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Houttuynia cordata Thunb. (*Saururaceae* Martinov): botany, ethnobotany, phytochemistry and biological activity (review)

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Abstract

Introduction. The purpose of the review is to present new and summarized data on morphology, ethnobotany, phytochemistry, and biological activity of the *Houttuynia cordata* Thunb. (*Saururaceae*), which is used in Asian folk medicine as a medical plant.

Text. *Houttuynia cordata* Thunb. Of the genus *Saururaceae* – a plant native to southeast Asia that grows in moist soil. In northeast India, it's used extensively in cooking. Actively used in folk medicine.

Conclusion. The phytochemical analysis of the plant showed that composition of the plant includes ethereal oils, terpenoids, steroids, phenylpropanoids, phenolcarboxylic acids, glycosides, lignans/neolignans, flavonoids, phenanthrene derivatives, alkaloids, and other compounds. There is a review of content and distribution of the biomarker compounds as well as of study of extracts and various isolated compounds of wide range of biological activities including powerful antiviral properties (such as flavonoids) acting against a range of viruses (such as HSV-1, H1N1, and DENV) and such coronaviridae as SARS-CoV and SARS-CoV-2. Bioavailability of the plant raw materials, lack of toxicity, wide range of biological activities, and therapeutic potential require further target study of the *Houttuynia cordata* to determine the prospect of using of the herb as modern medicinal plant raw material.

Keywords: *Houttuynia cordata* Thunb., morphology, ethnobotany, phytochemistry, biological activity

Conflict of interest. The authors declare that they have no obvious and potential conflicts of interest related to the publication of this article.

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Houttuynia cordata Thunb. (*Saururaceae* Martinov): ботаника, этноботаника, фитохимия и биологическая активность (обзор)

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Резюме

Введение. Цель обзора – представить новые и обобщенные данные по морфологии, этноботанике, фитохимии и биологической активности *Houttuynia cordata* Thunb. (*Saururaceae*), которая используется в азиатской народной медицине в качестве лекарственного растения.

Текст. *Houttuynia cordata* Thunb. из рода *Saururaceae* – растение родом из Юго-Восточной Азии, произрастающее во влажной почве. На северо-востоке Индии его широко используют в кулинарии. Активно используется в народной медицине.

Заключение. Фитохимический анализ растения показал, что в состав растения входят эфирные масла, терпеноиды, стероиды, фенилпропаноиды, фенолкарбоновые кислоты, гликозиды, лигнаны/неолигнаны, флавоноиды, производные фенантрена, алкалоиды и другие соединения. Представлен обзор содержания и распределения соединений-биомаркеров, а также продемонстрированы исследования экстрактов и различных выделенных соединений с широким спектром биологической активности, включая мощные противовирусные свойства (например, флавоноиды), действующих против ряда вирусов (ВПП-1, H1N1 и DENV) и коронавирусов, таких как SARS-CoV и SARS-CoV-2. Биодоступность растительного сырья, отсутствие токсичности, широкий спектр биологической активности и терапевтический потенциал требуют дальнейшего целенаправленного изучения *Houttuynia cordata* для определения перспектив использования травы в качестве современного лекарственного растительного сырья.

Ключевые слова: *Houttuynia cordata* Thunb., морфология, этноботаника, фитохимия, биологическая активность

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Вклад авторов. А. М. Анцышкина, Д. О. Боков, С. Г. Зайчикова участвовали в написании текста статьи, провели обзор литературы. Ее систематизацией и анализом занимались Т. В. Простодушева, А. В. Стреляева, Л. В. Федорова. Все авторы прочитали и согласились с опубликованной версией рукописи

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Introduction

Family *Saururaceae* Martinov (SRR [1]) includes 4 genres of (*Saururus* L., *Anemopsis* W.J. Hook & Arnott, *Houttuynia* Thunb., *Gymnotheca* Decaisne) and 7 kinds of perennial herbaceous plants widely used in

temperate, subtropical, and tropical regions of Northern Hemisphere such as East Asia, South-East Asia, and North America (south parts of USA and Mexico) [2–4]. Based on the mitochondrial gene sequence data, it is proven that the *Saururaceae* family is a deleted ancient monophyletic family, which ancestral gene has

been divided into two branches at an early development age. They are *Gymnotheca-Anemopsis* and *Saururus-Houttuynia* [5].

The *Houttuynia* Thumb is a monotypic genus named after Dutch physician and naturalist *Martinus (Maarten) Houltuyn* (1720–1798) [6, 7]. The *Houttuynia* Thumb includes the only polymorphic species of the species of three morphological variations (Chinese, Japanese, and poecilophyllous)[8].

Houttuynia cordata Thumb. (syn.: *Houttuynia emeien-sis* Z.Y. Zhu & S.L. Zhang; *Polypara cochinchinensis* Lour.; *P. cordata* Kuntze) is a perennial herbaceous stoloniferous colonizing plant up to (5-)15-60(-80) cm height with branchy thin creeping rootstalks up to 1 m long; the cataphylls are small, scale-shaped, and filmy. There are two ranges of cataphylls on the earthnut and on the aboveground stem base. The aboveground stem is upright or ascending, basal, usually simple, jointed, a bit zigzag, grooved, often reddish or purple, glabrous or downy-noded with simple, short, and upright root hair (figure 1).

The assimilating leaves are simple, whole, thin, alternating (they are often almost distichous), and herbaceous with stocks and persistent stipules. They are usually glabrous, shining, green or blue-gray-green, with the dotted and transparent glands and often with narrow, reddish, and marginal edges; the abaxial surface is matt; the midribs are convex; they are also glaucous, reddish or purple, glabrous, or downy with the simple, short, and upright hair. The blades are wide ovate, triangular ovate, or lanceolate ovate.

They are of 1.5–3.5–9–10 cm long and of 1.8–2.5–6.5–8 cm wide, with heart-shaped or kidney-heart-shaped bases, acuminate and often a bit tapered tops, and whole edges. The leaves are actinodromously (camptodromely) venated with 5–7 flat, thin, light, or reddish veinlets. Two inner veinlets are often 3–5 mm far from the basal node. The stocks of leaves are thin, cylindrical, grooved, glabrous, of (0.7-)1-4 cm long, light-green or reddish. The stipules are intrapetiolar, upright, united, basally adnate to the stocks, filmy and herbaceous, glabrous, blunt, oblong, of (0.5-)1-2.5 cm long, with amplexicaul bases and whole fringed edges. The prophyll is single-flowering, adaxial, small, acuminate, filmy, quickly exsiccant, and deciduous.

The inflorescences are spike-like, of (0.5-)1-3 cm long, and of (2-)5-6 mm diameter, upright, and bracteate; they flower on thin and glabrous peduncles. The peduncles are of 1.5-3 cm long. They are terminal and/or oppositifolious to leaves. The flowers are numerous (45–70), bisexual, 3-dimensional, zygomorphous, plain, and greenish, without perianth, sessile in axils of the cylindrical green bracts (with visible top hydathodes) of 0.5–1 mm long. The bracts are 4–6 basal flowers. The inflorescences are enlarged and horizontal. They form the corolla-shaped cover. Bracts are glabrous, petal-shaped, oblong or inversely egg shaped elliptic, (0.5-)1-1.5(-2) cm long and (0.3-)0.5-0.8(-1) cm wide, with round

or a bit acuminate tops and whole edges. The original terminal structure often develops on the top of inflorescence. Structure generally includes a terminal gynoeceum rounded by stamens, side reduced male flowers, and fertile bracts with rudimentary anthers.

Androeceum consists of 3(4) free oppositifolious for carpels stamens (they are longer than ovary) on glabrous and thin threads, which are three times longer than anthers. The basal part of stamens is adnate to the ovary. The stamen threads accrete in couples. Anthers are 0.3–0.5 mm long, a bit flattened, oblong-elliptic, yellow, tetrathecal, and latrorse-introrse; they are opened with longitudinal cracks; pollen is completely or almost completely sterile.

Gynoeceum is paracarp, it consists of 3(4) carpels with partially top unclosed, and free, and upright styles, which third top parts are reflected deccurrent stigmas. The ovary is glabrous, semi-interior, and unilocular; the placentation is parietal; there are 6–9 seedbuds on each placenta.

Fruit is a paracarp bridging sarcocarpous (pyrenocarp) round capsule of 2–3 mm diameter with the saved styles. It is usually polyspermous and opened with apical teeth. Then, the apomictic fruit usually develop. The seeds are round or elliptic-round, of 0.4–0.5 mm diameter, a bit acuminate, netted-ribbed, and deep brown. $2n = 24^*$, 96. Flowering: IV–IX (China), VI–VII (Japan); fruiting: VI–X (China) [9–17].

The areal covers East Asia (South China, Taiwan, Korea, and Japan, including the Ryukyu Islands), South-East Asia (Myanmar, Laos, Thailand, and Vietnam), India, Bhutan, and Nepal. The invasive and naturalized kind of the *Houttuynia cordata* grows in New Zealand, Australia, USA, Costa Rica, Brazil, and Madagascar. The *Houttuynia cordata* does well in dry habitats such as forests, bush, dry meadows, ravines, swamp peristomes, banks of ponds, shallow water, mountainsides, road borders, and cultivated plantations (as ruderal in tea and bamboo plantations) at a height of 2500 m above sea level [18].

Ethnobotany

The *Houttuynia* Thumb leaves and herb are used in Indian folk medicine for treatment of dysentery, diarrhea, measles, gonorrhea, helminthiasis, ulcer of the stomach, gastritis, anemia, allergy, asthma, tuberculosis, cholera, as well as against intoxication, insomnia, muscular pain, cardiovascular disorders, and bacillosis, and as anti-inflammatory, analgetic, astringent, and laxative drug. The root blood is used for treatment of wounds, injuries, skin diseases, abscesses, edemas, snakebites, indigestion, rectal prolapse, and difficult urination. Excess herb uptake reduces fertility [19–21]. In China, the herbal extracts and decoctions are used against chill, cough, tonsillitis, hemoptysis, pneumonia, tuberculosis, hydrops, malaria, dysentery, hemorrhoid, diarrhea, tympanic resonance, enteritis, cholecystitis, appendicitis, intoxication, snakebites, insect stings, edemas, mastitis, infantile diuresis, ischemia, and angina; the herbal ext-

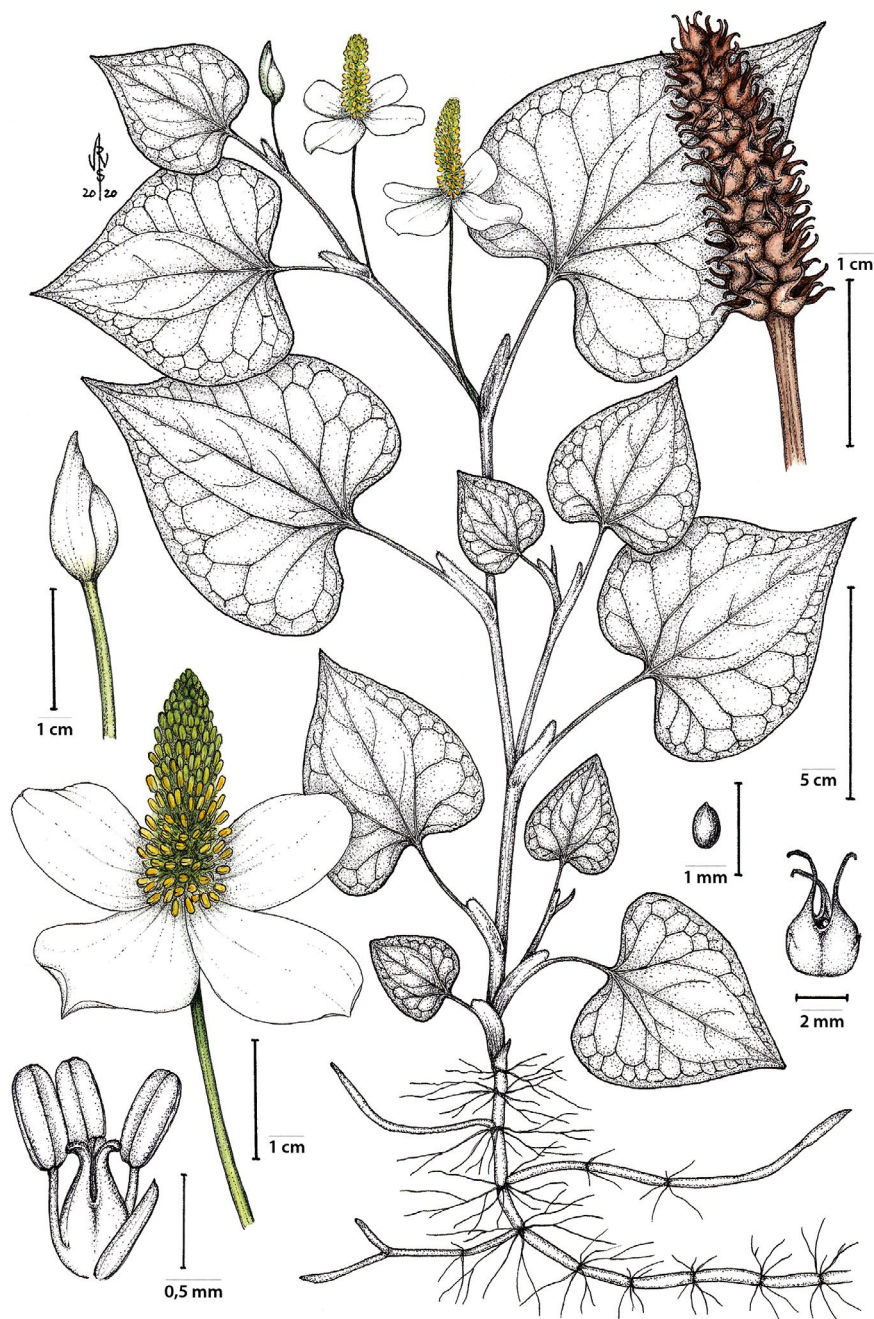


Figure 1. *Houttuynia cordata* Thumb.

racts and herbal decoctions are also used externally for treatment of skin diseases (dermatophytosis, shingles, and dermatitis), furunculosis, carbunculosis, purulent ulcers, lumbago, eczema, whitlow, syphilis, urethritis, and endometritis [22]. In Korean folk medicine, the plant is usually used for treatment of cough, bronchitis, pneumonia, chronic sinusitis, nasal polyps, hydrops, acneiform, eczema, herpes labialis, allergy, dysentery, leukorrhoea, and urethritis [23–25]. In Japan, the fresh leaves compress is high effective for treatment of such purulent skin diseases as furunculosis and carbunculosis [26]; the herbal drugs are used for treatment of ulcer of the

stomach, as well as the diuretic, antimicrobial, and antineoplastic drug; it is also combined with other herbal drugs for managing of atopic dermatitis, and other skin diseases. In Thailand, the herbal extract is widely used as an immunostimulant and as an antineoplastic drug [27]. In South America (in Argentina), the Chinese folk medicine followers widely use the *Houttuynia* to improve the cognitive abilities and as an adaptogenic substance, as well as for treatment of cough, dyspnea, chest pain, edemas, fever, fatigability, stress, epilepsy, rhinitis, sinusitis, bronchitis, pneumonia, light abscess, rheumatism, dysentery, hemorrhoid, skin diseases, nephritis, urinary tract infections, leukorrhea, and impotence [28].

The *Houttuynia cordata* (herb) is a medicinal plant. It is a part of the official list of Chinese and Japanese pharmacopeias. Since recently, it is included in European pharmacopeia [29].

The ethereal oil Tsi (China) is used in cosmetology and aromatherapy; it is extracted from the leaves under steam distillation or supercritical fluid extraction (CO₂). In Korea and in Japan, the herbal extract is used combining with other herbal drugs as cosmetic composition to accelerate the rejuvenation process, to lighten and to rejuvenate skin, to smooth out wrinkles, to remove freckles, to protect and to nutrice hair, as well as to prevent dandruff and skin cracking.

In the region, leaves, stems, and roots of the plant are used as a vegetable and spicy crop (*eng.*: Fish mint, Fishwort, Himalayan spinach); the plant is of specific "fish" taste. Fresh, boiled, and roasted plant is usually taken [30-32].

The *Houttuynia cordata* is planted as an ornamental and ground-covering plant. It is used as a decor fresh-water bank plant, decor shallow water plant, and dried swamp plant. Plant is simple, shade-loving, and moisture-loving. It is successfully introduced in parks placed in central Russia. It is intensively accrescent and tolerant at about -18 °C. The garden poecilophyllous "Chameleon" (tricolor) plants as well as double cultivars containing numerous white petal-shaped bracts of the inflorescences are widely used [33-35].

Biochemical composition

Carbohydrates and related compounds: 4-methyl-D-mannono- δ -lactone [36]; arabinose, galactose, glucose, xylose, mannose, rhamnose, galacturonic and glucuronic acids – in leaves and stems [37, 38].

Alicyclic compounds: 1-acetoxymethyl-3-isopropenyl-2-methyl-cyclopentane, bicyclo[3.1.1]heptene, bicyclo[2.2.1]hept-2-en-7-ol, 1-hexyl-2-propylcyclopropane, damascenone, decalin (decahydronaphthalene), 5,6-dimethylenecyclooctene, 6,6-dimethyl-2-methylenebicyclo[2.2.1]heptan-3-on, 1,1-dimethyl-2-(3-methylbuta-1,3-dienyl)cyclopropane, 7,9-di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione, α -ionene, 5-methyl-3-isopropylcyclohexene, 1-methyl-4-isopropyl-2-cyclohexen-1-ol, 1-methyl-6-(3-methylbuta-1,3-dienyl)-7-oxabicyclo[4.1.0]heptane, *trans*-1-methyl-4-(1-methylethyl)-2-cyclohexen-1-ol, 1-methyl-2-octylcyclopropane, 2-methyl-4-(2,6,6-trimethylcyclohex-1-enyl)but-2-en-1-ol, 1-methylene-4-(1-methylethenyl)cyclohexane, 5-methyl-3-(1-methylethenyl)-cyclohexene, 3-methylcyclohexanol, (1*R*)-nopione, oxacycloheptadecan-2-one, 1,1,4,4-tetramethylcyclohexane, 1,2,4,4-tetramethylcyclopentene, 1,5,5-trimethyl-6-methylidenecyclohexene, 3,7,7-trimethyl-1,3,5-cycloheptatriene, tris(methylencyclopropyl) methanol, cyclohexadecane, cyclohexa-2-en-1-ol, cyclohexanol, cyclohexene, cyclohexene-1-methanol, 1,3-cyclooctadiene, cyclooctane, cycloicosane, (2-endo,5-exo)-1,7,7-trimethylbicyclo[2.2.1]heptane-2,5-diol, 1,2-epoxy-1-vinylcyclo-dodecene, 3-ethenylcyclooctene [36]; vomifoliol, 6-

(9-hydroxy-but-7-ethyl)-1,1,5-trimethylcyclohexane-3,5,6-triol, 4-[(2*E*)-3-(β -D-glucopyranosyloxy)-2-butene-1-yl]-4-hydroxy-3,5,5-trimethyl-2-cyclohexene-1-one, dehydrovomifoliol, megastigmatrienone, 1-methyl-4-(5-methyl-1-methyl)cyclohexene, (1-propylheptadecyl)cyclohexane, (6*S*,9*S*)-roseoside, 4,4,6,6-tetramethylbicyclo[3.1.0]hex-2-ene, 7-(3,5,6-trihydroxy-2,6,6-trimethylcyclohexyl)-but-3-en-2-one, cyclododecanol – in aerial and underground parts [39-47]; 2,6-dimethylcyclohexanol, (3*S*,5*R*,6*R*,9*R*)-megastigman-7-en-3,5,6,9-tetrol, megastigman-7-en-3,5,6,9-tetrol-9-O- β -D-glucopyranoside, 5-methyl-3-(1-methylethyl)-*trans*-cyclohexene, 4-methyl-1-(1-methylethyl)-3-cyclohexen-1-ol, 3-oxo- α -ionyl- β -D-glucopyranoside – in aerial part [48, 49]; (3-isopropenyl-2-methylcyclopentyl)methylacetate – in leaves and inflorescences [50].

Tropolones: azulene

Monoterpenoids: artemisia alcohol, artemisiatriene, ascaridole, verbenol, (5*S*)-dihydrocitronellol, isoborneol, isopulegyl acetate, isocitronellene, ipsdienol (2-methyl-6-methylene-2,7-octadien-4-ol), camphene hydrate, *cis*-carveol, carvone, lavandulyl acetate, lavandulol, limonen-1,2-diol, limonene oxide, linalyl acetate, linalool oxide, menthol, myrtanol, nerol, perillol, pinocarvone, *trans*-piperitol, α -pyronene, terpinen-4-yl acetate, γ -terpineol, α - and β -terpinyl acetate, α -thujone, α -fenchyl acetate, fenchol, fenchone, 1,4-cineole, α -citral, citronellyl isovalerate [36]; (4*E*,6*Z*)-allo-ocimene, artemisia ketone, borneol, bornyl acetate, *neo*-verbenol acetate, geranyl acetate, geranyl propionate, geraniol, *neo*-dihydrocarveol, dihydrocarveyl acetate, isopinocampheol, camphene, campholenal, camphor, 2-carene, 3-carene, 4-carene, *D*-limonene, β -linalool, linalyl butyrate, *cis*- and *trans*-*p*-2-menthen-1-ol, *p*-menth-1-en-8-yl acetate, β -myrcene, myrtenol, neryl acetate, *cis*- and *trans*- β -ocimene, perillene, α - and β -pinene, *trans*-pinocarvyl acetate, *cis*-piperitol, β -sabinene, *cis*-sabinene hydrate, α -, β - and γ -terpinene, α -terpineol, (Z)- β -terpineol, 4-terpineol, α -terpinolene, tricyclene, α -thujene, 3-thujene, α -phellandrene, α -fenchene, *cis*-chrysanthenyl acetate, α -cyclogeranyl acetate, β -cyclocitral, *p*-cymene, 2-*p*-cymenol, *p*-cymen-8-ol, 1,8-cineol (eucalyptol), isobornyl acetate, 6,7-epoxymyrcene – in aerial and underground parts [51-55]; isoterpinolene, *cis*-*L*-carvyl acetate, *trans*-pinocarveol, β -phellandrene, α -cyclocitral, (Z)-citral, citronellyl acetate – in aerial part; acetyl borneol, *cis*-geraniol, α -pinene oxide, piperitone, rosefuran (α -naginatene), 1-terpinen-4-ol – in leaves [56-59]; *p*-menth-1-en-8-ol, *trans*-sabinene hydrate – in leaves and inflorescences.

Sesquiterpenoids: acoradiene, 12-acetoxy-6-hydroxymethyl-2,10-dimethyl-2,6,10-dodecatriene, α - and β -bisabolene, hexahydrofarnesyl acetate, germacrene D, *epi*-globulol, isocaryophyllene, zingiberene, γ -cadinene, α -cadinol, calamenene, cubenol, ledol, nerolidyl acetate, pachoulol, 4,11-selinadiene, γ -selinene, β -sesquiphellandrene, β -sinensal, farnesane, farnesyl acetate, farne-

syl acetone, chamigren, α -cedrene, α -cedrol, elemol, eremophylene, 10-*epi*- γ -eudesmol, γ -eudesmol; aromadendrene, globulol, α -humulene, α - and β -caryophyllene, caryophyllene oxide, (-)-clovan-2 β ,9 α -diol, 8 α -methyloctahydro-4(1H)-azulenone, muurola-4,10(14)-dien-1- β -ol, (*E*)-nerolidol, α -pachoulene, α - and β -selinene, 7-*epi*- α -selinene, spathulenol, α - and β -farnesene, (*E*)-farnesol, α -cyperene, β -eudesmol – in aerial and underground parts [60]; *epi*-bicyclosesquiphellandrene, germacrene B, δ -guaiene, δ -cadinene, α -copaene, α -muurolene – in aerial part; α -bisabolol, δ -cadinol, (*E,E*)- α -farnesene, γ -elemene – in leaves [57, 58]; β -elemene – in roots; α -guaiene, α -panasinsen – in leaves and inflorescences.

Diterpenoids: bigeranylidene, isophytadiene, methyl neoabietate, phytane; (*E*)-phytol – in aerial and underground parts [61]; isophytol – in leaves; neophytadiene, palustrol – in aerial part.

Triterpenoids: oleanolic and ursolic acids, acantrifoside E, sterculin A, cycloart-25-en-3 β ,24-diol – in aerial and underground parts [62].

Steroids: 3 β -amino-5 α -spirostan-6 α -ol, 4,4-dimethylcholester-5,7,9-trien-3-ol, 4,14-dimethyl-(3 β ,4,5 α)-9,19-cycloergost-24(28)-en-3-ol, 5 α -pregnan-3,11,20-trione; brassicasterol, 3 β -hydroxystigmast-5-en-7-one, spinasterol, 5 α -stigmast-3,6-dione, stigmast-4-en-3,6-dione, stigmast-4-en-3-one – in aerial part [63]; daucosterol, sitoindoside I, stigmast-3,6-dione – in rhizome [64]; β -sitosterol, β -sitosteryl glucoside, stigmast-4-en-3 β ,6 β -diol, stigmast-4-en-6 β -ol-3-one, stigmasterol – in aerial and underground parts.

Carotenoids: violaxanthin, β -caroten, lutein – in aerial and underground parts [65].

Derivatives of benzene: butyl isobutyl phthalate, butyl undecyl phthalate, dioctyl phthalate, diisooctyl phthalate, 3,5-ditert-butyl-4-hydroxybenzaldehyde, 1,4-diethyl-2-methylbenzene, diethyl phthalate, *p*-xylene, di-2-ethylhexylphthalate, mono-2-ethylhexyl isophthalate, mono-2-ethylhexyl phthalate, neopentylbenzene, syringaldehyde, 2-tert-butyl-1,4-dimethoxybenzene, benzeneacetaldehyde (phenylacetaldehyde), *p*-tolualdehyde, toluene, ethylbenzene; benzyl- β -D-glucopyranoside, benzoic acid, butyl-2-isopropylphthalate, butyl-2-methylpropylphthalate, 1-butyl-2-octylphthalate, 4-hydroxybenzaldehyde, 4(β -D-glucosyloxy)-3-hydroxybenzoic acid, 1,3-dibutyl phthalate, diisobutyl phthalate, α -4-dimethylbenzenemethanol, methyl-3-hydroxybenzoate, methyl 4-(hydroxymethyl)benzoate, 1-(4-methylphenyl)-1-pentanone, *m*-tolyl-dimethylacetaldehyde, 1,3,5-tridecanoylbenzene, houttuynoside A – in aerial and underground parts [66–68]; benzaldehyde – in leaves and inflorescences; guaiacylglycerol, threo-guaiacylglycerol, threo-guaiacylglycerol 8-O- β -D-glucopyranoside – in aerial part.

Derivatives of phenol: *m*-acetylphenol, *p*-acetylphenol (*p*-hydroxyacetophenone), acetovanillone, acetosyringone, 1-(2-hydroxy-5-methylphenyl)ethanone, (2,4,6-trimethylphenyl)methanol; 9-bromononyl-phenylcarba-

mate, vanillin, phenylethane – in aerial and underground parts; 2-phenylethanol – in aerial part.

Phenylpropanoids: β -asarone, bisphenol A, 2,6-ditert-butyl-4-methylphenol, 2,4-ditert-butylphenol, isosafrol, isoelemicin, coniferol, methylisoeugenol, 6-methoxyisoeugenol, 2-methyl-2-(3-methylphenyl)propanal, 2-ethyl-3-methylphenylpropanal; α -asarone, 2,6-bis(1,1-dimethylethyl)-4-methylphenol, 2,6-dimethoxy-4-(2-propenyl)phenol (methoxyeugenol), carvacrol, methylthymol, myristicin, thymyl acetate, elemicin – in aerial and underground parts [69]; 1,2-bis-(4-hydroxy-3-methoxyphenyl)propane-1,3-diol, thymol, eugenol – in aerial part; isoeugenol, methyleugenol – in leaves and inflorescences.

Phenolcarboxylic acids and derivatives: homovanillic acid, caffeic acid dimethyl ether; 3-hydroxybenzoic, caffeic, cryptochlorogenic, neochlorogenic and 4-hydroxycinnamic acids, methyl 4-hydroxybenzoate, methyl caffeate, cryptochlorogenic acid methyl ester, neochlorogenic acid methyl ester – in aerial part; vanillic, 4-hydroxybenzoic, protocathechuic and chlorogenic acids, methyl vanillate, methylparaben, *cis*- and *trans*-methyl ferulate, methyl chlorogenate – in aerial and underground parts [70, 71].

Phenolic glycosides and diglycosides: protocathechuic acid glucoside, sequinoside K, sequinoside L.

Phenylethanoid glycosides: hydroxytyrosol glucoside, 2-(3,4-dihydroxyphenyl)ethyl- β -D-glucopyranoside, 2-(4-hydroxyphenyl)ethyl- β -D-glucopyranoside (salidroside) – in aerial and underground parts; dopaol- β -D-glucopyranoside, undatuside A, 2-phenylethyl- β -D-glucopyranoside, β -phenylethoxy- β -D-glucopyranoside – in aerial part.

Lignans: (7*R*,8*S*,8'*S*)-isolariciresinol, sesamin, (+)-(8*S*,8'*S*)-secoisolariciresinol – in aerial part.

Neolignans: (7*S*,8*R*)-dihydrodehydrodiconiferyl alcohol, (7*S*,8*R*)-dehydrodiconiferyl alcohol, houttuylignan, *erythro*-1-(4-hydroxy-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]-propane-1,3-diol, *erythro*-(7*S*,8*R*)-4,7,9-trihydroxy-3,3'-dimethoxy-8-O-4'-neolignan-9'-O- β -D-glucopyranoside – in aerial part.

Coumarins: scopoletin – in aerial and underground parts.

Flavonoids: vicenin II, kaempferide, kaempferol-3-O- β -D-glucopyranoside; apigenin, quercetin 3-O- α -L-rhamnopyranosyl-7-O- β -D-glucopyranoside, kaempferol-3-O- α -L-rhamnopyranosyl-7-O- β -D-glucopyranoside, kaempferol-3-O- β -rutinoside, luteolin, houttuynoid G – in aerial part [72, 73]; avicularin, quercetin hexoside, phloridzin – in leaves [74]; afzelin, vitexicarpin, vitexin, 5-hydroxy-3,3',4',7-tetramethoxyflavonoids, 5-hydroxy-3,4',6,7-tetramethoxyflavonoids, hyperoside (hyperin), isoquercitrin, isorhamnetin, quercetin, quercetin 3-O- β -D-galactopyranosyl-7-O- β -D-glucopyranoside, quercitrin, kaempferitrin, kaempferol, kaempferol-3,7,4'-trimethylether, xanthol-3-O-glucoside, narirutin, rutin, houttuynoids A, B, C, D and E, chrysosplenol D – in aerial and underground parts [75,76].

Catechins: catechin – in aerial part.

Procyanidins: procyanidin B – in aerial part.

Heterocyclic compounds: (3Z)-3-butyldiene-2-benzofuran-1-one, dihydroactinidiolide, 3-(2-methyl-2-propenyl)-2,5-dihydrofurandione, 2,2,3-trimethyl-3-oxetanol, 2-ethyl-2-methyloxirane [36]; 2-propylfuran, 2-ethylfuran – in aerial part; hexadecyloxirane, 5-(hydroxymethyl)furfural, 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-on, tetradecyloxirane, 2-furfural – in aerial and underground parts.

Derivatives of phenanthrene: aristolactam All, aristolactam BII (cepharanone B), aristolactam FII, 3,4-dimethoxy-N-methyl aristolactam, caldensin, piperolactam A, sauristolactam – in aerial and underground parts [77–80]; piperolactam B, C and D – in aerial part [81].

Alkaloids / Amides: 4,6-dimethylpyridin-2-amine, 6-chloro-N,N'-dimethyl-1,3,5-triazine-2,4-diamine, hexanamide, 2(3-hydroxy-4-methoxyphenyl)acetamide, 1,2-dimethoxy-3-hydroxy-5-oxonoroporphine, lauramide, 1-methyl-4-stearoylpiperazine, oleamide, palmitamide, 1,2,3-trimethoxy-3-hydroxy-5-oxonoroporphine, N-(2-cyclopropylphenyl)-2-fluorobenzamide; adenosine, asimilobine, atherospermidine, 3-hydroxy-1,2-dimethoxy-5-methyl-5H-dibenzoindol-4-one, 4-hydroxy-1,2,3-trimethoxy-7H-dibenzoquinolin-7-one, N-(2-β-D-glucosidyl-2-phenylethyl)benzamide, 3-decanoyl-4-nonyl-5-dodecanoyl-1,4-dihydropyridine, 3-decanoyl-6-nonylpyridine, 5'-deoxy-5'-methylsulfinyladenosine, 3a,12a-dihydro-2H-furo[3,2-b]indolo[3,2,1-ij][1,5]naphthyridin-1,1(4H)-diol, 3,5-didecanoyl-4-nonyl-1,4-dihydropyridine, 3,5-didecanoyl-4-nonyl-1,4-dihydropyridine, 1,2-dimethoxy-3-hydroxy-5-oxonoroporphine, laurotetanine, liriodenine, N-methylasimilobine, N-methylaurotetanine, 3-methoxy-6H-benzodioxolo-benzoquinoline-4,5-dione, 3-methoxy-5-methyl-5H-benzodioxolo-benzoindol-4-one, 3-methoxy-6-methyl-6H-benzodioxolo-benzoquinoline-4,5-dione, nicotinamide, norisoboldine, N-nornuciferine, 7-oxodehydroasimilobine, orientaline, 1,2,3,4,5-pentamethoxy-dibenzoquinolin-7-one, perlolyrine, (S)-reticuline, 1,2,3-trimethoxy-3-hydroxy-5-oxonoroporphine, 1,2,3-trimethoxy-4H,6H-dibenzoquinolin-5-one, 1,2,3-trimethoxy-6-methyl-4H,6H-dibenzoquinolin-5-one, ouregidione, uridine, 4-[formyl-5-(methoxymethyl)-1H-pyrrol-1-yl] butanoic acid, houttuycorine, houttuynamide B and C, 2,3-quinoxalindione, quinoline, cepharadione A – in aerial part [82]; aurantiamide, aurantiamide acetate, aurantiamide benzoate, benzamide, 4-hydroxybenzamide, N-(1-hydroxymethyl-2-phenylethyl)benzamide, 4-hydroxy-3-methoxybenzamide, *cis*- and *trans*-N-(4-hydroxystiryl)benzamide, N-(4-hydroxyphenylethyl)benzamide, 2-nonyl-5-decanoylpyridine, 3,5-didecanoylpyridine, 6,7-dimethyl-1-ribitol-1-yl-1,4-dihydroquinoxalin-2,3-dione, 4,5-dioxodehydroasimilobine, isoboldine, (+)-isoboldin-β-N-oxide, indole-3-carboxylic acid, lysicamine (oxonucipherine), liriotalpiferine, N-methyl-5-methoxy-pyrrolidin-2-one, 3-nonylpyrasol, noraristolodione, norcepharadione B, oxymatrin, splendidine, telitoxinone, (S)-5,6,6a,7-tetrahydro-2,10-dimethoxy-4H-dibenzo[D,E,G]

quinolin-1,9-diol, N-phenethylbenzamide, N-*trans*-feruloyltyramine, houttuynamide A, 4-(1H)-quinolin-2-one, 7-chloro-6-demethyl cepharadion B, cepharadione B – in aerial and underground parts [83–85]; N-phenethylbenzamide – in rhizome.

Silicon-containing compounds: dimethyl(1-methylvinyl)chlorosilane – in aerial and underground parts.

Nitrogen-containing compounds: methyl-N-acetyl-L-leucinate – in aerial and underground parts.

Aliphatic hydrocarbons and derivatives: acetone, (Z)-9-hexadecenol, 3-hexadecyne, hexatriacontane, hexene, heneicosane, heptadecanol, 3-heptadecenal, 16-heptadecenol, heptacosane, heptane, 1-heptene, 2-heptene, 1-hepten-3-one, decane, decen, 2-decen-1-ol, 2,5-dimethyl-1,3-hexadiene, 2,5-dimethyl-1,5-hexadiene-3,4-diol, 2,2-dimethylheptane, 2,6-dimethyldecane, 3,6-dimethylene-1,7-octadiene, 2,7-dimethyl-2,6-octadien-1-ol, (Z,E)-2,5-dimethyl-2,4,6-octatriene, 2,6-dimethyl-3,5,7-octatrien-3-ol, 6,6-dimethylundecane, 6,10-dimethyl-2-undecanone, dodecane, 4-dodecanone, 2-dodecenal, 1-dodecen-3-ol, 1-dodecyne, isocitronellene (5,7-dimethyl-1,6-octadiene), isopropanol, isononadecane, 2-isopropenyl-5-methylhex-4-enal, 2-methylbutanal, 2-methyl-2-buten-1-ol, 3-methylbutanal, 3-methylhexane, (Z)-14-methyl-8-hexadecenal, 2-methylheptadecane, 6-methyl-2-heptanone, 6-methyl-1-heptene, 11-methyl-4-dodecanone, 2-methyldocosene, 3-methylenetridecane, 9-methyl-5-methylene-8-decen-2-one, 2-methyl-6-methylene-2-octene, 5-methyl-3-(1-methylethylidene)1,4-hexadiene, 2-methyl-3,13-octadecadienol, 5-methyl-3-octyne, 2-methyl-2-pentanol, 2-methyl-3-pentanone, 3-methyltridecane, 5-methylundecane, 1-methyloxy-1-butene, 1-methoxy-1-hexadecene (1-hexadecenyl methyl ether), 1-methoxy-3-(2-hydroxyethyl)nonane, nonadecane, 1-nonadecanol, 1,3,12-nonadecatriene, (E,E,Z)-1,3,12-nonadecatriene-5,14-diol, 1-nonene, (E)-3-nonene, (Z)-2-nonenal, 8-oxo-2-nonenal, octadecanal, octadecanol, 1-octadecene, (E)-9-octadecene, 1-octadecyne, 3-octadecyne, 9-octadecyne, 1-octen-3-one, 9-octylheptadecane, 3-octyne, pentadecanal, pentatriacontane, 1,13-tetradecadien-3-one, 1,14-tetradecanediol, 2-tetradecanol, tetracosane, 2,2,6,6-tetramethyl-4-ethylheptane, 2-tridecanol, 6-tridecanone, (E)-2-tridecenal, (E)-2-tridecen-1-ol, 2,2,4-trimethylhexane, 2,2,4-trimethyldecane, 2,2,5-trimethyldecane, 2,2,6-trimethyldecane, (Z)-9-tricosene, 3,3,5-trimethylheptane, 2,2,8-trimethyldecane, 2,4,6-trimethyldecane, 3,3,5-trimethyldecane, 2,3,3-trimethyloctane, 2,2,3-trimethyl-3-oxetanol, 6,10,14-trimethyl-2-pentadecanone, (E,E)-6,10,14-trimethyl-5,9,13-pentadecatrien-2-one, 2,6,10-trimethyltetradecane, 10-undecenal, 2-undecanol, 1-undecene, (E)-3-undecen-1-yne, 10-undecyn-1-ol, 1,4-eicosadiene, 9-eicosene, (E)-5-eicosene, 3-eicosyne, 1-ethenyloxyoctadecane, 2-ethyl-1-decene, 3-ethyl-3-methylheptane [36]; 3-buten-2-ol, 1-hexadecanol, 1-hexadecene, hexacosane, hexanal, (Z)-3-hexenal, 1-hexanol, (E)-2-hexene-1-ol, (Z)-3-hexen-1-ol, 1-decanal, 1-decanol, 2-decanol, 1-decen-3-one, 2,5-dimethyl-3-methylhepta-1,5-diene, 7,7-dimethyl-3-methyl-

lene-1,6,10-dodecatriene, 2,6-dimethyl-2,7-octadiene-1,6-diol, 3,7-dimethyl-1,6-octadiene-3-ol, 3,7-dimethyl-1,3,6-octatriene, 2,6-dimethyl-3,5,7-octatriene-2-ol, 1-dodecanal, 1-dodecanol, 2-dodecanone, dodecene, 2-methyl-6-methylene-octa-3,7-dien-2-ol, 3-methylundecane, 7-methoxy-3,7-dimethyloctanal, 1-methoxy-2-methyl-1-propene, nonacosane, *n*-nonane, *n*-nonanal, 1-nonanol, 2-nonanone, (*Z*)-2-nonenal, (*Z*)-2-nonene, octadecane, (*Z*)-13-octadecenal, octacosane, pentadecanol, tetradeccanal, 2,6,11,15-tetramethyl-hexadeca-2,6,8,10,14-pentene, 3,7,11,15-tetramethyl-2-hexadecen-1-ol, trideccanal, 2-tridecanone, 4-tridecanone, 1-tridecene, tricosane, 2,6,11-trimethyldodecane, 3,7-trimethyl-1,6,10-dodecatriene-3-ol, undecanal, 2-undecanone (methyl *n*-nonylketone), houttuynine (decanoyl acetaldehyde), 3-ethyl-5-methylene-heptane, 2-ethoxypropane – in aerial and underground parts; (*E*)-2-hexenal, (*Z*)-3-hexenal, hexadecanal, 4-decanol, (*E*)-2-decenal, 1,1-diethoxyethane, 2-dodecanol, 2-methyl-3-buten-2-ol, 2-methyl-1,4-hexadiene, 1-octen-3-one (pentyl vinylketone), (*E*)-2-pentenal, 1-penten-3-ol, (*Z*)-2-penten-1-ol, 1-penten-3-one, undecane – in aerial part; 2,3-butandiol, hexadecane, heptadecane, 2,3-dihydroxypropional, 2,2-dimethyldecane, 3-methyl-5-propylnonane, pentadecane, pentacosane, tetramethyloctane, 2,3,6-trimethylheptane, 2,5,9-trimethyldecane, eicosane – in leaves and inflorescences; 2-decanone, 2-methyl-2-pentenal, *n*-tetradecane, 1-undecanol – in leaves.

Alkyl glycosides: *n*-butyl-O- α -D-fructopyranoside – in rhizome; (*E*)-3-hexenyl- β -D-glucopyranoside (erigeside B) – in aerial part.

Macrolactones: 4,8,12,16-tetramethylheptadecan-4-olide; (*S*)-coriolide, (9*Z*,11*E*,13*S*,15*Z*)-octadeca-9,11,15-trien-13-olide – in aerial part.

Organic acid: succinic – in rhizome.

Fatty acids and derivatives: eicosanoic (arachidic), (*E*)-3-decenoic, (*Z*)-8-methyl-9-tetradecenoic, 18-nonadecenoic, 17-octadecynoic, octocosic, (*Z*)-6-octadecenoic (petroselinic), ricinoleic, acetic, elaidic, erucic [36]; octanoic, hexanoic, heptanoic, octadecadienic, octadecanoic, oleic, pentadecanoic, tridecanoic – in aerial part [86, 87]; isovaleric, capric (decanoic), lauric (dodecanoic), linoleic, linolenic, heptadecanoic, myristic (tetradecanoic), palmitic, palmitolinoleic (9-hexadecenoic), nonanoic, tricosanoic, undecanoic – in aerial and underground parts; 2,6,10,14-tetramethylpentadecanoic, 10-octadecenoic – in leaves and inflorescences. Amyl laurate, isoamyl laurate, butyl decanoate, (*Z*)-4-hexenyl acetate, heptadecyl heptadecanoate, heptyl decanoate, glyceryl linoleate, decanoic anhydride (decanoyl decanoate), decyl decanoate, decyl formate, 11,13-dimethyl-12-tetradecen-1-yl acetate, dodecyl acetate, isopropylpalmitate, methyl 2-acetoxy-9-octadecenoate, 3-methylbutyl pentadecanoate, methyl (R,R)-2,4-dimethylheptanoate, methyl 4,7,10,13,16,19-decosahexanoate, methyl 12-hexyloctadecanoate, 2-methylene-3-(1-methylethenyl) cyclohexanyl acetate, methyl 14-methylpentadecanoate, methyl pristanoate, methyl 10-octade-

cenoate, methyl tridecanoate, methyl elaidate, undecyl dodecanoate, vinyl decanoate, ethyl 5-methylnonanoate, ethyl palmitate, ethyl 2-ethoxyacetate; *t*-butylacetate, vinyl methacrylate, decyl acetate, 3,7-dimethyl-2,9-octadien-1-ol acetate, (3-isopropenyl-2-methylcyclopentyl)methylacetate, 3-methylbutyl heptanoate, methylisoleate, methyl linoleate, methyl-(2*E*)-6-(2-methylenecyclopropyl)-2-hexenoate, methyl 12-methyltetradecanoate, methyl-2,6,10,14-tetramethylpentadecanoate, ethyl decanoate (ethyl caprate), ethyl docosanoate, ethyl laurate, ethyl nonadecanoate, ethyltridecanoate – in aerial and underground parts; methyl decanoate, methyl laurate, methyloleate, methyl palmitate, methylundecanoate, ethylacetate – in aerial part; 4'-methylacetophenone – in leaves and inflorescences; *cis*-3-hexenyl acetate, decylcaprilate, octylacetate, pentylcaprilate – in leaves; glyceryl oleate – in rhizome.

Amino acid: alanine, arginine, asparagine, valine, hydroxyproline, histidine, glycine, glutamine, isoleucine, leucine, lysine, methionine, proline, serine, tyrosine, threonine, tryptophan, phenylalanine, cysteine, citrulline – in aerial and underground parts [88].

Vitamins: ascorbic acid – in leaves (35,6 mg/%) and underground part (14,2 mg/%).

Micro- and macronutrients: Fe, Cu – in leaves and underground part; Co, Zn – in underground part; Mn – in leaves.

Essential oil. Populations of plants growing in various places differ in percentage of chemical elements. There are two chemotypes of them. They are the decanal chemotype (D-chemotype) and the myrcene chemotype (M-chemotype). D-chemotype includes the plants of citrus aroma, high level of the aliphatic aldehyde, and low level of terpenoids. Myrcene chemotype (M-chemotype) includes the plants of coriander aroma caused by high level of myrcene and monoterpenoids. Besides, in South-West China (Province Sichuan), there is a plant population ring, content of ethereal oils of which does not include terpenoids. It may be caused by genetic mutation [89–91]. (ref.: table 1).

Biological activity

Antibacterial activity. Such extracts of whole plants as water and ethanol extracts are of moderate antibacterial activity against the *S. aureus* (*Staphylococcus aureus*) and *E. coli* (*Escherichia coli*) strains. The aqueous extract is of high activity [92–94, 96], as well as antimicrobial activity against gram-negative *Salmonella* (*Salmonella enterica*, *Salmonella typhimurium*) [97]; the ethanol extract is of high activity against the *S. aureus* strains (MRSA, *S. epidermidis*, *S. pyogenes*, *S. Mitis*) and *E. faecalis* (*Enterococcus faecalis*). The ethyl acetate rootstalk extract is of activity against the *Bacillus subtilis* and *Shigella dysenteriae*; the methanol extract is of activity against the *Streptococcus pneumoniae*; both extracts inhibit growth and development of *Klebsilla pneumoniae* [98]. The leaf extract (ethanol) is of activity against the *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Esche-*

Table 1. Main components of essential oil (%) *H. cordata* Thumb.

State	Plant part	Components	References
China	All	2-undecanone (2,1–40,36 %), bornyl acetate (0,4–8,61 %), β -myrcene (2,58–18,47 %)	[43]
China	All	β -pinene (23,65 %), 2-tridecanone (12,38 %), 2-undecanone (8,55 %), bornyl acetate (4,08 %), lauric acid (3,77 %), 1-tridecene (3,51 %), caryophyllene oxide (2,97 %), α -cyperene (2,59 %)	[52]
India	Ap 0,06–0,14 %	2-undecanone (19,4–56,3 %), β -myrcene (2,6–44,3 %), ethyl capilate (0–10,6 %), ethyl laurate (1,1–8,6 %), 2-tridecanone (0,5–8,3 %), 1-decanal (1,1–6,9 %)	[53]
Korea (cultivar)	Ap	β -myrcene (27,96 %), decanal (25,24 %), <i>cis</i> -ocimene (12,2 %), 2-undecanone (3,68 %), dodecanal (3,32 %), capric acid (3,1 %), β -caryophyllene (2,77 %), (Z)-3-hexenal (2,98 %)	[49]
India	Up 0,08–0,16 %	2-undecanone (29,5–42,3 %), β -myrcene (14,4–20,8 %), β -sabinene (6,0–11,1 %), 2-tridecanone (1,8–10,5 %), β -pinene (5,3–10 %), ethyl laurate (0,8–7,3 %)	[53]
Vietnam	L	β -myrcene (30,8 %), 2-undecanone (19,7 %), (Z)- β -ocimene (10,2 %)	[57]
China	L	decanal (42,64 %), capric acid (18,67 %), dodecanal (15,04 %)	[58]
China	L	2-undecanone (22,82 %), β -pinene (23,12 %), β -myrcene (12,76 %), α -pinene (11,63 %), limonene (7,69 %), bornyl acetate (4,46 %), camphene (1,96 %)	[59]
China (Sichuan)	L	decanal (42,64 %), decanoic acid (18,67 %), dodecanal (15,04 %)	[90]
China	All (dried) 0,34 %	myrcene (51,64 %), 2-undecanone (6,67 %), tridecan-2-one (6,06 %), <i>cis</i> - β -ocimene (5,72 %)	[95]

Note. All = all plant; Ap = aerial part; Up = underground part; L = leaf.

richia coli [99]. Components of the aqueous extract of the aboveground part of plant are of antibacterial properties against the *Bacillus cereus*, *B. subtilis*, *Vibrio cholerae*, and *V. parahaemolyticus* strains. The dried leaves decoction is of moderate antibacterial and antifungal action against the pathogen microorganisms of oral cavity: *Staphylococcus aureus* (MRSA), *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Streptococcus mutans*, *S. oralis*, and *Candida albicans* [100, 101]. The extracted from the whole plant alkaloid (3-nonilpirazol) inhibits growth of gram-positive *Staphylococcus aureus* and *Bacillus subtilis* bacteria as well as acts antifungally against *Trichophyton* sp., *Zygosaccharomyces saulus*, and *Aspergillus niger*. The ethereal oils extracted from aboveground and earthnut parts of plant are of antimicrobial activity against pathogenic *Candida albicans* fungi and a range of bacteria strains (*Enterococcus faecalis*, *Escherichia coli*, *Mycobacterium smegmatis*, *Pseudomonas aeruginosa*, *P. lachrymans*, *Ralstonia solanacearum*, *Salmonella enteritidis*, *Sarcina ureae*, *Shigella dysenteriae*, *Staphylococcus aureus*, *Streptococcus mutans*, *Vibrio parahaemolyticus*, and *Yersinia enterocolitica*); the *S. aureus* strain is of the most inhibiting action of ethereal oils [102, 103]. Aqueous extract and ethereal oil are good antibacterial agents in cultivating red tilapia (*Oreo-*

chromis mossambicus Linn. $\times$ *Oreochromis niloticus* Linn.); they are also of effective action against such fish pathogens as *Aeromonas hydrophila*, *Streptococcus* sp., and *Flavobacterium columnare*.

Antifungal activity. Ethyl acetate extract of the endophyte mycelium *Chaetomium globosum* extracted from the *Houttuynia cordata* plant is of wide range of high antimicrobial activity against phyto-genic fungus (*Bipolaris maydis*, *Aphanomyces raphani*, *Puccinia zoysiae*, *Fusarium moniliforme*, *Alternaria solani*); gray mold strains (*Botrytis cinerea*) and maize leaves mold strains (*Exserohilum turcicum*) are of the highest antimicrobial activity [104].

Anthelmintic activity. The *in vivo* experiment has shown that leaf methanol extract is of anticestodal activity against zoonosis tapeworm *Hymenolepis diminuta* (Cyclophyllidae: Taeniidae); it is shown that the containing in the extract terpenoids are of dose-dependent and anthelmintic action [105,106].

Anti-inflammatory activity. Dried and fresh material extracts (chloroform, water, ethanol, and *n*-butanol) are in use to inhibit the inflammation induced by xylol at the mouse ear edema model. All medicines are of significant anti-inflammatory activity, aqueous fresh material extract is of the best pharmacological activity [107].

According to the range of study, ethyl, ethanol, and supercritical level of CO₂-extracts are of anti-inflammatory activity. They can be used for treatment of inflammatory diseases (asthma, atopic dermatitis, pleurisy, and rheumatoid arthritis) [108–115]. Alkaloids and quercetin are of high anti-inflammatory activity against the acute inflammation [116]. In Chinese folk medicine, the «*Shuang-Qing-Cao*» tea containing Japanese honeysuckle (*Lonicera japonica*, Caprifoliaceae), dyer's woad (*Isatis tinctoria*, Brassicaceae), and *Houttuynia cordata* is effectively used for treatment of various inflammatory diseases. The *in vivo* experiment has shown that the «*Shuang-Qing-Cao*» tea extract is of effective action at the mouse acute pneumonia model [117]. Experiment of mouse acute pneumonia model show increased leukocyte level in epithelial fluid and increased cell infiltration of pathological lung tissue, confirming inhibiting action of herbal extract on the induced pneumonia [118]. Containing in aqueous herbal extract polysaccharides are of high anti-complementary activity and inhibiting action on overabundant macrophage activation facilitating the process of severe acute respiratory syndrome (SARS) and other lung infections [119, 120]. Inhibiting action of the *n*-hexane extract containing fatty acids on producing prostaglandins reducing the inflammatory process and the sensation of pain is *in vitro*. The experiment shows that ethyl and aqueous herbal extracts are of anti-neuro-inflammatory properties caused by inhibiting action of overabundant producing pro-inflammatory mediators [121, 122]. Aqueous extract of *Bacillus* strain fermented herb of high flavonoid (rutin, quercitrin, and quercetin levels) prevents the LPS-induced inflammatory processes [123]. Environment friendly synthesized by aqueous leaf extract silver nanoparticles (Ag-NPs) are of higher anti-inflammatory activity in comparison with normal Ag-NPs because of including phytochemicals [124].

Anti-allergic activity. The study was aimed to study action of aqueous herbal extract on passive cutaneous anaphylaxis (PCA) of mice and the IgE-mediated allergic reaction of the RBL-2H3 rat mast cells. It has been determined that eicosenoic fatty acids (oleic and linoleic acids) increase anti-allergic activity of the extract. Aqueous herbal extract is of anti-allergic action reducing regulation of expression of the immunoglobulin receptors, which reduces the histamine liberation. The results of study of aqueous herbal extract show that it is possible to apply aqueous herbal extract for anaphylactic reactions caused by mast cells [125]. Other study of aqueous and ethanol extracts show possibility of therapeutic application of these drugs against inflammatory allergic diseases [126–128].

Antioxidant and antidiabetic activity. The whole plant and the plant parts extracts (water, methanol, and ethyl acetate) are of antioxidant properties and expressed and dose-dependent inhibiting action for the lipid peroxidation [129–135]. The polysaccharide containing in aqueous herbal extract composition is one of the main

active components causing antioxidant activity. The aqueous leaf extract experiment shows high antioxidant activity; it has been determined, that chlorogenic acid is one of the main components of the extract. The herb extracted flavonoid extract is of significant antioxidant properties; it neutralizes oxidative action of radicals [136]. The *in vitro* experiment has shown that the leaf polyphenols are of antioxidant action on biological damage of proteins [137]. It has shown that there is protective action of natural herbal antioxidants (gentamicin sulfate) on the induced rat nephrotoxicity [138] as well as against the stress caused diseases (cancer, local asphyxia, and diabetes) [139]. The *in vivo* experiment has shown that the ethereal oil improves lipid metabolism, decreases the urine albumin level, increases organism tissues sensibility to insulin action, and takes protective effect on kidney tissues of diabetic rats [140–143]. The streptozocin induced rat diabetes study has established that it is possible to consider the ethanol herbal extract as a new factor of treatment of the disease; the factor is of positive influence on the liver functions [144]. The experiment has shown that containing in the whole plant ethanol extract flavonoids are of significant inhibit effect on production of the advanced glycation end products (AGEs) and on the rat lens aldose reductase (RLAR) activity of the rat eye lens [145]. The whole plant extract (ethanol) is of antidiabetic properties and of anti-hyperglycemic activity. Aqueous leaf extract inhibits increasing triglyceride level, increasing the unesterified fatty acid level and the glycerol level containing in mouse blood plasma; it also reduces or prevents the obesity caused by the high lipid level diet [146]. Leaf extract is of anti-cholesterol effect as well as biosynthesis inhibiting and increased lipid accumulation in the liver parenchymal tissues (hepatocytes) preventing effect [147]. Aqueous herbal extract reduces the critically increased lipid and/or lipoprotein level in blood; it is of a protective action during the prophylaxis of the hyperlipidemia diseases [148].

Other biological activity. The whole plant extract fraction containing of alkaloids/amides is of a strong inhibiting action on the ADP induced and the thrombin induced thrombocyte aggregation.

It is established that leaf extract reduces the aged male prostatic hyperplasia [149].

The flavonoids (quercitrin and isoquercitrin) containing in leafs, stems, inflorescences, and fruit extracts are of diuretic activity [150–152].

The herbal methanol extract is of anti-diarrheic activity, significantly reducing the gastrointestinal activity [153].

There are the study on the herbal tea used for treatment of alopecia and containing of perilla (*Perilla frutescens* and Lamiaceae), green China tea (*Camellia sinensis*, Theaceae), and *Houttuynia cordata*; the experimental data confirms regeneration of mouse fur [154].

The experiment has shown that the extracted from aboveground part and earthnut of plant ethereal oil is of anti-acetylcholinesterase activity.

Study of the bromobenzene induced rat hepatotoxicity has shown that the methanol extract of aboveground part of plant regenerates functional liver activity by reducing the aminopyrine-N-demethylase and the aniline hydroxylase activities as well as decreasing the epoxide hydrolase [155]. Other study has shown that the aboveground part extracts were also of significant hepatoprotective properties [156].

Aqueous, methanol, and chloroform herbal extracts are of anti-mutagenic action and of wide mechanism of reducing the mutagen substance levels, and of repressive action on metabolic process of mutagen substances [157].

Experiment has shown, that aqueous extract and ethereal oil are of allelopathic activity, inhibit germination of seeds, and initial development of germs [158].

Antiviral and immunomodulatory activity. The whole plant aqueous extract containing flavonoids (Houttuyniads A – E) is of strong antiviral activity (herpes simplex virus HSV-1). The whole plant aqueous extract inhibits development of the Herpes simplex virus (HSV-1, HSV-2, and acyclovir-resistant HSV-1), mainly via blocking viral binding and penetration in the beginning of infection; besides, quercetin and isoquercitrin inhibit activation of a transcription factor (NF- κ B) regulating the immune response gene expression, the apoptotic gene expression, and the cell cycle gene expression [159]. Experiment has shown that a 3-O- α -L-rhamnopyranosyl-7-O- β -D-glucopyranoside quercetin and B-norcedaphadin reduce replication of herpes simplex virus (HSV-1) at early age [160]. Acid pectin-like polysaccharide of aqueous herbal extract of leaves and stems is of antiviral action by deforming and inflating virus parts and inhibiting the introduction of viruses into the target cells. The data make it possible to suppose that plant may be a potential antiviral agent during treatment of virus diseases. The whole plant extract (hot water) is of activity against the HSV-1 and HSV-2 viruses; herpes simplex virus 2 (HSV-2) was of the best inhibiting indications. Fresh plant steam distillate is of a direct inhibitory action against herpes simplex virus (HSV-1), influenza virus, and the human immunodeficiency virus (HIV-1) without cytotoxicity; dodecanal is the strongest distillate component [161, 162]. Quercetin is of effective reduction of the Vpr function (an additional gene product of induced HIV-1 cell cycle anomaly) without influence on the expression and of the HIV replication inhibition [163]. Ethereal oil is of virucidal activity (*in vitro*) on influenza virus. Study confirm safe and effective use of aqueous herbal extract of plant against coronaviridae (SARS-CoV), which causes a severe form of acute respiratory syndrome (SARS). Extract is of significant dose-dependent inhibiting action on the coronaviridae 3-chymotrypsin-like cysteine protease /3C-likeprotease (3CLpro) / activity and the RNA poly-

merase (RdRp) [164,165], besides, aqueous methanol extracts of the above-ground part of plant and decrease the expression of PGE2, iNOS, IL-1 β , TNF- α , and IL-6 in LPS-stimulated RAW 264.7 cells. [166]. The modelling molecular docking to the main virus protease (Mpro) and the toll-like receptor (TLR) of the host showed that flavonoid rutin may influence viral functional protein assembly and host inflammatory suppression may be potential inhibitors of SARS-CoV-2. [167]. Ethyl acetate flavonoid (quercetin, quercitrin, and rutin) herbal fraction is of antiviral activity (*in vitro*) against the mouse hepatitis virus (MHV) and Dengue virus (DENV) [168]. The hyperoside, containing in aqueous and ethanol herbal extract, is of inhibiting action against Dengue virus of a serotype 2 (DENV-2, strain 16681) [169, 170], besides, experiment (*in vivo* и *in vitro*) shows that hyperoside and quercitrin decrease influenza virus A (H1N1) replication are of the TLR-inhibiting effect in cells [171]. Flavonoid quercetin 3-O- α -L-rhamnopyranosyl-7-O- β -D-glucopyranoside is of antiviral activity against the rotavirus and the rhinovirus as well as inhibition activity (by 50 %) replication of the pig epidemic diarrhea virus (PEDV) [172,173]. Herbal extracts are of inhibition activity against the swine pseudorabies virus (PrV), the epidemic viral hemorrhagic fever, and the enterovirus (EV71) [174-176]; besides, the amantadine, the ribavirin, and the herbal extract injections study has shown significant antiviral activity during treatment mouse pneumonia [177].

Cytotoxic and antitumor activity. The results of study on genotoxicity of the methanol herbal extracts confirm treatment safety. Negative effect on genes is not established [178]. Aqueous extract of *Bacillus* strain fermented herb of high flavonoid (rutin, quercitrin, and quercetin levels) inhibits growth of a human liver cancer cell line (HepG2). The *In vitro* experiment has shown that the ethereal oil is of concentration-dependent cytotoxic effect on four human cancer cell lines (HepG2, A2780, MCF-7, and SKOV-3); study has established the apoptosis induction in the human liver cancer cell lines (HepG2) [179]. The root methanol extract is of potential antineoplastic properties for human liver cancer cell lines (HepG2). The extracted from ethanol herbal extract flavonoid fraction is of dose-dependent antineoplastic activity in human lung cancer cell lines (A549) [180]. The total flavonoid herbal extract fraction is of a significant inhibitory effect on growth of the mouse sarcoma cells (S-180) [181], and induced apoptosis of the myeloid leukemia cells (HL60), and of the mouse melanoma (B16BL6) [182]. Methanol herbal extract is of anti-carcinogenic activity against induced mouse leukemia (L1210) [183]. Aqueous herbal extract herb is of anti-leukemic activity; the test of five leukemia cell lines (L1210, U937, K562, Raji, P3HR1) showed significant inhibitory effect [184]. Ethanol herbal extract fractions are of cytotoxic activity; they induce the apoptosis of human lymphoblastic leukemia line cells (MOLT-4) [185]. 6 alkaloids (A-aristolactam, B-aristolac-

tam, A-pyperolactam, B-norcepharadion, B-cepharadion, and splendidinin) were *In vitro* experimented against five human cancer line cells (A-549, SK-OV-3, SK-MEL-2, XF-498, and HCT-15); splendidinin is of the highest cytotoxicity against all samples; B-aristolactam inhibited the glioblastoma cells (XF-498) selectively. The whole plant extract (ethanol) is of the dose-dependent cytotoxicity and induced apoptosis in primary colorectal human cancer cells [186], the leaf extract is active against human melanoma line cells (A375) [187].

Conclusion

The review summarizes the data on morphology, phytochemistry, biological activity, and practical use of *Houttuynia cordata*. The phytochemical study shows presence of various chemical elements (ethereal oils, terpenoids, phenylpropanoids, lignins, phenanthrene-derivatives, flavonoids, alkaloids, etc.) and confirm valid use of the plant in folk medicine for treatment of many diseases. The extracted from plants biologically active compounds are of an interest for creation of various medicines. Antineoplastic activity of the *Houttuynia cordata* herbal drugs is of close attention. The antiviral action against SARS-CoV and SARS-CoV-2 is an actual and important pharmacological action. The presented data on the scientific and clinical evidence confirming application of the biological active substances of the plant is still inadequate. Further study is needed to use the plant in medical practice.

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