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The Genus *Asarum* L.: A Phytochemical and Ethnopharmacological Review

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ABSTRACT

Objective: This review aims to present updated and generalized data on ethnobotany, phytochemistry, and biological activity of some species of the genus *Asarum L. (Aristolochiaceae Juss.).* These species have been used as medicinal plants of traditional medicine in Asia (China, Japan, and India), Europe, and North America for a long time. This study included the 6 most widely known representatives of the genus *Asarum L.: A. europaeum L.* (European species); *A. heterotropoides F. Schmidt, A. himalaicum J.D. Hooker & Thomson ex Klotzsch* and *A. sieboldii Miq.* (Asian species); *A. canadense L.* and *A. caudatum Lindl.* (American species).

Materials and methods: Analysis of various literary sources of different years. Electronic scientific search systems (Pubmed, Springer, Wiley Online Library, Science Direct, Biodiversity library), electronic databases (Pubchem, Human Metabolome Database) and other Internet resources were used to search for the relevant literature and the necessary information.

Results: The phytochemical analysis of these species shows the presence of essential oils, terpenoids, steroids, phenylpropanoids, phenolcarboxylic acids, phenanthrene derivatives, lignans/neolignans, flavonoids, alkaloids, and other compounds. Studies of extracts and individual isolated compounds demonstrate a wide range of biological activity. They also provide evidence of nephrotoxicity and carcinogenic effects of phenanthrene derivatives (aristolochic acid – AAI and AAII).

Conclusions: Further study of genus *Asarum* L. species is required to determine the prospects for their use as sources of modern medicines, because of the bioavailability of raw materials, the wide range of biological activity and the therapeutic potential.

Keywords: *Asarum, A. europaeum, A. heterotropoides, A. himalaicum, A. sieboldii, A. canadense, A. caudatum*, biologically active substanthes, ethnopharmacology

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INTRODUCTION

Asarum is a genus of herbaceous plants in the birthwort *Aristolochiaceae* family, commonly known as wild ginger because the rhizome smells and tastes similar to ginger root. "Asarum" is the genitive plural of the Latin "āsa" (alternate form of "āra") that means altar or sanctuary. Representatives of the genus are perennial herbs with creeping rhizome and shortened stems. Leaves are kidney-shaped, heart-shaped, or spear-shaped; whole; with long stalks.

In this review, we try to present updated and generalized data on ethnobotany, phytochemistry, and biological activity of some species of the genus *Asarum L. (Aristolochiaceae Juss.).*

MATERIALS AND METHODS

Information search

Analysis of various literary sources of different years. Electronic scientific search systems (Pubmed, Springer, Wiley Online Library, Science Direct, Biodiversitylibrary), electronic databases (Pubchem, Human Metabolome Database) and other Internet resources were used to search for the relevant literature and the necessary information.

RESULTS AND DISCUSSION

3.1. Distribution and botanical description

Aristolochiaceae Juss. family includes 5-9 genera and more than 600 species. They are distributed mainly in the tropical and subtropical regions of both hemispheres (with a center of species diversity in Southeast Asia), as well as in temperate climatic zones [1, 2, 3]. The genus *Asarum* L. has about 100 plant species distributed in the temperate and partly subtropical regions of the Northern Hemisphere: in Europe (one species), North America (6-16 species), Japan and China (more than 80 species) as well as in Korea, Bhutan, Nepal, India (Sikkim, Jammu and Kashmir states), Vietnam and Taiwan [2, 4]. 3 species of the genus grow in Russia: *Asarum europaeum* L. (European part, Western Siberia), *Asarum heterotropoides* F. Schmidt (Sakhalin, Kuril Islands) and *Asarum sieboldii* Miq. (Seaside Territory, Sakhalin) [5, 6]. The modern genus Latin name comes from the ancient Greek – *asaron* (ασαρον), that was firstly mentioned in "De Materia Medica" by Pedanius Dioscorides (circa 40 AD) [7, 8].

3.2. Ethnobotany

Representatives of the genus *Asarum* L. were widely used in ancient Greece, medieval Europe, India, China, Korea, Japan, and American folk medicine. In folk medicine, infusions and decoctions of *Asarum europaeum L.* (Asarabacca, Hazelwort) are used for lung diseases: silicosis, bronchitis, bronchial asthma, pneumonia, acute respiratory infections, tuberculosis; in case of reproductive system disorders – menstrual irregularities, as an ecbolic in the early stages of pregnancy with diseases of the heart and blood vessels, including hypertension; with gastrointestinal tract disorders – diseases of the liver, enteritis, acute and chronic gastritis, diarrhea, inflammation of the biliary tract, intoxication, to improve digestion; with disorders of the central nervous system – epilepsy, neurotic conditions, hysteria, migraines; in children – with heart disease and convulsions; with other disorders – migraine, fever, malaria, gout, rheumatism, dropsy, with edema, [19,20]

The aerial part of Asarabacca is also used in folk medicine as an expectorant, bacteriostatic, antispasmodic, sudatory,

choleretic, and local anesthetic. It can be effective in the treatment of diseases of the kidneys, urine and biliary tract, as well as infections of the respiratory system [21]; A decoction of the roots is used externally for scabies, dermatoses, headaches, eye diseases, for washing suppurative wounds; paste from freshly chopped leaves are used in abscesses [19]. In medicine, an water infusion of leaves is used to enhance cardiac activity, as a bronchodilator in acute and chronic bronchitis. Decoction of the roots is also effective for the treatment of brain lesions, toothache, anemia, fever, as well as diseases of the eyes, diseases of the throat and oral cavity [20].

In Ayurvedic medicine, the powder from Asarabacca herb (in Sanskrit: Piṇḍatagara, Dvīpāntara Tagara) is used for rheumatism, epilepsy, amenorrhea, radiculitis, ascites, obstructive jaundice, hepatitis, pleurodynia, intercostal neuralgia, hemiplegia, intestinal colic, also diseases of the eyes and spleen [22]. In veterinary practice,rhizome with roots is used as a laxative and emetic; whole plant juice and tincture are applied externally against scabies and lichen in horses [23].

Rhizomes were used as a spice; when rubbed it emits a smell similar to the smell of allspice and camphor [15].

Essential oil from the underground part is locally used in dental practice, perfumery and food industry.

Indigenous peoples of North America used the aerial parts of *Asarum canadense L.* (Canadian snakeroot, Wild ginger) to treat spasmuses in children, to treat disorders of the gastrointestinal tract (including stimulating appetite), and for fever. It was also used as a tonic [24,25,26]. Rhizomes with roots were widely used to treat scarlet fever, colds, coughs, amenorrhea, urinary disorders, headaches, heart and blood diseases, nervous diseases, arthritis, gastrointestinal colic and as a remedy for gastrointestinal discomfort after eating. In herbal preparations, the plant was used in asthma as an anthelmintic and wound healing agent. Means from this plant are considered tonic, diuretic and lowering blood cholesterol. Also, these drugs have stimulating, sudatory, carminative and expectorant properties [24,25,27].

Water infusion on dry rhizomes was used as an oral contraceptive. The boiled root was applied externally for earaches [28,29]. In Ayurvedic practice in India Canadian snakeroot herb powder is used as a substitute for *A. europaeum (Asarabacca)* [22]. Wild ginger root was used as a spice due to the strong ginger smell. Indians also made candied fruit from pieces of rhizome [25,30,31].

Essential oil Canadian snakeroot Oil (USA) is used in the perfume industry. It is obtained by steam distillation from dried root material, [32].

The Indians of California used a decoction of the roots of *Asarum caudatum Lindl. (British Columbia wild ginger, Longtail wild ginger, Wild ginger)* for insomnia, anxiety, hysteria, fever, catarrhal diseases, indigestion and intestinal colic. It is also used as a laxative, analgesic and tonic.

Steamed leaves are used to treat furunculosis, skin infections and toothache, and are applied to the navel of a newborn baby to prevent infection.

A decoction of leaves and plants are used wholly for washing wounds and ulcers, treating rheumatism, headaches, intestinal and joint pains [24,33,34,35]. The whole plant has a strong smell of ginger and lemon. Its leaves are consumed by the natives of America as part of a tea drink. Dry rhizome is used in amulets "for good luck" and to protect against negative influences [36,37,38,39].

Genetically close Asian species and subspecies of *Manchurian wild ginger Asarum heterotropoides F. Schmidt (A. heterotropoides var. Mands-huricum (Maxim.) Kitag .; A. sieboldii var. Mands-huricum Maxim.)* And *A. sieboldii Miq . (A. sieboldii var. Seoulensis Nakai)* are used as sources of a single medicinal plant material (Herba Asari, Asari Radix et Rhizoma, Asiasari radix) under the general name Xi Xin [40]. In Chinese medicine, the *herb Manchurian wild ginger (Herba Asari)* is used as an analgesic and antitussive agent for treating flu, asthma, headache, toothache, and rheumatic pain [41,42]; In the herbal mixtures it is used for migraine, toothache, rheumatism, rheumatoid arthritis, cough, shortness of breath and nasal stuffiness. Herb powder is used for sinusitis [43]. In China and Japan, a decoction of the herb is used for inflammation in the oral cavity, sicchasia, headache and toothache. In Korea, decoction of this plant is used to treat colds and as an insecticide [44].

In traditional Chinese medicine, drugs, that consists of rhizome with roots (Asiasari radix) are used to treat epilepsy, rheumatism, rhinitis, sinusitis, cough, headache and toothache, aphthous stomatitis and nasal polyps. These drugs are also used for inflammation, accumulation of spit in the lungs and various infectious diseases. Also, these drugs have diaphoretic, diuretic, emetic and laxative effects. [44,45,46,47]. In China, Asiasari radix (Xi Xin) is used in the food industry because of its odorous properties [48].

The aerial part of *A. heterotropoides* is used to treat colds, as an analgetic, antitussive, and antiallergic drug [49]. Rhizome with roots is used to treat headache and toothache, cough, colds, sinusitis and rheumatic arthralgia [50]. All parts of the plant *A. sieboldii* have anesthetic, anti-bacterial, antipyretic, antitussive, diaphoretic, diuretic and hypotensive effects. Tinctures and decoctions of herbs are used to treat cavities, periodontal disease, colds and chronic bronchitis, toothache and rheumatic pain [51,52].

In Chinese medicine, rhizome with roots is used as a diuretic, diaphoretic, expectorant, antitussive, antipyretic, analgesic, sedative, wound healing, anthelmintic, improves digestion and laxative. Preparations from the underground part of the plant are used to treat rheumatism, respiratory infections, bronchitis, bronchial asthma, flu, stomatitis, paralysis and liver disease, diseases of the nervous system, headache and toothache, and colic. It is also used as an emetic for intoxication. In Korea, Herba Asari is used to treat pleurisy and pneumonia [53,54,55].

In Tibetan medicine, a decoction of the herb *Asarum himalaicum* J.D. Hooker & Thomson ex Klotzsch (Himalayan wild ginger, Himalayan claw) is used for fever, phlegmon, rheumatism, headache and toothache treatment. The drug has expectorant and analgesic properties [56].

3.3. Medicinal plant raw material and herbal drugs in official medicine

Medicinal plant raw material *A. europaeum* was previously included in the pharmacopoeia of the Netherlands, Germany, Switzerland, Poland, Sweden and Russia (USSR). At the moment, raw materials are excluded from the monographs of the European Pharmacopoeia and the State Pharmacopoeia of the Russian Federation (XIV) [55, 57, 58]. *A. europaeum* (underground and aboveground parts) and *A. canadense* (rhizome with roots) are included in the homeopathic Pharmacopoeias of the USA and India. Homeopathic drugs from these plants (granules and drops) are indicated for treatment of nervous diseases, increased emotionality, distracted attention, craving for alcoholic beverages [23,59,60,61]. The state Pharmacopoeia of the Russian Federation (XIV) includes the "homeopathic mother tincture" monograph for alcohol extract from fresh rhizomes with roots of *A. europaeum*, which is used for the manufacture of homeopathic medicines [58]. A similar homeopathic tincture is used in Germany [62].

Based on the extract from the rhizome with the roots of *A. europaeum* in Europe, a number of medicines were produced ["Escarole" (Germany), "Azarina" (Poland), "Asaropect" (Hungary)]. They were used for bronchitis and bronchial asthma treatment as an expectorant [55,63]. In Russia, *A. europaeum* leaves are one of the constituent components of the "Stopal", "Iscelenie", and "Narcodel" dietary supplements. These drugs are used in the treatment of alcoholism, relief of manifestations of alcohol withdrawal syndrome and alcohol hepatosis [64]. Tincture of fresh leaves is a part of the domestic combined preparation "Acofit",that is used externally for acute radiculitis, sciatica and neuralgia treatment [55].

In addition, the aerial part of *A. europaeum* and *Aristolochia clematitis (Aristolochiaceae)* is a part of the patented mixture herbal product "Herbal Tea of 77 Herbs" with tonic properties. The rhizome of *A. europaeum* (Piṇḍatagara Rhizome) is included in the Ayurvedic Pharmacopoeia of India [22]. The underground part of the Asian species *A. heterotropoides* and *A. sieboldii* is included in the Japanese Pharmacopoeia (Asiasarum Root), as well as in the South Korean Pharmacopoeia and Taiwan's Herbal Pharmacopoeia (Asari Radix et Rhizoma) [65, 66, 67]. Herb (Herba Asari; Xi Xin) of *A. heterotropoides* and *A. sieboldii* [50] is included in the Chinese Pharmacopoeia as medicinal plant raw materials.

3.4. Chemical constituents

Longstanding (1956-2018) phytochemical studies of six representatives of the genus *Asarum L.* made it possible to obtain numerous raw materials chemical components, presented in Table. 1. They are essential oils, alicyclic compounds, terpenoids, steroids, phenylpropanoids, phenolcarboxylic acids, phenanthrene primers, lignans / neolignans, flavonoids, alkaloids / amides, benzenoids, aliphatic compounds, fatty acids and other components. The main components of essential oils are presented in Table 2.

Table 1: Chemical constituents isolated from *Asarum* species: *A. canadense, A. caudatum, A. europaeum, A. heterotropoides, A. himalaicum, A. sieboldii*

Compound	Species	Plant part	Refs
ALICYCLICS:			
4-(Chlormethyl)cyclohexene	*A. heterotropoides*	Rh,R	[68]
Cyclopentadecane	*A. sieboldii*	Up	[69]
Dihydro-β-ionone	*A. himalaicum*	All	[56]
4-(3,3-Dimethyl-but-1-ynyl)-4-hydroxy-3,5,5-trimethyl-cyclohex-2-enone	*A. himalaicum*	All	[56]
1-(6,6-Dimethyl-1,2-epoxycyclohexyl)-1-butyn-3-one	*A. himalaicum*	All	[56]
1,8-Dimethyl-8,9-epoxy-4-isopropyl-spiro[4.5]decan-7-one	*A. himalaicum*	All	[56]
2-(3,3-Dimethyl-2-[(1E)-3-methyl-1,3-butadienyl] cyclopentyl)-2-oxoethyl acetate	*A. himalaicum*	All	[56]
2,2-Dimethyl-1-(3-oxo-but-1-enyl) cyclopentanecarboxaldehyde	*A. himalaicum*	All	[56]
4-(3-Hydroxy-6,6-dimethyl-2-methylenecyclohexyl)-3-buten-2-one	*A. himalaicum*	All	[56]
1(4-Hydroxy-3-isopropenyl-4,7,7-trimethyl-cyclohept-1-enyl)-ethanone	*A. himalaicum*	All	[56]
6-Hydroxy-5-methyl-6-vinyl-bicyclo[3.2.0]heptan-2-one	*A. himalaicum*	All	[56]
2-Hydroxy-4-trimethyl-3-cyclohexene-1-methanol	*A. himalaicum*	All	[56]
3-Isopropyl-5,5-dimethylcyclohexanone	*A. himalaicum*	All	[70]

1-Isopropyl-4,8-dimethylspiro[4.5]decan-7-one	*A. himalaicum*	All	[56]
2-Methyl-2-adamantanol	*A. himalaicum*	All	[56]
3-Methylcyclopentanone	*A. canadense*	R(*)	[32]
3-Methyl-4-(1,3,3-trimethyl-7-oxabicyclo[4.1.0]heptan-1-yl)-3-buten-2-one	*A. himalaicum*	All	[56]
2,3,4,5-Tetramethylcyclopent-2-en-1-ol	*A. himalaicum*	All	[56]
2,2,7,7-Tetramethylcyclo[6.2.1.0(1,6)]undec-4-en-3-one	*A. himalaicum*	All	[56]
4,6,10,10-Tetramethyl-5-oxatricyclo[4.4.0.0(1,4)]dec-2-en-7-ol	*A. himalaicum*	All	[56]
4-(2,6,6-Trimethyl-1-cyclohexen-1-yl)butanoic acid	*A. himalaicum*	All	[56]
1-(1,2,3-Trimethyl-cyclopent-2-enyl)-ethanone	*A. himalaicum*	All	[56]
(1,2,3-Trimethyl-cyclopent-2-enyl)-methanol	*A. himalaicum*	All	[56]
2,4,4-Trimethyl-3-(3-oxobutyl)-2-cyclohexen-1-one	*A. himalaicum*	All	[56]
2,4,6-Tris(cyclohexyl)hept-1-ene	*A. himalaicum*	All	[56]
MONOTERPENS:			
Asarinol *A*	*A. heterotropoides*	R	[45,47]
	A. sieboldii	R	[47,71,72]
Asarinol *B*	*A. sieboldii*	R	[72]
Asarinol *C*	*A. sieboldii*	R	[73]
(+)-Asarinol *D*	*A. heterotropoides*	R	[45]
	A. sieboldii	R	[73]
Asiarinol A	*A. heterotropoides*	Rh,R	[74]
Asiasarinol	*A. heterotropoides*	Rh,R	[74]
	A. sieboldii	Up	[75]
Bois de rose oxide (*Limetol*)	*A. canadense*	R	[76]
Borneol	*A. canadense*	R	[32]
	A. europaeum	All	[21]
	A. heterotropoides	Up,L	[77,78,79,80,81]
	A. himalaicum	All	[56]
	A. sieboldii	Up	[69,77,80]
Bornyl acetate	*A. canadense*	Rh,R	[32,82,83]
	A. europaeum	All	[21]
	A. himalaicum	All	[70]
Camphene	*A. canadense*	R	[32,76]
	A. europaeum	All	[21]
	A. heterotropoides	Up,L	[77,78,79,80,81]
	A. himalaicum	Up	[80]
	A. sieboldii	Up	[77,80]
Camphor	*A. heterotropoides*	Up,L	[77,79,80]
	A. sieboldii	Up	[69,77,80]
2-Carene (*3,7,7-Trimethylbicyclo(4,1,0)hept-3-ene*)	*A. heterotropoides*	All	[84]
δ–3-Carene	*A. europaeum*	All	[21]
	A. heterotropoides	Up,L	[77,78,79,80,81]
	A. sieboldii	Up	[69,77,80]
Car-3-en-2,5-dione	*A. heterotropoides*	Rh,R	[47,74]
	A. sieboldii	Rh,R	[47,71,72,85]
3-Caren-2-one	*A. sieboldii*	Up	[69]

(E)-Carvil acetate	*A. europaeum*	All	[21]
1,4-Cineole	*A. canadense*	R(*)	[32]
1,8-Cineol (*Eucalyptol*)	*A. canadense*	R	[32,76,82]
	A. heterotropoides	Up,L	
[77,78,79,80,81]			
	A. himalaicum	Up	[80]
	A. sieboldii	Up	[69,77,80]
Citronellyl acetate	*A. europaeum*	All	[21]
m-Cymene	*A. heterotropoides*	Up	[80]
	A. himalaicum	Up	[80]
	A. sieboldii	Up	[80]
n-Cymene	*A. europaeum*	All	[21,86]
o-Cymene	*A. himalaicum*	All	[70]
p-Cymene	*A. canadense*	R	[32,82]
	A. europaeum	All	[21,76]
	A. heterotropoides	Up	[77]
	A. sieboldii	Up	[69,77]
p-Cymen-7-ol	*A. sieboldii*	Up	[69]
p-Cymen-8-ol (*2-p-Tolylpropan-2-ol*)	*A. canadense*	R	
[76]			
	A. heterotropoides	Up	[77,80]
	A. sieboldii	Up	[77,80]
m-Cymol	*A. heterotropoides*	L	[79]
o-Cymol	*A. heterotropoides*	Up	[79]
2,3-Dehydro-1,8-cineol	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
1,2-Dimyrtenyl-1,2-ethanediol	*A. himalaicum*	All	[56]
Eucarvone	*A. heterotropoides*	All	
[78,79,80,81,84,87]			
	A. sieboldii	Up	
[69,71,77,80,88]			
2-exo-O-β-D-glucosyl-5-hydroxy-borneol	*A. heterotropoides*	Rh,R	[74]
Fenchene	*A. heterotropoides*	R,Up	[78,81]
Fenchone	*A. heterotropoides*	Up,R	[77]
	A. sieboldii	Up	[77]
Geraniol	*A. canadense*	Rh,R	[32,76,82,83]
Geranyl acetate	*A. canadense*	Rh,R	[32,76,82]
Hodiendiol (*2,6-Dimethyl-3,7-octadiene-2,6-diol*)	*A. canadense*	R	[76]
Hotrienol (*3,7-Dimethyl-1,5,7-octatrien-3-ol*)	*A. canadense*	R	[32,76]
Isoverbenil acetate	*A. europaeum*	All	[21]
Limonene	*A. canadense*	Rh,R	
[32,76,82,83]			
	A. europaeum	All	[21]
	A. heterotropoides	Up,L	
[77,78,79,80,81]			
	A. himalaicum	All	[70]
	A. sieboldii	Up	
[69,77,80,88]			
Limonene oxide	*A. himalaicum*	Up	[80]
Linalool	*A. canadense*	Rh,R	[32,76,82,83]
	A. europaeum	All	[21]
	A. heterotropoides	R,Up	[78,81]
(Z)-Linalool hydrate (*2,6-Dimethyl-7-octene-2,6-diol*)	*A. canadense*	R	[76]
Linalool oxide	*A. canadense*	R	[32,76]
Linalyl acetate	*A. canadense*	Rh,R	[32,82,83]

	A. europaeum	All	[21]
p-Mentha-1,4-dien-7-ol	*A. canadense*	R	[76]
p-Mentha-1,8-diol	*A. canadense*	R	[76]
p-Menth-3-en-1,2,8-triol	*A. sieboldii*	R	[85]
(E)-p-Menthen-1-ol	*A. canadense*	R(*)	[32]
Mint furanon (*3,6-Dimethyl-1,4,5,6,7,7a-hexahydroinden-2-one*)	*A. himalaicum*	All	[56]
Myrcene	*A. canadense*	Rh,R	[32,76,82]
	A. europaeum	All	[21]
	A. heterotropoides	Up,R	[77,78,80,81]
	A. sieboldii	Up	[69,77,80]
β-Myrcene	*A. heterotropoides*	Up	[80]
	A. sieboldii	Up	[80]
Myrcenol	*A. sieboldii*	Up	[80]
Myrtenal	*A. canadense*	R(*)	[32]
Nerol	*A. canadense*	Rh,R	[76,82]
Neryl acetate	*A. canadense*	Rh,R	[32,76,82]
(*Z*)-Ocimene	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[69,77]
(E)-β-Ocimene	*A. canadense*	Rh,R	[76,82]
	A. europaeum	All	[21]
(Z)-β-Ocimene	*A. canadense*	Rh,R	[76,82]
Phellandral	*A. sieboldii*	Up	[80]
Phellandrene	*A. heterotropoides*	Up	[80]
	A. sieboldii	Up	[80]
α-Phellandrene	*A. canadense*	R	[76,82]
	A. heterotropoides	Up,L	[77,78,80,81,89]
	A. himalaicum	All	[70]
	A. sieboldii	Up	[69,77,80]
β-Phellandrene	*A. canadense*	Rh,R	[76,82]
	A. heterotropoides	Up	[80]
	A. himalaicum	Up	[80]
	A. sieboldii	Up	[80]
α-Pinene	*A. canadense*	R	[32,76]
	A. europaeum	All	[21]
	A. heterotropoides	All	[77,78,80,81,84,89]
	A. sieboldii	Up	[69,77,88]
β-Pinene	*A. canadense*	R	[32,76]
	A. europaeum	All	[21]
	A. heterotropoides	Up,All	[77,78,80,81,84,89]
	A. himalaicum	Up, All	[70,80]
	A. sieboldii	Up	[69,77,80,88]
(E)-Pinocarveol	*A. canadense*	R	[32,76]
	A. himalaicum	All	[56]
Sabina ketone	*A. canadense*	R	[76]
Sabinene	*A. canadense*	R	[32,76]
	A. heterotropoides	Up	[77,80]
	A. himalaicum	Up	[80]
	A. sieboldii	Up	[77,80]
Sabinyl acetate	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
Sylvestrene	*A. heterotropoides*	Up	[89]

α-Terpinene	*A. canadense*	Rh	[82]
	A. heterotropoides	Up	[77]
	A. sieboldii	Up	[77]
γ-Terpinene	*A. canadense*	Rh,R	[76,82]
	A. heterotropoides	Up,R	
[77,78,80,81,89]			
	A. sieboldii	Up	[69,77,80]
Terpinen-4-ol	*A. canadense*	Rh,R	[32,76,82]
	A. europaeum	All	[21]
	A. heterotropoides	Up,L	
[77,78,80,81,89]			
	A. sieboldii	Up	[69,77,80]
Terpinen-4-yl acetate	*A. europaeum*	All	[21]
	A. sieboldii	Up	[77]
α-Terpineol	*A. canadense*	Rh,R	[32,76,82,83]
	A. heterotropoides	Up,L	
[77,78,80,81,89]			
γ-Terpineol	*A. canadense*	R(*)	[32]
Terpin-hydrate	*A. canadense*	R	[76]
Terpinolene	*A. canadense*	Rh,R	[32,76,82]
	A. europaeum	All	[21]
	A. heterotropoides	Up,L	
[77,78,80,81,89]			
	A. sieboldii	Up	
[69,77,80,88]			
Terpinyl acetate	*A. heterotropoides*	Up	[77]
cis-4-Thujanol	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
α-Thujene	*A. heterotropoides*	Up,L	[77,89]
	A. sieboldii	Up	[77]
β-Thujone	*A. sieboldii*	Up	[77]
Tricyclene	*A. heterotropoides*	L	[89]
Verbenol	*A. himalaicum*	All	[56]
	A. sieboldii	Up	[69]
Verbenone	*A. canadense*	R(*)	[32]
	A. europaeum	Rh	[90]
	A. heterotropoides	R	[78,81]
	A. himalaicum	All	[56]
SESQUITERPENS:			
β-Acoradiene	*A. europaeum*	All	[21]
α-Agarofuran	*A. europaeum*	All	[90]
Alloaromadendrene	*A. canadense*	Rh	[82]
	A. heterotropoides	L	[89]
	A. himalaicum	All	[70]
α-Amorphene	*A. canadense*	R	[82]
δ-Amorphene	*A. canadense*	R	[82]
γ-Amorphene (*1-Isopropyl-7-methyl-4-methylene-* *-1,2,3,4,4a,5,6,8a-octahydronaphthalene*)	*A. heterotropoides*	Up	[80]
Aristolene	*A. heterotropoides*	Up	[77]
Aristolene epoxide	*A. himalaicum*	All	[56]
Aristolone	*A. canadense*	Rh,R	[32,83]
6,7-*epi*-Aristolone	*A. himalaicum*	Up	[80]
Aromadendrene	*A. europaeum*	All	[21]
Artemether (*β-n-propylether of 11-epi-dihydroartemisinin*)	*A. himalaicum*	All	[56]
5-Azulenemethanol,1,2,3,3a,4,5,6,7-			

octahydro-a,a,3,8-tetramethyl	*A. himalaicum*	Up	[80]
(E)-α-Bergamotene	*A. canadense*	R	[82]
Bicyclo-4(15)-oppositene	*A. canadense*	R	[82]
α-Bisabolene	*A. himalaicum*	All	[70]
β-Bisabolene	*A. canadense*	R	[82]
α-Bulnesene	*A. canadense*	R	[82]
β-Burbonene	*A. europaeum*	St,L	[21]
Cadinene	*A. himalaicum*	Up	[80]
γ-Cadinene	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
τ-Cadinol	*A. himalaicum*	All	[56]
Calarene	*A. heterotropoides*	Up	[80]
	A. himalaicum	Up,All	[56,80]
	A. sieboldii	Up	[80]
	A. heterotropoides	L	[89]
β-Caryophyllene	*A. heterotropoides*	Up,R	[78,81]
Caryophyllene oxide	*A. heterotropoides*	L	[89]
Cascarilladiene	*A. canadense*	R	[82]
β-Cedrene	*A. europaeum*	All	[21]
α-Copaene	*A. europaeum*	All	[21]
ar-Curcumene	*A. canadense*	Rh,R	[82]
β-Dihydroagarofuran	*A. europaeum*	All	[21]
(E)-Dracunculifoliol	*A. canadense*	R	[82]
β-Elemene	*A. europaeum*	St,L	[21]
	A. heterotropoides	Up	[80]
	A. sieboldii	Up	[80]
γ-Eudesmol	*A. canadense*	R	[76]
	A. europaeum	Rh,R	[82]
5-*epi*-7-α-Eudesmol	*A. canadense*	R	[76]
(E)-β-Farnesene	*A. canadense*	R	[82]
	A. heterotropoides	Up	[77]
	A. sieboldii	Up	[69,77]
(Z)-β-Farnesene	*A. heterotropoides*	L	[89]
Furopelargone A	*A. europaeum*	Rh	[91]
Germacrene *A*	*A. canadense*	R(*)	[82]
Germacrene *B*	*A. canadense*	R	[82]
	A. europaeum	All	[21]
Germacrene *D*	*A. canadense*	Rh,R	[82]
	A. europaeum	All	[21]
Globulol	*A. himalaicum*	Up,All	[56,80]
Guaia-6,9-diene	*A. canadense*	Rh,R	[82]
α-Guaiene	*A. canadense*	R	[82]
	A. heterotropoides	Up	[77]
	A. sieboldii	Up	[77]
β-Guaiene	*A. heterotropoides*	Up	[80]
	A. himalaicum	Up	[80]
	A. sieboldii	Up	[80]
δ-Guaiene	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
α-Gurjunene	*A. europaeum*	All	[21]
β- Gurjunene	*A. europaeum*	All	[21,86]
	A. heterotropoides	Up,L	[89]
1,2,3,3*a*,4,5-Hexahydro-1,1,4,4-tetramethyl--2,3*b*-methano-3*b*H-cyclopenta (1,3)cyclopropa(1,2)benzene	*A. himalaicum*	Up	[80]

α-Himachalene	*A. himalaicum*	All	[70]
α-Humulene	*A. canadense*	R	[82]
	A. europaeum	All	[21]
β-Humulene	*A. europaeum*	All	[21]
Humulene epoxide II	*A. heterotropoides*	L	[89]
Isoledene	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
Isovelleral	*A. himalaicum*	All	[56]
Junenol	*A. canadense*	Rh,R	[32,82]
10-*epi*-Junenol	*A. canadense*	R	[82]
Juniper camphor (*Eudesm-7(11)-en-4-ol*)	*A. canadense*	R	[82]
Longifolene	*A. himalaicum*	All	[70]
γ-Muurolene	*A. canadense*	R	[82]
8-*oxo*-Neoisolongifolene	*A. himalaicum*	All	[56]
(E)-Nerolidol	*A. europaeum*	All	[21]
1,2,3,4,4a,5,8,8a-Octahydro-7,8a-acetate-dimethyl-3-(1-methylvinyl)-1-naphthyl	*A. himalaicum*	Up	[80]
Oplopanone	*A. canadense*	R	[76]
Opposita-4(15),7-diene	*A. canadense*	R	[82]
α-Patchoulene	*A. canadense*	R	[82]
	A. heterotropoides	Up,L	[80,89]
γ-Patchoulene	*A. himalaicum*	Up	[80]
Patchoulol	*A. canadense*	R	[82]
	A. heterotropoides	L	[89]
	A. himalaicum	Up,All	[56,80]
α-Santalene	*A. himalaicum*	All	[70]
Sativene	*A. sieboldii*	Up	[69]
Selininan-5,11-diol	*A. europaeum*	Rh	[90]
β-Selinene (*Eudesma-4(14),11-diene*)	*A. himalaicum*	All	[56]
δ-Selinene	*A. canadense*	R	[82]
	A. himalaicum	All	[56]
Selin-11-en-4-α-ol	*A. canadense*	Rh,R	[82]
	A. himalaicum	All	[56]
Selin-5(6)-en-11-ol	*A. europaeum*	Rh	[90]
β-Sesquiphellandrene	*A. canadense*	R	[82]
Seychellene	*A. canadense*	Rh,R	[82]
Spathulenol	*A. europaeum*	L	[21]
	A. himalaicum	Up	[80]
Valencene	*A. himalaicum*	Up	[80]
Zingiberene	*A. canadense*	R	[82]
DITERPENS:			
Phytol	*A. himalaicum*	All	[56]
TRITERPENS:			
24α-Aethylcholestadien-5,22-ol-3β	*A. europaeum*	Up,L	[92]
24α-Aethylcholestanol-3β	*A. europaeum*	Up,L	[92]
24α-Aethylcholesten-5-ol-3β	*A. europaeum*	Up,L	[92]
Cholesten-5-ol-3β	*A. europaeum*	L	[92]
Cycloartenol acetate	*A. himalaicum*	All	[56]
24α-Methylcholesten-5-ol-3β	*A. europaeum*	Up,L	[92]
IRIDOIDS:			
6-*O*-(3,4-Dimethoxy-)cinnamoyl-ajugol	*A. sieboldii*	Up	[75]

STEROIDS:			
Campesterol	*A. sieboldii*	Up	[93]
β-Sitosterol	*A. canadense*	Rh	[83]
	A. europaeum	L	[94,95]
	A. himalaicum	All	[96]
	A. sieboldii	Up	[93]
4,22-Stigmastadiene-3-one	*A. himalaicum*	All	[56]
Stigmasterol	*A. sieboldii*	Up	[93]
BENZEN DERIVATIVES:			
5-Allyl-1,2,3-trimethoxybenzene	*A. heterotropoides*	All	[84]
Benzaldehyde	*A. canadense*	R(*)	[32]
3,4-Benzocyclodec-3-ene-1,5-diyn-7-one	*A. heterotropoides*	Up	[87]
(*R*)-5-(2,3-Dihydroxypropyl)-1,3-benzodioxole	*A. heterotropoides*	R	[45]
1-(3′,4′-Dihydroxy)phenyl-6,7-dihydroxy-isochroman	*A. heterotropoides*	Up	[74]
2-(3,4-Dihydroxy)phenylethyl-*O*-*β*-D-glucopyranoside	*A. heterotropoides*	Up	[74]
3,4-Dimethoxybenzaldehyde	*A. canadense*	R	[76]
2,4-Dimethoxycinnamaldehyde	*A. canadense*	Rh	[83]
3',4'-Dimethoxycinnamaldehyde	*A. sieboldii*	R	[97]
4,6-Dimethoxy-5-methylphthalide	*A. heterotropoides*	Rh,R	[87]
2,5-Dimethoxytoluene	*A. europaeum*	Up,St	[21]
3,5-Dimethoxytoluene	*A. heterotropoides*	Up,L,All	[78,80,81,84,87,89]
	A. sieboldii	Up	[69,77,80,98]
Ethyl-methylterephthalate	A. *himalaicum*	All	[70]
1,4,5,6,7,7a-Hexahydro-7a-methyl-(S)-2H-inden-2-one	*A. himalaicum*	All	[56]
p-Hexylacetophenone	*A. himalaicum*	All	[56]
3-Methoxy-5-methylbenzene-1-*O*-*β*-D-glucopyranoside	*A. heterotropoides*	Up	[74]
3-(3,4-Methylenedioxyphenyl)-1,2-propanediol	*A. heterotropoides*	Up	[74]
Methylbenzoate	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
(1′*R*,2′*R*)-4-*O*-Methylguaiacylglycerol	*A. sieboldii*	R	[85]
2,3,4,5-Tetramethoxyallylbenzene	*A. canadense*	Rh	[83]
2,4,5-Trimethoxybenzaldehyde (*Asarylaldehyde*)	*A. europaeum*	Up	[99]
3,4,5-Trimethoxybenzaldehyde	*A. himalaicum*	All	[56]
2,3,5-Trimethoxytoluene	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[69,77]
3,4,5-Trimethoxytoluene	*A. heterotropoides*	Up,L	[77,78,80,81,89]
	A. sieboldii	Up	[77,80,98]
2,3,5-Trimethyl-1,4-benzenediol	*A. himalaicum*	All	[56]
POLYCYCLIC AROMATIC COMPOUND:			
Cyclohepta[*de*]naphthalen-7(8*H*)-one	*A. sieboldii*	Up	[69]
PHTHALIDES:			
n-Butylphthalide	*A. canadense*	R	[32]
Sedanolide	*A. canadense*	R	[32]
PHENYLPROPANOIDS:			
Asaricin	*A. canadense*	Rh	[82]

	A. heterotropoides	Up	[77,80]
	A. himalaicum	Up	[80]
	A. sieboldii	Up	
[77,80,88,98,100]			
Asaricin A and B	*A. heterotropoides*	Rh,R	[74]
α-Asarone	*A. canadense*	R(*)	[82]
	A. europaeum	All	[21,101]
	A. heterotropoides	Up	[81]
	A. himalaicum	All	[56]
	A. sieboldii	Up,R	[69,102]
β-Asarone	*A. europaeum*	All	[21]
	A. heterotropoides	R	[47,78]
	A. sieboldii	R	[47,102]
γ-Asarone	*A. heterotropoides*	Up	[77,103]
	A. sieboldii	Up,R	[71,97]
Asaronic acid	*A. europaeum*	Up	[99]
Croweacin	*A. heterotropoides*	Up	[77,81]
	A. sieboldii	Up	[77]
Cuminol	*A. canadense*	R	[32,76]
Diasarone I and II	*A. europaeum*	Up	[104]
1-(2,5-Dimethoxyphenyl)propane	*A. heterotropoides*	Up	[81]
Elemicin	*A. canadense*	Rh,R	[32,82,83,76]
	A. europaeum	Up,St	[21]
	A. heterotropoides	Up,L	[77,80,89]
	A. himalaicum	Up,All	[56,80]
	A. sieboldii	Up	
[69,72,77,80,97,102]			
Estragol (*4-Allylanisole; Methylchavicol*)	*A. canadense*	R(*)	
[32]			
	A. heterotropoides	Up,L	
[77,78,80,81,89]			
	A. sieboldii	Up	[69,77,80]
Eugenol	*A. canadense*	R	[32]
Hydroxyelemicin	*A. canadense*	R	[76,82]
(E)-Hydroxyisoelemicin	*A. canadense*	R	[82]
(Z)-Hydroxyisoelemicin	*A. canadense*	R(*)	[82]
(E)-Isocroweacin	*A. sieboldii*	Up	[69]
	A. heterotropoides	Up	[87]
Isoelemicin	*A. canadense*	R	[76,82]
(E)-Isoelemicin	*A. canadense*	R	[32]
	A. europaeum	All	[86]
(E)-Isoeugenol	*A. europaeum*	Up	[86]
	A. heterotropoides	Up	[80]
Kakuol	*A. heterotropoides*	Up	
[77,80,105,106]			
	A. sieboldii	Up	
[77,98,100,105]			
Methoxy-elemicin	*A. canadense*	R	[76,82]
(E)-Methoxy-isoelemicin	*A. canadense*	R	[76,82]
(Z)-Methoxy-isoelemicin	*A. canadense*	R	[82]
2-Methoxy-4,5-methylene-dioxypropiophenone	*A. heterotropoides*	Rh,R	[105,106]
	A. himalaicum	Rh,R	[105]
	A. sieboldii	Rh,R	
[106]			
Methyl eugenol	*A. canadense*	Rh,R	[32,76,82,83]
	A. europaeum	All	[21]

	A. heterotropoides	All	[47,77,78,80,81,84,87,89,103,105]
	A. sieboldii	Up,Ap	[47,69,71,72,77,80,85,88, 97,98,100,102,105,107]
Methyl isoeugenol	*A. canadense*	R	[32,82]
	A. heterotropoides	Up	[80]
(E)-Methyl isoeugenol	*A. europaeum*	All	[21,101]
Methyl kakuol	*A. sieboldii*	R	[98,100]
Methyl thymol (*2-Isopropyl-5-methylanizole*)	*A. canadense*	R	[32,82]
	A. europaeum	All	[21]
	A. heterotropoides	Up,L	[77,80,89]
	A. sieboldii	Up	[69,77,80]
3,4-Methylene-dioxypropiophenone	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
Myristicin	*A. heterotropoides*	Up,L	[77,78,80,81,87,89,105]
	A. himalaicum	Up	[80]
	A. sieboldii	Up,Ap	[69,80,105,107]
Safrol	*A. europaeum*	All	[108]
	A. heterotropoides	Up,L	[77,78,80,81,87,89,105]
	A. himalaicum	Rh,R	[105]
	A. sieboldii	Up,Ap	[69,77,80,88,98,102,105,107]
Thymol	*A. heterotropoides*	Up	[77]
	A. himalaicum	Up	[80]
	A. sieboldii	Up	[69,77]
CARBOXYLIC ACIDS THEIR DERIVATIVES:			
Caffeic acid	*A. europaeum*	Rh,L	[109]
Chlorogenic acid	*A. europaeum*	Rh	[110]
Cichoric acid	*A. europaeum*	Rh	[110]
Cinnamic acid	*A. europaeum*	Rh	[110]
n-Coumaric acid	*A. europaeum*	L	[109]
2,3-Dihydro-2-methyl-6-hydroxybenzofuran-5-carboxylic acid	*A. heterotropoides*	Up	[74]
3′,5′-Dimethoxy-4′-*O*-*β*-*D*-glucopyranosil-cinnamic acid	*A. sieboldii*	Rh,R	[111]
Ferulic acid	*A. europaeum*	Rh,L	[109]
(E)-Ferulic acid	*A. heterotropoides*	Up	[74]
Gallic acid	*A. europaeum*	Rh	[110]
Gallotannic acid	*A. europaeum*	Rh	[110]
4-Hydroxybenzoic acid	*A. heterotropoides*	R	[45]
	A. himalaicum	All	[96]
4-Hydroxycinnamic acid	*A. himalaicum*	All	[96]
Isovanillic acid	*A. heterotropoides*	R	[45]
Protocatechuic acid (*3,4-Dihydroxybenzoic acid*)	*A. himalaicum*	All	[96]
Sinapinic acid	*A. europaeum*	Rh	[112]
Vanillic acid1-*O*-*β*-D-glucopyranoside	*A. heterotropoides*	Up	[74]
PHENANTHRENE DERIVATIVES:			

Aristolactam A-II	*A. heterotropides*	Ap	[113]
Aristolactam-I [45,105,113,114]	*A. heterotropoides*	Up,Ap	
	A. himalaicum	Up,All	[96,105]
	A. sieboldii	Rh,R	[105,113]
Aristolactam-Ia *N*-β-D-glucoside	*A. heterotropoides*	Rh,R	[114,115]
Aristolactam-II	*A. heterotropoides*	Ap	[113]
Aristolactam-II *N*-β-D-glucoside	*A. heterotropoides*	Rh,R	[114]
Aristolactam-III	*A. heterotropoides*	R,Ap	[113,116]
	A. sieboldii	R	[116]
Aristolactam-IIIa	*A. heterotropoides*	Ap	[113]
Aristolactam-IV	*A. heterotropoides*	Up,Ap	[113,114]
Aristolactam-IVa [113,114]	*A. heterotropoides*	Up,Ap	
Aristolactamoside-I and -II	*A. heterotropoides*	Rh,R	[114]
Aristolic acid-II	*A. himalaicum*	All	[96]
Aristolochic acid-I [117,118,119]	*A. canadense*	Up	
	A. caudatum	Up	[117,119]
	A. europaeum	Up,Ap	[62]
	A. heterotropoides	Up,All	
[105,113,114,119,120]			
	A. himalaicum	Up,All	
[96,105,113,119,120]			
	A. sieboldii	Up,All	
[102,105,113,119,120]			
Aristolochic acid-Ia	*A. himalaicum*	All	[96]
Aristolochic acid-II	*A. heterotropoides*	Ap	[113]
	A. sieboldii	Rh,R	[102,113]
Aristolochic acid-IIIa	*A. heterotropoides*	Ap	[113]
Aristolochic acid-IV	*A. heterotropoides*	Ap	[113]
	A. himalaicum	All	[96]
	A. sieboldii	Rh,R	[113]
Aristolochic acid–IVa [45,105,113,114]	*A. heterotropoides*	Up,Ap	
	A. himalaicum	Rh,R	[105]
	A. sieboldii	Rh,R	
[105,113]			
Aristothiolactamoside	*A. heterotropoides*	Rh,R	[114]
Cepharadione A	*A. heterotropoides*	Rh,R	[114]
Debilic acid	*A. himalaicum*	All	[96]
4-Demethoxyaristolochic acid-BII	*A. himalaicum*	All	[96]
9-Ethoxyaristolactam-I and -IV	*A. heterotropoides*	Rh,R	[114,115]
9-Ethoxy-7-methoxyaristolactam-IV	*A. heterotropoides*	Rh,R	[114,115]
9-Hydroxyaristolactam-I	*A. himalaicum*	All	[96]
7-Hydroxyaristolochic acid-I	*A. heterotropoides*	Ap	[113]
	A. himalaicum	All	[96]
7-Methoxyaristolactam-IV	*A. heterotropoides*	R	[45,114]
	A. himalaicum	All	[96]
Norcepharadione-A *N*-β-D-glucoside	*A. heterotropoides*	Rh,R	[114,115]
LIGNANS, NEOLIGNANS:			
Asarinin	*A. heterotropoides*	Rh,R	[49,105]
	A. himalaicum	Rh,R(*)	[105]
	A. sieboldii	Rh,R	[105]
(-)-Asarinin [45,47,74,103,106]	*A. heterotropoides*	Rh,R	

	A. sieboldii	Rh,R	[47,71,72,97,98,100]
Asarinin A and B	*A. heterotropoides*	Rh,R	[74]
Asatone	*A. heterotropoides*	Up	[121]
	A. himalaicum	Up	[121]
	A. sieboldii	Up	[121]
4-((1*S*,3a*R*,4*R*,6a*R*)-4-(Benzo[d][1,3]dioxol-5-yl) hexahydrofuro[3,4-c]furan-1-yl)benzene-1,2-diol	*A. heterotropoides*	Rh,R	[49]
Clemaphenol A	*A. heterotropoides*	Rh,R	[74]
Epipinoresinol	*A. heterotropoides*	Rh,R	[45,49,74]
	A. sieboldii	R	[85]
Episesamine	*A. sieboldii*	R	[85]
Episesaminone	*A. heterotropoides*	Rh,R	[49,74]
(7′*R*)-7′-Hydroxylariciresinol	*A. heterotropoides*	Rh,R	[74]
(+)-7'-Methoxylariciresinol	*A. heterotropoides*	R	[45]
(7*S*,8*R*,7'*S*,8'*S*)-3-Methoxy-3',4'-methylenedioxy-7,9'-epoxylignane-4,7',9-triol	*A. heterotropoides*	R	[45]
(7α,7'β,8α,8'α)-3,4-Methylenedioxy-3',4'-dihydroxy-7,9':7',9-diepoxylignane	*A. heterotropoides*	R	[45]
(1*R*,2*S*,5*R*,6*R*)-5'-*O*-Methylpluviatilol	*A. heterotropoides*	Rh,R	[45,49,74]
Morinols *G*	*A. heterotropoides*	Rh,R	[74]
Neoasarinin A, B and C	*A. heterotropoides*	Rh,R	[74]
Neoasarininoside A and B	*A. heterotropoides*	Rh,R	[74]
Neo-olivil	*A. heterotropoides*	Rh,R	[74]
Piperitol	*A. heterotropoides*	Rh,R	[49]
	A. sieboldii	R	[85]
(-)-Piperitol	*A. heterotropoides*	Rh,R	[45,74]
Pluviatilol	*A. heterotropoides*	Rh,R	[49,105,106]
	A. sieboldii	Rh,R	[85,105]
(-)-Pluviatilol	*A. sieboldii*	R	[100]
Sesamin	*A. heterotropoides*	Rh,R	[105]
	A. himalaicum	Rh,R(*)	[105]
	A. sieboldii	Rh,R	[85,105]
(-)-Sesamin	*A. heterotropoides*	Rh,R	[45,47,49,74,87,106]
	A. sieboldii	Rh,R	[47,71,72,97,98]
Sesaminone	*A. heterotropoides*	Rh,R	[49]
(-)-Tanegol	*A. heterotropoides*	Rh,R	[74]
Tanegool	*A. heterotropoides*	Rh,R	[74]
(-)-Tanegool-7'-methyl ether	*A. heterotropoides*	R	[45]
Xanthoxylol	*A. heterotropoides*	Rh,R	[45,74,103]
	A. sieboldii	Rh,R	[71,97]
	A. sieboldii	R	[85]
FLAVONOIDS:			
1-*O*-*p*-Coumaroyl-xylopyranosyl-glucoside	*A. heterotropoides*	Rh,R	[105]
	A. sieboldii	Rh,R	[105,111]
1-*O*-*p*-Coumaroyl-xylopyranosyl-glucoside heptaacetate	*A. heterotropoides*	Rh,R	[111]
	A. sieboldii	Rh,R	[111]
(*E*)-*p*-Feruloyl-β-D-glucoside	*A. heterotropoides*	R	[45]

1-*O*-Feruloyl-xylopyranosyl-glucoside	*A. heterotropoides*	Rh,R	[105]
	A. sieboldii	Rh,R	[105,111]
1-*O*-Feruloyl-xylopyranosyl-glucoside heptaacetate	*A. heterotropoides*	Rh,R	[111]
	A. sieboldii	Rh,R	[111]
Isorhamnetin	*A. europaeum*	L	[122,123]
Isorhamnetin 3-*O*-galactoside	*A. europaeum*	L	[123]
Isorhamnetin 3,7-*O*-glucoside	*A. sieboldii*	L	[124]
Isorhamnetin 3-*O*-rhamnosyl-galactoside	*A. canadense*	L	[125]
	A. europaeum	L	[123]
Kaempferol	*A. europaeum*	Rh,L	[109]
	A. heterotropoides	Ap	[126]
Kaempferol 3-*O*-galactoside (*Trifolin*)	*A. canadense*	L	[125]
	A. europaeum	L	[123,125,127]
Kaempferol 3-*O*-galactoside-7-*O*-rhamnoside	*A. canadense*	L	[125]
Kaempferol 3,7-di-*O*-glucoside	*A. canadense*	L	[128]
	A. heterotropoides	L,Ap	[129]
	A. sieboldii	L	[124]
Kaempferol 3-*O*-glucoside (*Astragaline*)	*A. canadense*	L	[125]
	A. europaeum	L	[122]
	A. heterotropoides	L,Ap	[124,126]
Kaempferol 3-*O*-rhamnosyl-rutinoside	*A. heterotropoides*	L	[124]
Kaempferol 3-O-rutinoside	*A. europaeum*	L	[123,127]
	A. heterotropoides	L	[124]
(2*S*)-Liquiritigenin 7-O-glucoside	*A. heterotropoides*	Rh,R	[74]
Luteolin	*A. europaeum*	Rh	[110]
Luteolin 7-O-glucoside (*Cynaroside*)	*A. europaeum*	Rh	[110]
(2*S*)-Naringenin	*A. heterotropoides*	Rh,R	[45,74]
Naringenin 5,4′-di-*O*-glucoside	*A. heterotropoides*	Rh,R	[74]
(2*R*)-Naringenin 5,7-di-*O*-glucoside	*A. heterotropoides*	Rh,R	[105]
	A. sieboldii	Rh,R	[105,111]
	A. himalaicum	Rh,R	[105]
(2*R*)-Naringenin 5,7-di-*O*-glucoside (*isomer*)	*A. heterotropoides*	Rh,R	[105]
	A. himalaicum	Rh,R	[105]
	A. sieboldii	Rh,R	[105]
(2*S*)-Naringenin 5,7-di-*O*-glucoside	*A. heterotropoides*	Rh,R	[74,105]
	A. himalaicum	Up,All	[96,105]
	A. sieboldii	Rh,R	[105,111]
(2*S*)-Naringenin 5-*O*-glucoside	*A. heterotropoides*	Rh,R	[45,74]
(2*S*)-Naringenin 7-*O*-glucoside	*A. heterotropoides*	Rh,R	[45,74]
Quercetin	*A. europaeum*	Rh,L	[123,127]
Quercetin 3-*O*-galactoside (*Hyperoside*)	*A. canadense*	L	[125]
	A. europaeum	L	[122,123]
Quercetin 3-*O*-galactoside-7-*O*-rhamnoside	*A. canadense*	L	[125]
Quercetin 3-*O*-glucoside (*Isoquercitrin*)	*A. europaeum*	L	[123,127]

	A. heterotropoides	L,Ap	[129]
Quercetin 3-*O*-glucoside-7-*O*-rutinoside	*A. heterotropoides*	L	[124]
	A. sieboldii	L	[124]
Quercetin 3,7-di-*O*-glucoside	*A. canadense*	L	[128]
Quercetin-3-methyl ether 7-*O*-glucoside	*A. canadense*	L	[128]
Quercetin 3-*O*-robinobioside	*A. canadense*	L	[125]
Quercetin 7-*O*-rutinoside (*Rutin*)	*A. europaeum*	Rh,L	[110,122]
CATECHINS:			
Epicatechin	*A. europaeum*	Rh	[122]
Epigallocatechin gallate	*A. europaeum*	Rh	[122]
CHALCONE GLYCOSIDES:			
Chalcononaringenin 2'-*O*-glucoside-4'-*O*-gentiobioside	*A. canadense*	L	[125]
Chalcononaringenin 2',4'-di-*O*-glucoside	*A. canadense*	L	[125]
	A. heterotropoides	Rh,R	[124]
	A. sieboldii	Rh,R,L	[124]
Chalcononaringenin 4,2',4'-tri-*O*-glucoside	*A. heterotropoides*	Rh,R	[124]
	A. sieboldii	Rh,R,L	[124]
2',4',6',4-Tetrahydroxychalcon-4',6'-*O*-glucoside	*A. europaeum*	Rh	[123]
ANTHOCYANINS:			
Cyanidin 3-*O*-glucoside	*A. canadense*	Fl	[130]
Malvidin 3-*O*-glucoside	*A. canadense*	Fl	[130]

avonoids of Asarum canadense L., which is native to North America. The ¯avonoids of A. canadense have been partially characterized as kaempferol 3,7-di-O-glycoside, quercetin 3,7-di-O-glycoside and quercetin 3-methyl ether 7-O

CYANOGENIC GLYCOSIDES:			
Acacipetalin	*A. himalaicum*	All	[70]

avonoids of Asarum canadense L., which is native to North America. The ¯avonoids of A. canadense have been partially characterized as kaempferol 3,7-di-O-glycoside, quercetin 3,7-di-O-glycoside and quercetin 3-methyl ether

ALKALOIDS, AMIDES:			
Asaramid	*A. heterotropoides*	Rh,R	[74]
Asaramid-II	*A. heterotropoides*	Rh,R	[74]
Asaramid-III	*A. heterotropoides*	Rh,R	[74]
N-trans-Coumaroyltyramine	*A. heterotropoides*	Rh,R	[74]
Higenamine	*A. heterotropoides*	Rh,R	[71,93,131]
N-Isobutyl-2*E*,4*E*,8*Z*-decatrienamide	*A. heterotropoides*	Rh,R	[105]
	A. sieboldii	Rh,R	[85,100,105]
N-Isobutyl-2*E*,4*Z*,8*Z*,10*E*-dodecatetraenamide	*A. heterotropoides*	Rh,R	[87]
N-Isobutyl-2*E*,4*E*,8*Z*,10*E*-dodecatetraenamide	*A. heterotropoides*	Rh,R	[105,132]
	A. himalaicum	Rh,R(*)	[105]
	A. sieboldii	Rh,R	[85,97,98,100,105]
N-Isobutyl-2*E*,4*E*,8*Z*,10*Z*-dodecatetraenamide	*A. heterotropoides*	Rh,R	[105,132]
	A. himalaicum	Rh,R(*)	[105]
	A. sieboldii	Rh,R	[85,100,105]

N-Isobutyl-3,4-methylenedioxy cinnamide	*A. heterotropoides*	Rh,R	[74]
Pellitorine	*A. heterotropoides*	Rh,R	[47,74,93,132]
	A. sieboldii	Rh,R	[47,71]
HETEROCYCLIC COMPOUNDS:			
(3*S*)-7,8-Dihydroxy-3-methyl-1*H*-2-benzopyran-4(3H)-one	*A. heterotropoides*	Ap	[129]
(10*bS*)-8,9-Dihydroxy-1,5,6,10*b*-tetrahydro-2*H*-pyrroloisoquinolin-3-one	*A. heterotropoides*	Ap	[126]
2,6-Dimethylpyrazine	*A. canadense*	R(*)	[32]
Methyl-1*H*-indole-3-carboxylate	*A. heterotropoides*	Ap	[129]
OXYGEN HETEROCYCLIC COMPOUNDS:			
Acetylfuran	*A. canadense*	R(*)	[32]
3,5-Dihydroxy-2-methyl -4*H*-pyran-4-one (*5-Oxymaltol*)	*A. heterotropoides*	Ap	[129]
Furfural	*A. canadense*	R(*)	[32]
5-Hydroxymethylfurfural	*A. heterotropoides*	R	[126]
5-Hydroxymethylfuroic acid	*A. heterotropoides*	Ap	[126]
5-Methylfurfural	*A. canadense*	R(*)	[32]
2-Methyltetrahydro-3-furanone	*A. canadense*	R(*)	[32]
2,10,10-Trimethyl-6-methylene-1-oxaspiro[4.5]decan-7-one	*A. himalaicum*	All	[56]
(7E)-2,6,6-Trimethyl-3-methylene-7-(3-oxobutylidene)oxepanyl acetate	*A. himalaicum*	All	[56]
5,6,6-Trimethyl-5-(3-oxobut-1-enyl)-1-oxaspiro[2.5]octan-4-one	*A. himalaicum*	All	[56]
NITROGEN CONTAINING COMPOUNDS:			
1,1-Dicyano-2-methyl-4-(*P*-cyanophenyl)propene	*A. sieboldii*	Up	[69]
ORGANIC ACIDS:			
(E)-Aconitic acid	*A. europaeum*	All	[133]
Succinic acid	*A. heterotropoides*	Ap	[126]
ALIPHATIC HYDROCARBONS AND THEIR DERIVATIVES:			
n-(Z)-Decen-9-ol	*A. europaeum*	Rh,L	[95]
n-Docosanol	*A. europaeum*	R	[95]
n-Dodecanol	*A. europaeum*	R	[95]
n-Eicosanol	*A. europaeum*	L	[95]
8-Heptadecene	*A. heterotropoides*	Rh,R	[77]
	A. sieboldii	Rh,R	[77]
Hexanal	*A. canadense*	R(*)	[32]
n-Hexadecanol	*A. europaeum*	R	[92]
(Z)-3-Hexenol	*A. canadense*	R	[76]
4-Hydroxy-4-methyl-2-pentanone	*A. canadense*	R(*)	[32]
5-Isopropyl-6-methyl-hepta-3,5-dien-2-ol	*A. himalaicum*	All	[56]
3-Methylbutanal	*A. canadense*	R(*)	[32]
3-Methylbutanol	*A. canadense*	R(*)	[32]
3-Methyl-2-butenal	*A. canadense*	R(*)	[32]
n-Octadecanol	*A. europaeum*	L	[95]
n-Pentadecane	*A. heterotropoides*	Rh,R	[77,78,81,87]
	A. sieboldii	Rh,R	[77,93]
1-Pentadecene	*A. heterotropoides*	Up	[77]

	A. sieboldii	Up	[77]
Pentanol	*A. canadense*	R(*)	[32]
n-Tetracosanol	*A. europaeum*	Rh,L	[95]
Tetradecane	*A. heterotropoides*	Up	[77]
	A. sieboldii	Up	[77]
n-Tetradecanol	*A. europaeum*	R	[95]
3,7,11,15-Tetramethylhexadecen-1-ol	*A. europaeum*	Rh,L	[95]
1-Tridecene	*A. sieboldii*	Up	[77]
2-Undecane	*A. sieboldii*	Rh,R	[134]
ALKYL GLUCOSIDES:			
n-Butyl fructopyranoside	*A. heterotropoides*	R	[106]
FATTY ACIDS AND THEIR DERIVATIVES:			
2,7-Dimethyl-octa-4-enedioic acid	*A. heterotropoides*	Ap	[129]
2,7-Dimethyl-4-octenedioic acid	*A. heterotropoides*	Ap	[129]
2,3-Dihydroxypropyl-16-hydroxyhexadecanoate	*A. heterotropoides*	Rh,R	[74]
Glyceryl-1-stearate	*A. heterotropoides*	Rh,R	[74]
(*Z*)-3-Hexenyl isobutyrate	*A. himalaicum*	All	[56]
Linoleic acid (*9Z,12Z-Octadecadienoic*)	*A. europaeum*	L,S	[92,135]
	A. heterotropoides	Rh,R	[87]
α-Linolenic acid (*9Z,12Z,15Z-Octadecatrienoic*)	*A. europaeum*	L,S	[92,135]
	A. himalaicum	All	[56]
Methyl linolenate	*A. himalaicum*	All	[56]
Oleic acid (*(Z)-9-Octadecanoic*)	*A. europaeum*	L,S	[92,135]
Palmitelaidic acid (*9-hexadecenoic*)	*A. himalaicum*	All	[56]
Palmitic acid (*Hexadecanoic*)	*A. europaeum*	L,S	[92,135]
	A. himalaicum	All	[56]
Stearic acid (*Octadecanoic*)	*A. europaeum*	L	[92]
	A. himalaicum	All	[56]
cis-Vaccenic acid (*(Z)-11-Octadecenoic*)	*A. himalaicum*	All	[56]
MONO- AND OLIGOSACCHARIDES:			
Fructose, Glucose, Sucrose	*A. europaeum*	L	[122]
VITAMINS:			
Ascorbic acid (Vitamin C)	*A. europaeum*	All	[136]
Nicotinic acid (Vitamin PP)	*A. heterotropoides*	Ap	[126]
AMINO ACIDS:			
Arginine, Alanine, Cysteine, Glycine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Serine, Threonine, Tryptophane, Tyrosine, Valine	*A. europaeum*	L	[122]

Rh = rhizome; R = root; L = leaf; St = stem; Fl = flowers; S = seeds; Ap = aerial part; Up = underground part; All = all plant; (*) – trace

Table 2: Major components of the essential oils of *Asarum* species: *A. canadense, A. europaeum, A. heterotropoides, A. himalaicum, A. sieboldii*

Species	Components	Plant part; (%)	Refs
	Methylisoeugenol (53,8%) Linalool (12,5%)	Rh; (1,3%)	[82]

	α-Terpineol (6,6%) Geraniol (3,3%)		
1. *Asarum canadense*	(*E*)-Isoelemicin (20%) Elemicin (4,9%) Junenol (13,0%) Guaia-6,9-diene (3,7%) Zingiberene (3,0%)	R; (1,96%)	[82]
	Methyleugenol (36,1-44,5%) Linalyl acetate (8,0-41,4%) Geraniol (0,8-7,2%) Linalool (5,0-5,3%)	Rh,R; (3,0%)	[32,83,137]
2. *Asarum europaeum*	Chemiotypes: 1. α-Asaron - type: α-Asaron (70%) (*E*)-Methylisoeugenol (0,5%) (*E*)-Isoelemicin (0,5%) 2. (*E*)-Methylisoeugenol - type: (*E*)-Methylisoeugenol (40%) α-Asaron (30%) (*E*)-Isoelemicin (0,5%) 3. (*E*)-Isoelemicin - type: (*E*)-Isoelemicin (45%) α-Asaron (35%) (*E*)-Methylisoeugenol (1%) 4. Eudesmol - type: Eudesmol (40%) α-Asaron (0,5%) (*E*)-Methylisoeugenol (0,5%) (*E*)-Isoelemicin (0,5%)	Ap,Up; (0,7-4,1%)	[138,139]
	α-Asaron (30-50,2%) Methylisoeugenol (15-20%) 2,4,5-Trimethoxybenzaldehyde (2-3%) (*Asarylaldehyde*)	Rh,R; (2,13-3,69%)	[140,141]
3. *Asarum heterotropoides*	Methyleugenol (28,7%) Safrol (19,6%) 3,5-Dimethoxytoluene (12,6%) δ-3-Carene (6,1%)	R; (5,01%)	[89]
	Methyleugenol (27,0%) Safrol (15,7%) α-Pinene (6,8%) 3,5-Dimethoxytoluene (6,4%)	L; (4,85%)	[89]
	Eucarvone (1,8-16,8%) 3,5-Dimethoxytoluene (6,6-26,5%) 3,4,5-Trimethoxytoluene/Methyleugenol (6,4-31,7%) 2,3,5-Trimethoxytoluene (1,6-6,7%)	Up	[77]
	Methyleugenol (37,6%)	Up	[87]

		Sesamin (22,1%) Safrol (14,7%)		
	S.Korea:	Eugenol (22,6%) Pentadecane (6,8%) 2,3,5-Trimethoxytoluene (5,5%) 4-(Chlormethyl)cyclohexene (3,4%) Myristicin (3,3%) Sesamin (3,2%) Kakuol (2,6%)	Up	[68]
		Methyleugenol (59,4%) Eucarvone (24,1%) 5-Allyl-1,2,3-trimethoxybenzene (5,7%) 3,7,7-Trimethylbicyclo(4,1,0)hept-3-ene (4,9%)	All	[84]
		Methyleugenol (20,2-62,9%) Safrol (2,7-32,4%) 3,5-Dimethoxytoluene (2,0-18,6%) Eucarvone (1,5-19,2%) 3,4,5-Trimethoxytoluene (1,2-11,1%)	Up; (1,9-2,6%)	[80]
4. *Asarum himalaicum*		Patchoulol (27,4-52%) Elemicin (13,1-42,2%) β-Pinene (3,9-4,2%) Sabinene (2,3-3,4%) Calarene (2,1-3,4%)	Up; (0,6-0,8%)	[80]
		1,8-Cineol (*Eucalyptol*) (14,1-24,9%) Croweacin (5,6-13,5%) Pentadecane (8,4-20,8%) Asaricin (7,0-13,4%)	Up	[77]
5. *Asarum sieboldii*		Methyleugenol (48,3-61,1%) Eucarvone (11,1-13,9%) Elemicin (4,8-11,1%) δ-3-Carene (4,0-6,4%) 3,5-Dimethoxytoluene (0,9-5,6%)	Up; (1,9-2,3%)	[80]
	S.Korea:	Methyleugenol (56,3%) Eucarvone (11,5%) (*E*)-Isocroweacin (8,6%) Safrol (5,8%) 3,5-Dimethoxytoluene (5,6%) δ-3-Carene (2,1%)	Up	[69]

Rh = rhizome; R = root; L = leaf; Ap = aerial part; Up = underground part; All = all plant.

3.5. Biological activity

3.5.1. Antimicrobial activity

Phenylpropanoids *A. europaeum* show antimicrobial activity against gram-positive bacteria. In the experiment, the methanol extract proved to be the most effective against *Staphylococcus epidermidis*, and the ethanol extract against *S. aureus* [142,143]. The methanolic root extract of Manchurian wild ginger *(Asarum heterotropoides var. Manshuricum / A. sieboldii)* shows strong antimicrobial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) KCCM 11812, 40510 and *S. aureus* ATCC 25923 [144]. This extract also exhibits an inhibitory effect on the growth of gram-positive bacilli bacteria *Listeria monocytogenes*, that are a food pathogen. Also they cause listeriosis. The four components of the extract of [(±) -car-3-en-2,5-dione, (–)-azarinin, (–)-sesamine, methyleugenol] demonstrated a potent antimicrobial effect in vitro in *L. monocytogenes* strains [47].

Essential oil from the underground part of the *A. heterotropoides var. mandshuricum* exhibits antimicrobial and inhibitory activity against five types of epidermal bacteria, producing human body odor (*Staphylococcus epidermidis*, *Propionibacterium freudenreichii*, *Micrococcus luteus*, *Corynebacterium jeikeium* and *Corynebacterium xerosis*) [87]. This essential oil also has an inhibitory effect on the growth and development of *Streptoccus* sp., *Shigella* sp. and *Salmonella typhi* [145]. The ethanol and aqueous extracts from Herba Asari (*A. sieboldii*) experimentally inhibited the growth and synthesis of acidic production of *S. mutans*., Significantly reduced the adhesion of bacteria on the surface of tooth enamel. *Streptococcus mutans* plays a major role in the formation of plaque and dental caries [52].

3.5.2. Antifungal activity

The methanol extract from the aerial part of *A. caudatum* exhibits moderate antifungal activity in relation to Aspergillus flavus, A. fumigatus, Candida albicans, Fusarium tricuictum, Microsporum cookerii, M. ypseum, Saccharomyces cerevisiae, Tricodermaagirida 6 virida girida cereviaida [146]. Essential oil from the roots of *A. sieboldii* demonstrated very high antifungal activity against human pathogenic fungi (*Aspergillus fumigatus*, *A. niger*, *Cryptococcus neoformans* and *Candida albicans*) [147]. Methyleugenol isolated from the raw materials of the same plant showed antifungal properties against mycotoxin-producing fungi (*Aspergillus flavus*, *A. parasiticus*, *A. ochraceus*, and *A. versicolor*) [148]. Essential oil (methyleugenol) from the roots of *A. heterotropoides* var. *mandshuricum* exhibits significant fungicidal activity against phytopathogenic fungi *Alternaria humicola*, *Colletotrichum gloeosporioides*, *Rhizoctonia solani*, *Phytophthora cactorum* and *Fusarium solani* [84], *Gloeosporium* sp., *Pestalotiopsis* sp., *Actinonema rosae*, *Alternaria* sp., *Fusarium* sp., *Bipolaris* sp., *Curvularia lunata* and *Ustilago maydis* [149,150].

Essential oil from the roots of *A. sieboldii* exhibits fungicidal activity against the *Neolentinus lepideus* (*Basidiomycota*, *Gloeophyllaceae*), that destroys the treated wood of sleepers and pillars [69]. The ethanol extract from this plant shows an inhibitory effect on the growth of the mycelium of the phytopathogenic fungus *Verticillium alboatrum*, that causes verticilliosis wilt and early withering of vegetable and industrial cultures [151]. The kakoul phenylpropanoid isolated from the root of *A. sieboldii* showed fungicidal activity against the phytopathogenic fungus *Colletotrichum orbiculare*, that causes cucumber anthracnose. This substance also completely inhibited the mycelial growth of the fungi *Botrytis cinerea* and *Cladosporium cucumerinum*, causing gray rot and olive spotted of cucumber [152].

3.5.3. Acaricidal activity

Ethanol extract of the roots of *A. heterotropoides* and preparations of steam distillate (methyleugenol, safrole, δ-3-karen, α-azarone, pentadecane) show acaricidal activity against the chicken tick Dermanyssus gallinae (Mesostigmata, Dermanyssidae), a parasitizing wild bird [81]. Petroleum ether extract and essential oil from the roots of *A. heterotropoides / A. sieboldii* show acaricidal toxicity to Dermatophagoides farinae dust mites (Acari, Pyroglyphidae). Ticks of this species cause tick-borne sensibilization in humans. This type of sensibilization occurs by asthma attacks, diffuse neurodermatitis, allergic rhinitis and conjunctivitis. Metilevgenol showed the highest mortality rate among adult mites of D. Farinae (during bioassay of components of essential oil for contact toxicity) [153].

3.5.4. Insecticidal and repellent activities

Toxic and repellent effect of essential oil from the roots and leaves of *A. heterotropoides var. mandshuricum* manifested itself in relation to pests of stocks of plant products and biological museum collections – the Lasioderma serricorne tobacco beetle (Coleoptera, Ptinidae) and the Liposcelis bos-trychophila haymaker (Psocoptera, Liposcelididae) [89]. The same effect was shown by the essential oil from the roots of *A. sieboldii* against L. serricorne (Coleoptera, Ptinidae) [69] and rice weevil Sitophilus oryzae (Coleoptera, Curculionidae). A bioassay of the components of the essential oil from the roots of *A. sieboldii* revealed a high fumigant toxicity of eukarvon and safrole [154].

3.5.5. Larvicidal and nematocidal activities

The high larvicidal and nematocidal activity of *A. europaeum* against larvae of the yellow-fever mosquito (Aedes aegyptii, Culicidae) and free-living roundworms (Caenorhabditis elegans and Panagrellus redivivus, Rhabditidae) was revealed [155]. The larvicidal activity of a number of compounds isolated from the roots of *A. heterotropoides* has been established in relation to the larvae of non-malarial mosquitoes (Culex pipiens pallens, Aedes aegypti and Ochlerotatus togoi, Culicidae). Safrol was the most toxic component for C. p. pallens and *A. aegypti*, while terpinolene was the most toxic to Ochlerotatus togoi [78]. Other studies have shown the highest larvicidal activity of (–)-azarinin and pellitorin in relation to populations of common mosquito larvae (C. p. Pallens), that are resistant to synthetic insecticides [156].

Phenylpropanoids (methyleugenol, myristicin, and safrol) from the aerial part of *A. sieboldii* showed significant fumigant toxicity to the larvae of Lycoriella ingenua and Coboldia fuscipes (Diptera, Scatopsidae) during bioassay. These larvae are the most important pests of cultivated fungi [107]. The methanol extract of the roots of *A. sieboldi* showed high larvicidal activity against larvae of the housefly Musca domestica (Diptera, Muscidae) [157].

3.5.6. Anti-inflammatory and antinociceptive activities

Lignan-containing water and ethanol extracts from the underground part of *A. heterotropoides var. mandshuricum/A. sieboldii* exhibited the high antinociceptive and anti-inflammatory pharmacodynamics in experiments [74,158,159,160]. The methanol extract of radix *A. sieboldii* shows an antinociceptive and anti-inflammatory effect in a rat experiment. It's analgesic effect is stronger than that of aspirin [85,161]. Amphoterin

Nuclear Protein (HMGB1) is a cytokine mediator. With necrosis of cells and tissues, it can be released and bind to the innate immunity receptor TLR4. This leads to the secretion of cytokines by macrophages and subsequent inflammatory reaction. In the experiment, episesamine potentially inhibits the release of HMGB1 and HMGB1-dependent inflammatory responses in human endothelial cells. It also inhibits HMGB1-mediated hyperpermeability and leukocyte migration in mice. The results of the study suggest the use of epi-sesamine for the treatment of various severe vascular inflammatory diseases [162].

The active components (phenylpropanoids) of *A. europaeum* infusion showed broncholytic and anti-asthma effects [163]. α-Asarone (one of the phenylpropanoids of this plant) exhibits a local anesthetic activity, that is close to benzocaine [101]. Herb extract of *A. heteropoides var. mandshuricum / A. sieboldii* when administered intravenously effectively relieves bronchospasm in an animal experiment. The alcohol solution of the essential oil of this plant in a mixture with borneol, when applied sublingually in patients with angina pectoris and coronary heart disease, has a therapeutic effect similar to that of nitroglycerin. Clinical trials of a paste from a mixture of grass *A. heteropoides var. mandshuricum* / *A. sieboldii* with glycerin have been shown to be effective in aphthous ulcers.

Asiasari radix essential oil shows an anti-inflamatory and anesthetic effect in animal experiments. When administratered intraperitoneally, it reduces edema in the legs of rats [145]. The traditional herbal medicine of Japan and China (from Japanese: Mao-bushi-saishin-to; from Chinese: Ma-Huang-Fu-Zi-Xi-Xin-Tang) consists of three ingredients: Ephedrae Herba (4 g), Asiasari Radix (3 g) and Aconiti Tuber (1 g). In clinical trials of this drug, it was shown that the drug reduces the level of C-reactive protein (CRP) and body temperature in elderly patients infected with Pseudomonas aeruginosa [164]. In China, a patented patch of essential oil of *A. Himalaicum* leaves is produced. It is used for headaches and migraines. Anti-nociceptive effect is achieved by transdermal absorption [165].

3.5.7. Antitussive activity

Roots from *A. heterotropoids* contain active components that suppress the cough reflex (higenamine and methylenegenol). It was found that higenamine amide is a β-adrenergic agonist (stimulator of β-adrenergic receptors), and phenylpropanoid methyleugenol has a relaxing effect on smooth muscle fibers of the trachea [131]. *A. europaeum* grass exhibits expectorant properties [166].

3.5.8. Anti-allergic activity

The aqueous extract of Asiasari radix (*A. heteropoides* var. *mandshuricum* / *A. sieboldii*) has anti-allergic activity. In vivo and in vitro extract showed an inhibitory effect on blood IgE immunoglobulin and its products that cause hypersensitivity and are directly involved in allergic reactions [167]. The methanol extract of A. sieboldi roots exhibits in vitro and in vivo antiallergic properties [97]. The tablet preparation from Asiasari radix (in an experiment on Guinea pigs) shows a significant effect on nasal hypersensitivity, prevents allergic rhinitis by reducing the amount of histamine in the nasal mucosa and blocking the activity of nitric oxide synthase (NOS) [168]. Azarinin isolated from Herba Asari extract may play an important role in suppressing immune graft rejection after heart transplantation, prolong allograft survival time, and protect the donor organ [151].

3.5.9. Inotropic and chronotropic effects

Extract of *A. heteropoda* var. *mandshurica* / *A. sieboldii* herb when administered intravenously increases heart rate and stroke volume in animal experiments [145]. The same stimulating effect is demonstrated by the *A. europaeum* herb [169].

3.5.10. Hypolipidemic effect and antithrombotic activity

α-azarone showed a significant decrease in blood lipid levels (lipid-lowering effect) and showed antithrombotic properties in in-vitro and in-vivo experiments on rats and mice [170]. Sesamine and episesamine contained in the roots of *A. sieboldii* exhibit antithrombotic properties. What is more, the inhibitory activity on anticoagulation by episesamine was stronger. Anticoagulant activity was studied by monitoring activated partial thromboplastin time (aPTT), prothrombin time (PT), cell thrombin activity and activated factor X (FXa) [171]. In addition, the amide compound pellitorin found in the subterranean parts of *A. sieboldii* / *A. heterotropoides* also has antithrombotic activity and causes anticoagulant effects in mice [172].

3.5.11. Antisecretory and antiulcer activities

Aqueous and ethanol extracts of a mixture of *A. europaeum* root and *Symplocos racemosa* bark (*Symplocaceae*) show a potent antisecretory and antiulcer effect in an in vivo experiment on rats. This justifies the traditional use of this herb for the treatment of peptic ulcer disease [173].

3.5.12. Hepatoprotective activity.

Injection of an aqueous extract of Asiasari radix showed significant hepatoprotective activity, showed a decrease in the content of total cholesterol and phospholipids in the blood serum in an experiment on rats. [174].

3.5.13. Antioxidant protection

A. heterotropoides flavonoids showed antioxidant activity under experimental conditions [175]. A similar effect is demonstrated by the essential oil from the underground part of *A. heterotropoides* var. *mandshuricum* [87]. Asiasari xixin drugs were tested in the D-galactose induced mice aging model. This study investigated the effect of the herb on the activity of superoxide dismutase (SOD), glutahione peroxidase (GSH-Px) and nitric oxide synthases NOS, to know the damages degree of body caused by free radicals. An increase in the activity of enzymes was revealed and an anti-aging effect was shown [176].

3.5.14. Neuroprotective activity

The components of the root extract of *A. sieboldii,* (–)-sesamine, kakoul, N-isobutyl-2E, 4E, 8Z, 10E-

dodecatatetraenamide and 3,4,5-trimethoxytoluene, showed significant inhibitory activity against lipopolysaccharide-induced production of nitric oxide (NO) in the microglial immune cells of BV-2 of the central nervous system and can be recommended for inflammation and neurodegenerative diseases [98].

Essential oil *A. heterotropoides* var. *mandshuricum* rhizome with roots effectively suppresses depressive behavioral responses in a mouse experiment. Therefore, it can be prescribed in stressful situations to reduce anxiety [68]. Methanol extract and its subfractions from Asiasari radix can exert memory-enhancing effects and have a protective effect in brain cells due to activation of insulin receptors and ERK I/II, show inhibition of rat cholinesterase activity [177]. These substances contain active components that significantly inhibit cell death induced by α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) in PC12 (differentiated cell lines) and neuroglia, and also take part in the inhibition of AMPA receptors [178].

3.5.15. Hair growth promoting effect

Ethanol extract of Radix Asiasari showed potent stimulation of hair growth in experiments in mice [179].

3.5.16. Antiviral activity

Aqueous *A. heterotropoides* var. *mandshuricum* herbal extracts have been shown to be effective against human papillomavirus (HPV) [180].

3.5.17. Anti-melanogenesis activity

The methanol chromatographic fraction of Asiasari Radix extract from the ethyl acetate layer (PPAR) shows an inhibitory effect on melanin synthesis in the experiment. The fraction of PPAR extract in B16F10 melanoma cells leads to a decrease in tyrosinase activity and melanin synthesis, as well as protein expression associated with the process of melanogenesis [181].

In addition, PPAR inhibits α-MSH-induced melanogenesis in melanoma cells of B16F10 mice through activation of mitogen-activated protein kinase/extracellular signal-activated kinase (MEK/ERK) and the intracellular signaling pathway PI3K/Akt through the destruction of MITF, that may lead to a decrease in tyrosinase content [182]. Individual root compounds of *A. sieboldii* influence the biosynthesis of melanin in the body. Lignan (–)-azarinin showed the strongest inhibitory effect on melanogenesis [71].

3.5.18. Cytotoxic and anticancer activities

Asiasari Radix, used in the herbal formulation of anticancer drugs with some plant extracts, improves clinical outcomes in cancer chemotherapy [183]. Ethanol extract from Asiasari Radix significantly increased the sensitivity of HeLa tumor cells to paclitaxel (cytostatic anticancer drug) [179]. Preparations from Asiasari Radix enhance neurotrophic factors in the mouse myoblast cell line (C2C12), that stimulate growth and stabilize the formation of neurites in cancer cell lines (PC12D) [184]. *A. sieboldii* var. *seoulense* and *A. himalaicum* herb extracts showed cytotoxic selective activity against one or two of the four tumor cell lines studied (HL-60, BGC-823, KB, and Bel-7402) [185].

Intraperitoneal administration of *A. himalaicum* and *A. heterotropoides* var. *mandshuricum* inhibits granuloma proliferation induced by implantation of cotton granules in an experiment on rats (this may be due to a decrease in the content of zinc in blood serum) [186]. Lignan (–)-azarinin isolated from the *A. sieboldii* roots showed potent cytotoxicity against human ovarian cancer cells (A2780 and SKOV3) and immortalized cells of the surface ovarian epithelium (IOSE80PC), causing their apoptotic death [100]. Hydrophobic lignans (–)-azarinin and xanthoxylol isolated from the roots of *A. heterotropoides* var. *mandshuricum* demonstrated antitumor activity in a two-step carcinogenesis test on the skin and lungs of mice. In addition, the phenylpropanoids methyleugenol and γ-azarone exhibited an inhibitory effect upon activation of the early Epstein-Barr virus antigen (EBV-EA). These results suggest that these compounds may be antitumor stimulants [103].

Phenylpropanoids (methyleugenol, elemicin, and γ-azarone) isolated from the *A. heterotropoides* roots showed a suppression of the genotoxic activity of chemical mutagens in DNA damage reaction (SOS, umu test Salmonella typhimurium TA1535 / pSK1002) [187,188]. Phenanthrene derivatives (aristolactams) Isolated from *A. heterotropoides* var. *mandshuricum* showed cytotoxic activity in tests of cell lines (HK-2) of the human epithelium of the proximal tubule of the kidney [114].

(E)-aconitic acid isolated from the herb *A. europaeum* protects against cancer in an in vitro experiment [133]. An aqueous extract of this herb also showed positive results of tests of anti-tumor activity [143]. Human colorectal cancer affects 6% of the world's population. It is the third most common oncological disease in Western countries [189]. Ethanolic extract of *A. heterotropoides* var. *mandshuricum* roots exhibited an antitumor effect on HCT-116 human colon cancer cells in an in vitro experiment [190]. *A. heterotropoides* roots extract inhibits the growth of human lung cancer A549 cell lines (NSCLC). Isolates (7-methoxyaristolactam-IV and (7α, 7'β, 8α, 8'α)-3,4-methylenedioxy-3',4'-dihydroxy-7.9': 7 ', 9-diepoxylignane) induce reduced regulation of NO production, FOXP3 expression, and transcriptional activity of HIF-1α [45].

3.5.19. Toxic and nephrotoxic effects

Toxicity studies have shown that safrole and methyleugenol from Asari radix et rhizoma (Xixin) can be hepatocarcinogenic and/or genotoxic substances. The amount of safrole decreases by more than 92% and reaches therapeutic doses after 1-hour boiling of raw materials [191]. The phenylpropanoids α- and β-azarone exhibit genotoxic and carcinogenic properties [21,192]. Large doses of *A. europaeum* herb cause sting in the mouth and throat, nausea, vomiting, gastric bleeding, gastroenteritis with diarrhea, digestive problems, uterine bleeding, and central nervous system disorder, in some cases leading to death from central apnea [193,194]. Almost all representatives of the *Asarum* L. genus contain phenanthrene derivatives

(aristolochic acids), that have nephrotoxic and carcinogenic effects [119,195,196,197].

A study of the nephrotoxicity of *A. himalaicm* and *A. heterotropides* leaves in laboratory animals showed that even one leaf causes kidney damage in rabbits and leads to partial death of mice. It was found that the renal toxicity of *A. himalaicm* leaves is lower than that of *A. heterotropides* [198,199]. Clinical evidence suggests that aristolochic acid (AAI and AAII) is a genotoxic mutagen that forms DNA adducts after metabolic activation and is a potent cytotoxin with an extremely short latency. For this reason, patients develop a destructive fibrous process in the kidneys (nephropathy), as well as urothelial carcinoma of the upper urinary tract (UTUC) [62,113]. In the United States, the Food and Drug Administration (FDA), Asarum sp., as well as other plants containing or presumably containing aristolochic acid, are included in the base of poisonous plants [200].

In Russia, all *Asarum* L. species (all parts, essential oil, oil from the roots and rhizomes) are included in the list of plants containing potent, narcotic or toxic substances that are prohibited for use in the composition of food supplements [64]. Species of *Aristolochia* and *Asarum* genera are prohibited for therapeutic use in Australia, but are not included in the lists of toxic herbs in Asian countries [201]. More than 250 traditional Chinese proprietary drugs containing aristocholium acid and its derivatives are still sold in Chinese markets today. All products containing or presumably containing aristolochic acid or its derivatives should be prohibited for use on the world market [202, 203]. Most synthetic dyes are very resistant to various chemical and physical methods of removing them from wastewater, so there is a problem of environmental pollution. Platinum and gold nanoparticles (Au-Pt) have catalytic properties and contribute to the elimination of toxic chemicals. Therefore, the biological synthesis of metal nanoparticles is an important area of nanotechnology research. The biosynthesis of Au-Pt metal nanoparticles using the aqueous extract of *A. europaeum* raw materials in the experiment turned out to be safe and environmentally friendly, economically efficient. It ensured the complete reclamation of malachite green and methylene blue in wastewater [204].

CONCLUSION

The review summarizes information on phytochemistry, biological activity, medical use, and utilitarian use of six species of the *Asarum* L genus. Phytochemical studies show the presence of various chemical components (essential oils, terpenoids, phenylpropanoids, lignins, phenanthrene derivatives, flavonoids, alkaloids, etc.) and confirm the validity of the use of these plants in traditional medicine for the treatment of many diseases. Biologically active compounds isolated from plants are of interest for the creation of new drugs. Although insufficient scientific and/or clinical evidence has been provided to justify their applicability in modern medical practice.

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CONFLICT OF INTEREST

None.

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