiac to increase "love charm" [45, 60, 80]. In particular, there is evidence of a high assessment of the magical properties of this agent by American bachelor Indians of the Ponca tribe [45] (Nebraska and Oklahoma) [5, 8, 9].

Several Indian tribes used the rhizome in teas and powders to treat colds, constipation, and flu-like symptoms [25].

The Ojibwe Tribe of Wisconsin used the blood root as candy by adding it to a cube of maple sugar. Such a remedy helped with throat ailments, in particular with angina [84]. The same tribe used small pieces of sanguinaria rhizomes to make maple sugar cakes [25].

Currently, sanguine products are widely sold in the world as a herbal dietary supplement. In particular, the American company Walmart Inc (formerly Wal-Mart Stores Inc), which operates the world's largest wholesale and retail chain (headquartered in Bentonville, Arkansas) [92], offers non-alcoholic drops (water extract) from wild-growing rhizomes. sanitary facilities as a Herbal dietary supplement starting at \$ 18.49 [24]. The main regions of this company are the USA and Mexico; there is also a significant presence in Canada, South America, Great Britain (Asda), South Africa, China and Japan [92].

#### 7. Other areas of application

Sanguinaria has historically been used as a dye for wood and fabric due to the presence of latex in the root, giving rise to a bright red-orange color (hence the name bloody root) [25].

#### CONCLUSIONS

1. Conducted information and analytical research *Sanguinaria canadensis* L. in terms of botanical characteristics of the plant, problems of synonymy, as well as modern ideas about the chemical composition, nutritional use and use of this plant in dentistry, homeopathy and veterinary medicine.

2. It has been shown that an erroneous automatic translation, including scientific publications in PubMed, leads to terminological confusion in the definition of the botanical name, synonymy and the spectrum of medical use of Canadian sanguinaria.

3. Revealed many years of experience in homeopathic use and the absence of toxicity for matrix tinctures and low

dilutions of homeopathic medicines from sanguinaria in therapeutic doses.

4. Homeopathic provings suggest a wide range of biological activities for extracts from sanguinaria and the prospects of their use in official medico-pharmaceutical practice.

5. Experience in food use, as well as a wide range of actions and lack of toxicity established for *Sanguinaria canadensis* L. in veterinary medicine, allow us to consider the prospects for the creation of dietary supplements for food and specialized food products based on Canadian sanguinaria.

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