*Review*

Natural Product Communications
Volume 15(9): 1–19

DOI: 10.1177/1934578X20957752
journals.sagepub.com/home/npx

SAGE

# A Review of the Traditional Uses, Botany, Phytochemistry, Pharmacology, Pharmacokinetics, and Toxicology of *Corydalis yanhusuo*

**Jingxia Zhang[1,2], Surong He[1,2], Jing Wang[1], Changli Wang[1,2], Jianhua Wu[1], Weifeng Wang[3], Fan Li[3], Shasha Li[3], Chongbo Zhao[1,2], and Fang Li[1,3]**

## Abstract

*Corydalis yanhusuo* W. T. Wang (Papaveraceae) is a traditional Chinese herbal medicine that has long been used to treat several conditions and is widely distributed in Asian countries. This review focuses on the traditional uses, botany, phytochemistry, pharmacology, pharmacokinetics, and toxicology of *C. yanhusuo*. The literature on *C. yanhusuo* was reviewed using several resources, including classic books on Chinese herbal medicine and scientific databases, namely, PubMed, Springer, Web of Science, Science Direct, and China National Knowledge Infrastructure. Based on information from these databases regarding the chemical components of *C. yanhusuo*, we evaluated the underlying interaction network between chemical components, biological targets, and associated diseases using Cytoscape software. To date, more than 160 compounds have been isolated and identified from *C. yanhusuo*, including alkaloids, organic acids, volatile oils, amino acids, nucleosides, alcohols, and sugars. The crude extracts and purified compounds of this plant have analgesic, antiarrhythmic, and antipeptic ulcer properties, along with hypnotic effects. However, studies on the pharmacokinetics of *C. yanhusuo* extracts remain limited. *C. yanhusuo* has therapeutic potential in diseases such as cancer and depression, probably due to glaucine and corydaline. Our network pharmacology analysis revealed interactions between 20 compounds, 54 corresponding targets, and 4 health conditions. We found that leonticine, tetrahydroberberine, and corydalmine may regulate the expression of *PTGS2*, *PTGS1*, *KCNH2*, *SCN5A*, *RXRA*, *CAMKK2*, *NCOA2*, and *ESR1*, representing a potential treatment strategy against pain, gastric ulcers, inflammation, and cardiac arrhythmias. Additionally, this article discusses the future directions of research on *C. yanhusuo*.

## Keywords

alkaloids, corydalis yanhusuo, pharmacokinetics, pharmacology, phytochemistry, traditional medicine

Received: May 4th, 2020; Accepted: August 13th, 2020.

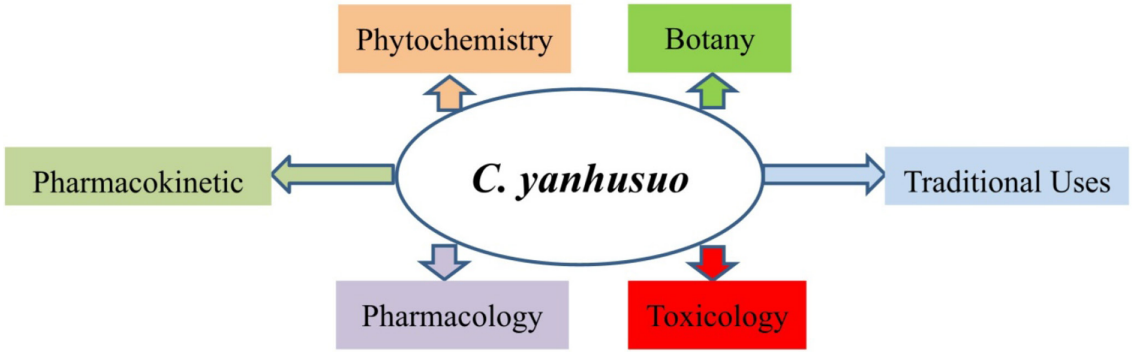
*Corydalis yanhusuo*, also known as Yanhusuo or Xuanhu, is a perennial herb widely distributed in China, Japan, Korea, Russia, and other Asian countries.[1,2] In China, *C. yanhusuo* is mainly distributed in the Zhejiang Province. *Corydalis yanhusuo* has been shown to improve blood circulation, alleviate pain caused by blood stasis, promote movement of Qi, and alleviate Qi stagnation-induced pain.[3]

Details regarding the pharmacological efficacy of *C. yanhusuo* are reported in the *Chinese Pharmacopoeia* (2015 edition). To date, more than 160 compounds have been isolated and identified from *C. yanhusuo*, including alkaloids, organic acids, volatile oils, amino acids, nucleosides, alcohols, and sugars.[1] This herb is often used to treat symptoms such as the chest, abdominal, and menstrual pain[4] and has been demonstrated to have several pharmacological effects: antinociceptive, antitumor, antibacterial, anti-inflammatory, and antidepressant effects, among others.[5,6]

Herein, we comprehensively reviewed available literature on *C. yanhusuo*, including its traditional uses and botany, as well as

[1]College of Pharmacy, Shaanxi University of Chinese Medicine, Xianyang, P. R. China
[2]College of Pharmacy, Engineering Technology Research Center of Shaanxi Administration of Chinese Herbal Pieces, Shaanxi University of Chinese Medicine, Xianyang, P. R. China
[3]Institute of Tradition Chinese Medicine, Shaanxi Provincial Academy of Traditional Chinese Medicine, Xi'an, P. R. China

**Corresponding Authors:**
Chongbo Zhao, College of Pharmacy, Shaanxi University of Chinese Medicine, Shiji Avenue, Xianyang 712046, P. R. China.
Email: 218030112382@email.sntcm.edu.cn
Fang Li, Shaanxi Provincial Academy of Traditional Chinese Medicine, Xi'an, Shaanxi 710003, P. R. China.
Email: 218030112382@email.sntcm.edu.cn




advances in phytochemistry, pharmacology, pharmacokinetics, and toxicology, from Chinese medicine books and scientific databases, namely, PubMed, Science Direct, Web of Science, Springer, Baidu Scholar, Elsevier, and China National Knowledge Infrastructure. Additionally, we present potential research pathways and new perspectives on *C. yanhusuo*.

## Traditional Uses

*Corydalis yanhusuo* was first reported in Lei Gong Pao Zhi Lun (Northern and Southern Dynasties, 618-907 AD) and has been used as an analgesic agent in traditional Chinese medicine for over 1100 years,[7] primarily for the treatment of chest pain. According to Hai Yao Ben Cao (Tang Dynasty, 907-960 AD), *C. yanhusuo* was used to treat postpartum blood stasis, whereas Yi Xue Qi Yuan (Jin and Yuan Dynasties, 1115-1368 AD) reported the use of this plant to treat spleen and stomach stasis and as an adjuvant to digestion. Ben Cao Gang Mu (Ming Dynasty, 1551-1578 AD) also reported its use in improving blood circulation and Qi, relieving pain, and micturition.[8] In China, Japan, Korea, Russia, and other Asian countries, *C. yanhusuo* has been used to treat Qi stagnation, blood stasis, chest pain, abdominal pain, amenorrhea, dysmenorrhea, and postpartum stasis.[2,5] Moreover, *C. yanhusuo* is commercially available in the United States as a dietary supplement.[9]

*Corydalis yanhusuo* has been reported to have various pharmacological effects; over 20 different prescriptions of this plant are listed in the *Chinese Pharmacopeia*, *Han Fang Bao Dian*, *Dong Yi Shi Shou Bao Yuan, Dong Yi Bao Jian,* and *Zhongyao chengfang zhiji*. The forms of these prescriptions include tablets, granules, and powders, among which tablets are the most commonly used form (Table 1). However, owing to the poor analgesic effect of raw *C. yanhusuo*, vinegar-processed products are widely used in the clinical setting. Alkaloids present in the herb are insoluble in water; therefore, they are processed with acetic acid to enhance their activity. Briefly, the rhizoma of *C. yanhusuo* is soaked in vinegar (20 L of vinegar per 100 kg of *C. yanhusuo*), first, sealed infiltration for 30 minutes then 150-160°C temperature and at a frequency of 40 times per minute turn, fried for 6 minutes and then cooled. Vinegar-processed *C. yanhusuo* effectively promotes blood circulation and Qi and relieves pain.[10]

## Botany

*Corydalis yanhusuo* belongs to the genus *Corydalis* of the Papaveraceae family. It is a glabrous perennial herb, approximately 10-20 cm in height, with spherical or oblate spheroid-shaped tubers (0.5-2.5 cm in diameter) and a yellowish interior. Its leaves are either 2-lobed or 3-lobed, with lanceolate segments that are often 2-3 parted, and its racemes contain 5-15 sparse flowers. The sepals are small and caducous with a symmetrical corolla. It has 4 petals, which are either purple or red; the upper part of the outer wheel is the largest, with a length of 1.5-2 cm; its top is dimpled, and its tail extends cylindrically having a length of 1.1-1.3 cm. Male flowers have 6 stamens bundled into 2 filaments, whereas female flowers have an oblate-columnar ovary, a subcircular stigma, and a linear capsule. Flowering occurs during April, while fruiting occurs from May to June(Figure 1).[16]

*Corydalis yanhusuo* is distributed in China, Japan, Korea, Russia, and other Asian countries, with a wide ecological niche.[2] In China, it is primarily distributed in Anhui, Jiangsu, Zhejiang, Hubei, Henan, and Shaanxi provinces.[17] The Zhejiang province is famous for its high production and quality of *C. yanhusuo*, as it has the largest areas for cultivation.[1]

## Phytochemistry

To date, more than 160 constituents of *C. yanhusuo* have been isolated and identified.[18] Alkaloids and terpenoids were identified as the characteristic components of this species. The following section details phytochemical studies conducted on *C. yanhusuo*. The compounds identified from this plant are listed in the relevant tables, and their structures are also presented.

### *Alkaloids*

The earliest known study of *Corydalis* alkaloids was published in 1928.[18] Alkaloids are the primary constituents of *C. yanhusuo*

**Table 1.** Traditional and Clinical Applications of *Corydalis yanhusuo*.

| Preparation name | Main composition | Traditional and clinical applications | References |
|---|---|---|---|
| Yuan Hu Zhi Tong Pian | Rhizoma *Corydalis*, Radix *Angelicae dahuricae* | Treating stomachache, headache, and dysmenorrhea caused by qi stagnation and blood stasis | [11] |
| Qi Zhi Wei Tong Pian | Radix *Bupleuri*, Rhizoma *Corydalis*, Fructus *Aurantii*, Rhizoma *Cyperi*, Radix *Glycyrrhizae*, Radix *Paeoniae Alba* | Treating abdominal pain | [4] |
| An Zhong Pian | Ramulus *Cinnamomi*, Rhizoma *Corydalis*, Concha *Ostreae*, Fructus *Foeniculi*, Fructus *Amomi*, Rhizoma *Alpinia officinarum*, Radix *Glycyrrhizae* | Treating stomachache caused by yang deficiency | [2,4] |
| An Wei Pian | Rhizoma *Corydalis*, *Alumen*, Endoconcha *Sepiae* | Treating epigastric stabbing pain caused by Qi stagnation and blood stasis | [4] |
| Fu Le Ke Li | Caulis *Lonicerae japonicae*, Radix *Glycyrrhizae*, Folium *Isatidis*, Herba *Taraxaci*, Cortex *Moutan*, Radix *Paeoniae rubra*, Fructus *toosendan*, Rhizoma *Corydalis*, Radix *Rehmanniae Prepared* | Treating abdominal pain and pelvic inflammation | [4] |
| Kuai Wei Pian | Endoconcha *Sepiae*, *Alumen*, Rhizoma *Corydalis*, Rhizoma *Bletillae*, Radix *Glycyrrhizae* | Treating abdominal pain, vomiting, acid reflux, appetite loss, and gastritis | [4] |
| Shen Yang Hong Yao Jiao Nang | Radix and Rhizoma *Notoginseng*, Rhizoma *Chuanxiong*, Radix *Angelicae Dahuricae*, Radix *Angelicae Sinensis*, Eupolyphaga *Steleophaga*, Rhizoma *Corydalis*, Flos *Carthami* | Treating wind dampness caused by blood stasis | [4] |
| Jin Fo Zhi Tong Pills | Radix *Paeoniae Alba*, Rhizoma *Corydalis*, Radix and Rhizoma *Notoginseng*, Radix *Curcumae*, Fructus *Citri sarcodactylis*, Rhizoma *Curcumae longae*, Radix *Glycyrrhizae* | Treating abdominal pain, dysmenorrhea, peptic ulcer, and chronic gastritis caused by Qi stagnation and blood stasis | [4] |
| Gu You Ling Cha Ji | Flos *Carthami*, Radix *Aconiti cocta*, Radix *Polygoni Multiflori Praeparata*, Radix *Dipsaci*, Radix and Rhizoma *Clematidis*, Rhizoma *Corydalis*, Radix *Saposhnikoviae*, Caulis *Spatholobi*, Periostracum *Cicadae* | Treating osteoarthritis and joint swelling | [4] |
| Du Sheng Huo Xue Pian | Radix and Rhizoma *Notoginseng*, Rhizoma *Cyperi*, Radix *Angelicae sinensis*, Rhizoma *Corydalis*, Caulis *Spatholobi*, Radix and Rhizoma *Rhei*, Radix *Glycyrrhizae* | Promoting blood circulation, treating dysmenorrhea caused by blood stasis | [4] |
| Yang Xue Qing Nao Pills | Radix *Angelicae Sinensis,* Rhizoma *Chuanxiong*, Radix *Paeoniae Alba*, Radix *Rehmanniae Prepared*, Ramulus *Uncariae Cum Uncis*, Caulis *Spatholobi*, Spica *Prunellae*, Semen *Cassiae*, Concha *Margaritifera*, Rhizoma *Corydalis*, Herba *Asari* | Treating headache and insomnia | [4] |
| Jing Tong Ke Li | Radix and Rhizoma *Notoginseng*, Rhizoma *Chuanxiong*, Rhizoma *Corydalis*, Rhizoma and Radix *Notopterygii*, Radix *Paeoniae Alba*, Radix and Rhizoma *Clematidis*, Radix *Puerariae* | Treating neck, shoulder, and upper limb pain caused by Qi stagnation and blood stasis | [4] |
| Zhen Xin Tong Kou Fu Ye | Radix *Codonopsis*, Radix and Rhizoma *Notoginseng*, Rhizoma *Corydalis*, *Pheretima*, Bulbus *Allii Macrostemonis*, Semen *Descurainiae*, Cortex *Cinnamomi*, Borneolum *Syntheticum*, *Mentholum* | Treating chest pain caused by Qi and blood stasis | [4] |
| Xuan Hu Suo San | Rhizoma *Corydalis*, Radix *Achyranthis Bidentatae*, Radix *Angelicae Sinensis*, Fructus *Psoraleae* | Clearing postpartum blood stasis | [12] |
| Fu Nv Tong Jing Wan | Rhizoma *Corydalis*, Feces *Trogopterorum*, Radix and Rhizoma *Salviae Miltiorrhizae*, Pollen *Typhae* | Treating abdominal pain caused by Qi and blood stasis | [12] |
| Yan Bing Pian | Rhizoma *Corydalis*, Borneolum *Syntheticum* | Treating coronary heart disease and angina pectoris | [12] |
| Ba Wei Tong Jing Pian | Radix *Cyathulae*, Cortex *Moutan*, Radix *Angelicae Sinensis*, Radix *Paeoniae Alba*, Rhizoma *Corydalis*, Semen *Persicae*, Ramulus *Cinnamomi*, Radix *Aucklandiae* | Treating dysmenorrhea | [13] |
| Ru Shen Tang | Rhizoma *Corydalis*, Radix *Angelicae Sinensis*, Cortex *Cinnamomi*, Rhizoma *Cyperi,* Radix *Aucklandiae* | Treating pain caused by Qi and blood stasis | [14] |
| Fu Yuan Tong Qi San | Fructus *Foeniculi*, Squama *Manis*, Radix *Aucklandiae*, Rhizoma *Corydalis*, Semen *Pharbitidis*, Pericarpium *Citri Reticulatae*, Radix *Glycyrrhizae* | Treating pain caused by Qi stagnation | [15] |
| Xuan Hu Suo San | Radix *Angelicae Sinensis*, Radix *Paeoniae Rubra,* Rhizoma *Corydalis*, Pollen *Typhae*, Ramulus *Cinnamomi*, Frereana *Boswellia*, Commiphora *myrrha* | Clearing postpartum blood stasis | [15] |

**Table 2.** Alkaloids Isolated From *Corydalis yanhusuo*.

| Identifier | Name | Plant part | References |
|---|---|---|---|
| 1 | Glaucine | Aerial part | [20] |
| 2 | Norglaucine | Aerial part | [20] |
| 3 | *N*-methyllaurotetanine | Roots | [21] |
| 4 | Isoboldine | Roots | [22] |
| 5 | Nantenine | Aerial part | [23] |
| 6 | Thaliporphine | Roots | [6] |
| 7 | Lirioferine | Roots | [6] |
| 8 | *O*-methylbulbocapnine | Roots | [23] |
| 9 | Dehydrocorydaline | Roots | [24] |
| 10 | Berberine | Roots | [24] |
| 11 | Palmatine | Roots | [25] |
| 12 | Coptisine | Roots | [24] |
| 13 | Columbamine | Roots | [26] |
| 14 | Dehydroyuanhunine | Roots | [23] |
| 15 | 13-Methylpalmatrubine | Roots | [24] |
| 16 | Yanhusuine | Roots | [27] |
| 17 | Corydayanine | Roots | [27] |
| 18 | Dehydrocorybulbine | Roots | [21] |
| 19 | Jatrorrhizine | Roots | [21] |
| 20 | 13-Methyl-dehydrocorydalmine | Roots | [21] |
| 21 | Tetrahydropalmatine | Roots | [28] |
| 22 | Tetrahydrocoptisine | Roots | [24] |
| 23 | Yuanhunine | Roots | [21] |
| 24 | (−)-Corypalmine | Roots | [24] |
| 25 | Corydalmine | Roots | [29] |
| 26 | Scoulerine | Roots | [21] |
| 27 | Tetrahydrojatrorrhizine | Roots | [21] |
| 28 | Tetrahydrocorysamine | Roots | [26] |
| 29 | Tetrahydroberberine | Roots | [24] |
| 30 | Corydaline | Roots | [28] |
| 31 | Isocorybulbine | Roots | [24] |
| 32 | Corybulbine | Roots | [24] |
| 33 | Didehydroglaucine | Roots | [24] |
| 34 | Dehydronantenine | Roots | [30] |
| 35 | 7-Formyldidehydroglaucine | Roots | [31] |
| 36 | Protopine | Roots | [28] |
| 37 | *α*-Allocryptopine | Roots | [32] |
| 38 | Oxoglaucine | Roots | [33] |
| 39 | Corunine | Roots | [29] |
| 40 | Dihydrosanguinsrine | Roots | [34] |
| 41 | Dihydrochelerythrine | Roots | [35] |
| 42 | 8-Oxocoptisine | Roots | [24] |
| 43 | Pontevedrine | Roots | [24] |
| 44 | 6-Acetonyl-5,6 dihydrosanguinarine | Roots | [29] |
| 45 | Homochelidonine | Roots | [29] |
| 46 | Saulatine | Roots | [21] |
| 47 | Nordelporphine | Roots | [21] |
| 48 | Leonticine | Roots | [34] |
| 49 | Bicuculline | Roots | [32] |
| 50 | Coryphen-anthrine | Aerial part | [21] |
| 51 | *N*-methylcanadine | Roots | [31] |
| 52 | *N*-methyltetrahydropalmatine | Roots | [31] |
| 53 | 1-[2-(*N*-methylaminoethy)]-3,4,6,7-tetramethoxyphenanthrene | Aerial part | [20] |
| 54 | *N*,*N*-dimethyl-*N*′,*N*′- dimethyl-diphenyl-one | Roots | [33] |
| 55 | *N*,*N*-dimethyl-*N*′-methyl-diphenyl-one | Roots | [33] |
| 56 | Noroxyhydrastinine | Roots | [24] |
| 57 | Taxilamine | Roots | [21] |
| 58 | Epiberberine | Roots | [6] |
| 59 | Dehydrocorydaline chloride | Roots | [36] |
| 60 | Cryptopine | Roots | [32] |
| 61 | 8-Trichloromethyl-7,8-dihydrocoptisine | Roots | [24] |
| 62 | Tetrahydrocolumbamine | Roots | [37] |
| 63 | Stepharanine | Roots | [26] |

(Continued)

**Table 2.** Continued

and play an important role in pain relief. To date, 64 alkaloids have been isolated from the plant; they are primarily categorized as isoquinoline alkaloids based on their structure. Other alkaloids include berberine, aporphine, proto-opioid base, isoquinoline benzylimidazole, and benzophenanthridine.[19] Alkaloids are presented in Table 2, and their structures are shown in Figure 2.

## *Water-Soluble Nonalkaloids*

Water-soluble nonalkaloids present in *C. yanhusuo* have high polarity due to their hydroxyl, amino, and carboxyl groups. Water-soluble components, such as organic acids, amino acids, and carbohydrates are commonly separated by alumina adsorption, column chromatography, gel column chromatography, reverse-phase adsorption column chromatography, and gas chromatography-mass spectrometry.[38-40] Analysis of 80% ethanol extract of *C. yanhusuo* isolated using a DA201 type macroporous adsorption resin revealed that the fraction eluted with

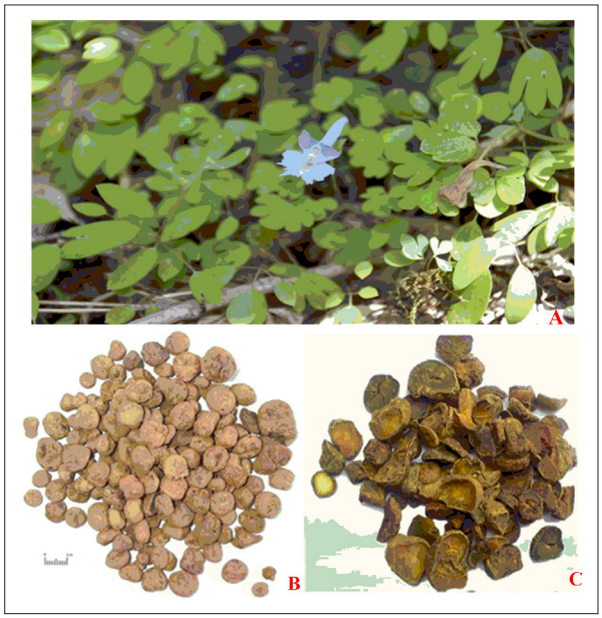



**Figure 1.** *Corydalis yanhusuo* plant (A), *C. yanhusuo* rhizoma (B), vinegar-fried *C. yanhusuo* (C).

**Table 3.** Organic Acids Isolated From *Corydalis yanhusuo*.

| Identifier | Name | Plant part | References |
|---|---|---|---|
| 1 | 4-Hydroxybenzoic acid | Roots | 38 |
| 2 | Vanillic acid | Roots | 38 |
| 3 | Lactic acid | Roots | 39 |
| 4 | Butanedioic acid | Roots | 40 |
| 5 | 2,3-Dihydroxypropionic acid | Roots | 39 |
| 6 | Malic acid | Roots | 39 |
| 7 | Palmitic acid | Roots | 39 |
| 8 | Stearic acid | Roots | 39 |
| 9 | Citric acid | Roots | 39 |
| 10 | 2-Piperidinecarboxylic acid | Roots | 40 |
| 11 | *trans*-9-Octadecenoic acid | Roots | 40 |
| 12 | Docosanoic acid | Roots | 22 |
| 13 | *trans*-13-Octadecenoic acid | Roots | 40 |
| 14 | Ethanedioic acid | Roots | 40 |
| 15 | Propionic acid | Roots | 18 |
| 16 | Benzoic acid | Roots | 40 |
| 17 | Dodecanoic acid | Roots | 40 |
| 18 | Xylonic acid | Roots | 40 |
| 19 | Propanetricarboxylic acid | Roots | 40 |
| 20 | 2-Propenoic acid | Roots | 40 |
| 21 | Glucaric acid | Roots | 40 |
| 22 | Pantothenic acid | Roots | 40 |
| 23 | 2-Hydroxyacrylic acid | Roots | 39 |
| 24 | 2-Butenedioic acid | Roots | 40 |
| 25 | Ribonic acid | Roots | 40 |
| 26 | Galacturonic acid | Roots | 40 |

pure water shows anti-ischemic effects.[39] Moreover, the polysaccharide YHP-1 extracted from *C. yanhusuo* exhibited antitumor activity.[41] Therefore, it is important to extract and isolate its water-soluble compounds. Organic acids, amino acids, and alcohols and sugars isolated from *C. yanhusuo* are presented in Tables 3–5, respectively. The structures of these compounds are shown in Figures 3–5, respectively.

## *Volatile Oils*

Most volatile oils obtained from plants have various medicinal and health-promoting effects. The most abundant volatile oil in *C. yanhusuo* is 2′-hydroxy-4′-methoxyacetophenone, which is known to show analgesic, antimicrobial, anti-inflammatory, and antitumor activities and can be used to treat cardiovascular diseases.[42] Moreover, another volatile oil in *C. yanhusuo*—*a*-bisabolol—has been demonstrated to have anti-inflammatory and spasmolytic properties and is widely used in some European countries.[43] Volatile oil from the rhizoma of *C. yanhusuo* is extracted using the heating reflux, rope extraction, and ultrasonic extraction methods.[44] The chemical constituents of volatile oils have been analyzed using Fourier-transform infrared spectroscopy and gas chromatography-mass spectrometry.[42] Volatile oils

**Table 4.** Amino Acids Isolated From *Corydalis yanhusuo*.

| Identifier | Name | Plant part | References |
|---|---|---|---|
| 1 | L-Valine | Roots | 40 |
| 2 | L-Threonine | Roots | 40 |
| 3 | D-Ornithine | Roots | 40 |
| 4 | L-Isoleucine | Roots | 40 |
| 5 | L-Aspartic acid | Roots | 40 |
| 6 | *N-a*-acetyl-L-lysine | Roots | 40 |
| 7 | L-Proline | Roots | 40 |
| 8 | L-Citrulline | Roots | 40 |
| 9 | *N*5-acetylornithine | Roots | 38 |
| 10 | L-Tyrosine | Roots | 40 |
| 11 | Serine | Roots | 1 |
| 12 | Alanine | Roots | 40 |
| 13 | Phenylalanine | Roots | 26 |

from *C. yanhusuo* are presented in Table 6, and their structures are shown in Figure 6.

## *Nucleosides*

Nucleosides have various biological functions and are crucial for living cells. They participate in deoxyribonucleic acid metabolic processes, show anticancer and antiviral activities, and can be used in gene therapy. For example, adenosine improves cardio-cerebral blood circulation, prevents arrhythmia, inhibits neurotransmitter release, and regulates adenylate cyclase activity.[46] Nucleosides isolated from *C. yanhusuo* are presented in Table 7, and their structures are shown in Figure 7.

## *Other Compounds*

In addition to the aforementioned components, anthraquinones (emodin and physcion), terpenoids (3*β*-hydroxy-olean-11,13(18)-dien-28-oic acid), steroids (stigmasterol, *β*-sitosterol, and daucosterol),[35] inorganic acids (phosphoric acid),[39] some trace elements (Pb, Cr, Cd, Cu, Mn, Fe, Zn, Al, Ba, B, Ca, Mg,

**Table 5.** Alcohols and Sugars Isolated From *Corydalis yanhusuo*.

| Identifier | Name | References |
|---|---|---|
| 1 | Cyclohexane-1,2,3,4,5,6-hexol | 39 |
| 2 | Glycerol | 39 |
| 3 | Ribonolactone | 39 |
| 4 | D-Glucopyranose | 39 |
| 5 | Lactose | 39 |
| 6 | D(+)-Ribonic acid gamma-lactone | 40 |
| 7 | D-Glucuronic acid | 40 |
| 8 | D-Fructose | 40 |
| 9 | D-Mannose | 40 |
| 10 | D-Turanose | 40 |
| 11 | Galacturonic acid | 40 |
| 12 | Polysaccharide | 41 |

P, Sr, Ti, and V),[47-49] and some unsaturated fatty acids (*trans*-linoleic acid and hexadecanoic acid) have also been isolated from *C. yanhusuo*.[50]

## Pharmacology

*Corydalis yanhusuo* has various pharmacological effects on the digestive, nervous, and cardiovascular systems and has therapeutic benefits in treating complications associated with thrombosis and cancer. In the following section, the primary pharmacological activities of *C. yanhusuo*, including its active ingredients, minimum effective concentration, and relevant in vitro and in vivo research, are discussed (Table 8).

### *Effects on the Central Nervous System*

*Corydalis yanhusuo* primarily shows analgesic, sedative, and hypnotic effects on the central nervous system, with alkaloids mostly contributing to the analgesic effects. Vinegar-processing can enhance the effects of *Rhizoma Corydalis* to facilitate blood flow and relieve stasis,[98,99] while water extracts of *C. yanhusuo* effectively attenuate acute inflammatory and neuropathic pain in mice.[9] Tetrahydropalmatine extracted from *C. yanhusuo* is widely used to treat chronic dull pain and persistent pain.[29] Moreover, both tetrahydropalmatine and corydaline significantly increase mechanical and thermal pain threshold in rats,[51] with similar analgesic effects.[8]

Tetrahydropalmatine from *Corydalis* L and *Corydalis* J show sedative and hypnotic activities in rabbits, mice, dogs, and monkeys, and significantly reduce spontaneous and passive activities.[52,53] Tetrahydropalmatine also has anxiolytic effects[54] and is effective against depression.[55] Lastly, the total alkaloid of *C. yanhusuo* showed antifatigue, antihypoxia, and antistress activity in mice.[56]

### *Effects on the Digestive System*

The pharmacological effects of *C. yanhusuo* on the digestive system include antigastric ulcer and hepatoprotective activities and effects on smooth muscle activation and contraction. The active components of *C. yanhusuo* with such properties are tetrahydropalmatine and protopine. In particular, tetrahydropalmatine protected rats from gastrointestinal injury, an effect that may be associated with its impact on gastric mucosal blood flow and regulation of dopamine transmitters.[100] Another study in mice demonstrated the hepatoprotective effect of tetrahydropalmatine.[57] Oral administration of tetrahydropalmatine (20, 40, 80, 160, and 320 mg/kg) reduced intestinal motive force in healthy mice; at 320 mg/kg it inhibited spontaneous contractions in isolated rabbit duodenum, thereby inhibiting

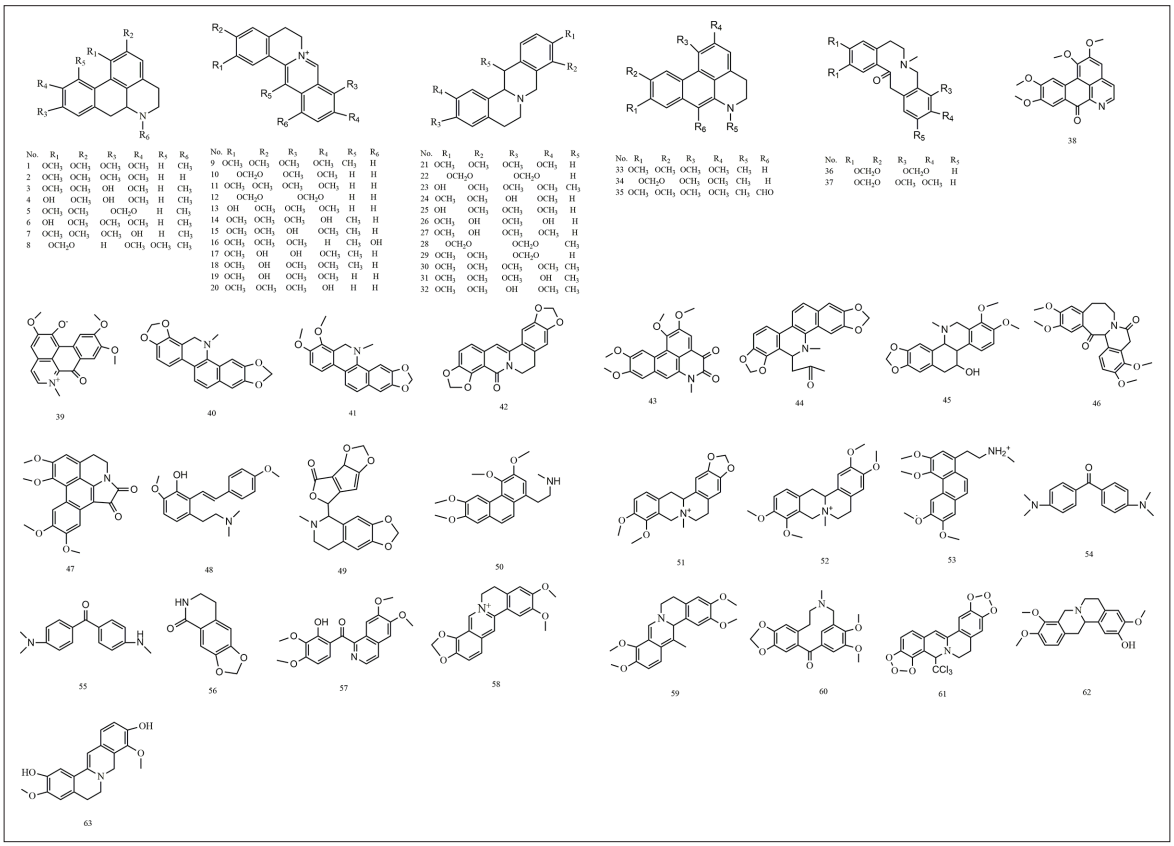


**Figure 2.** Chemical structures of alkaloids in *Corydalis yanhusuo*.

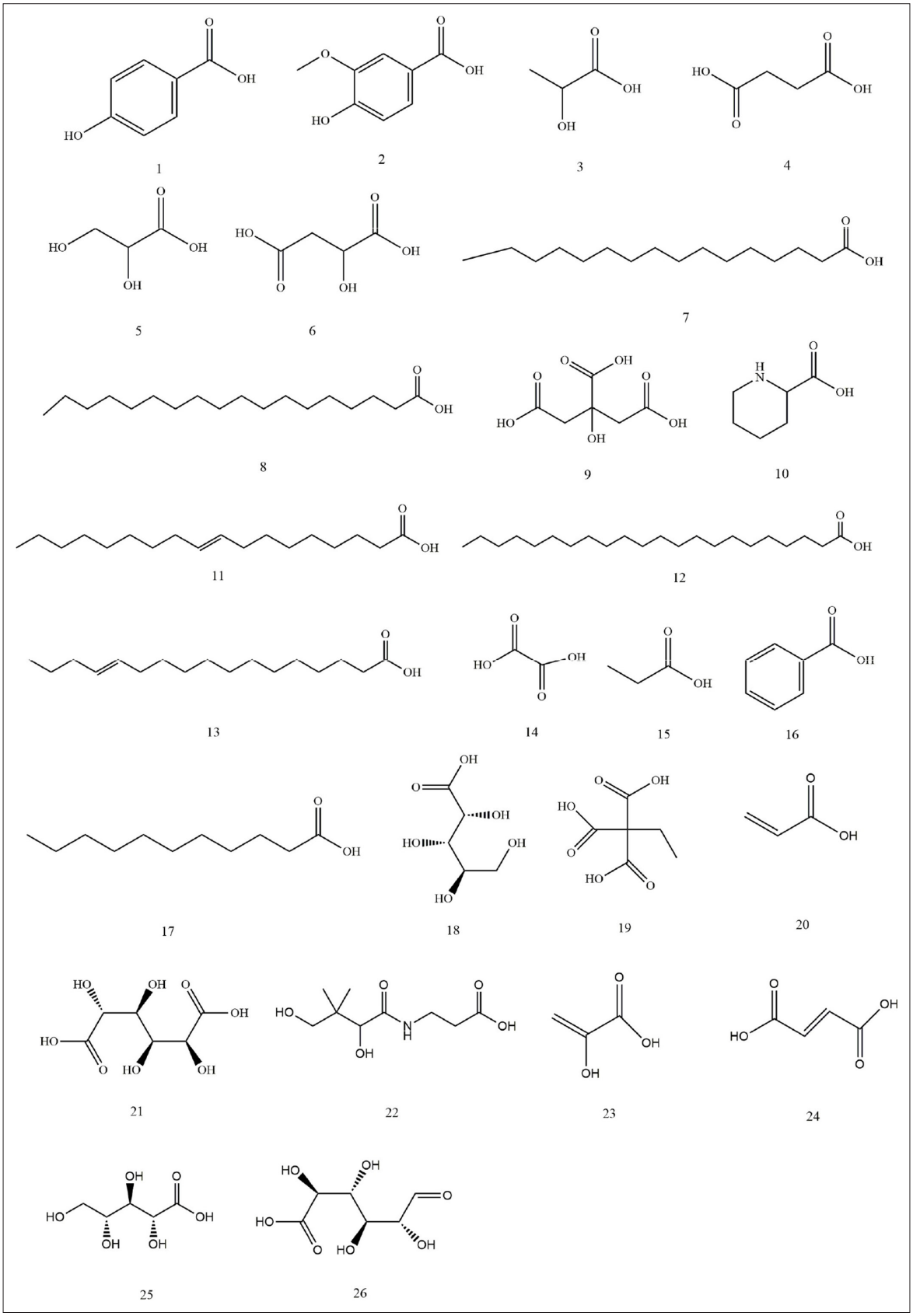



**Figure 3.** Chemical structures of organic acids in *Corydalis yanhusuo*.

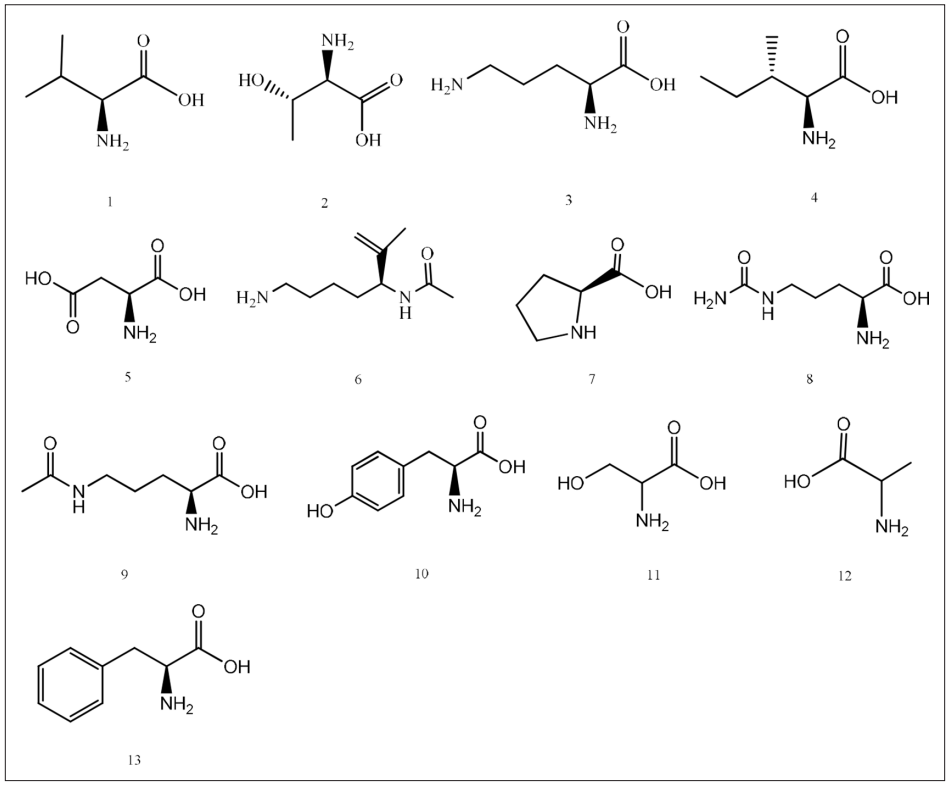



**Figure 4.** Chemical structures of amino acids in *Corydalis yanhusuo*.

intestinal smooth muscle activity.[58,101] Lastly, corydaline was shown to promote gastric emptying and small intestinal transit, as well as facilitate gastric accommodation.[59]

## *Effects on the Cardio-Cerebrovascular System*

*Corydalis yanhusuo* can promote coronary artery dilation, protect against arrhythmia and myocardial and cerebral ischemia-reperfusion injury, and alleviate myocardial infarction.[1,102] Tetrahydropalmatine can decrease norepinephrine and catecholamine in rat blood vessels and peripheral tissues, respectively, which may subsequently contribute to reduced heart rate and blood pressure.[60,61] This compound can also lower blood pressure by blocking voltage-dependent calcium channels.[62] In contrast, the total alkaloids from *C. yanhusuo* were found to exhibit protective effects in experimental models of acute myocardial ischemia, alleviate oxidative stress induced by isoproterenol, protect cardiac function, and reduce myocardial injury and apoptosis in rats with myocardial infarction.[63–65] Kang et al described similar effects of total alkaloids in dogs.[66]

Tetrahydropalmatine alleviates cerebral ischemia/reperfusion injury by antagonizing free radicals and calcium ions and by regulating $Ca^{2+}$-ATPase activity.[65] It significantly reduces arrhythmias during ischemia/reperfusion injury and reduces lipid peroxides in the myocardium to prevent myocardial injury.[67] This compound significantly increased the activity of $Na^{+}$-$K^{+}$-ATPase and $Ca^{2+}$-ATPase in the cell membrane, alleviated intracellular $Ca^{2+}$ overload, and ultimately reduced cerebral ischemia-reperfusion injury in rats.[68,69] Moreover, it showed protective effects in focal cerebral ischemia-reperfusion injury in rats, which is related to lipid peroxidation.[70] However, another study showed that the antimyocardial ischemic effect of *C. yanhusuo* could be related to the direct protective effect of tetrahydropalmatine, dehydrocorydaline, berberine, and palmatine on myocardial cells, rather than its antioxidative mechanisms.[71] *Corydalis yanhusuo* rhizoma extract regulates the expression of Bcl-2 family proteins to inhibit cardiomyocyte apoptosis.[72]

*Corydalis yanhusuo* alkaloids were shown to protect against coronary heart disease and arrhythmia.[73] High concentrations of tertiary amine base and quaternary ammonium hydroxide were also found to prolong the duration of action potentials in ventricular myocytes of guinea pigs. However, these 2 alkaloids can also have the opposite effect when administered at low concentrations.[74] *Corydalis yanhusuo* extract can protect against myocardial damage and provide resistance to arrhythmia.[75]

Other studies have also revealed that *C. yanhusuo* extract can improve hemorheology in rats in a hypercoagulable state and inhibit the formation of venous, arterial, and arteriovenous bypass thromboses.[76,77] Tetrahydropalmatine inhibits platelet aggregation induced by adenosine diphosphate, arachidonic acid, and collagen, resulting in antithrombotic activity.[78]

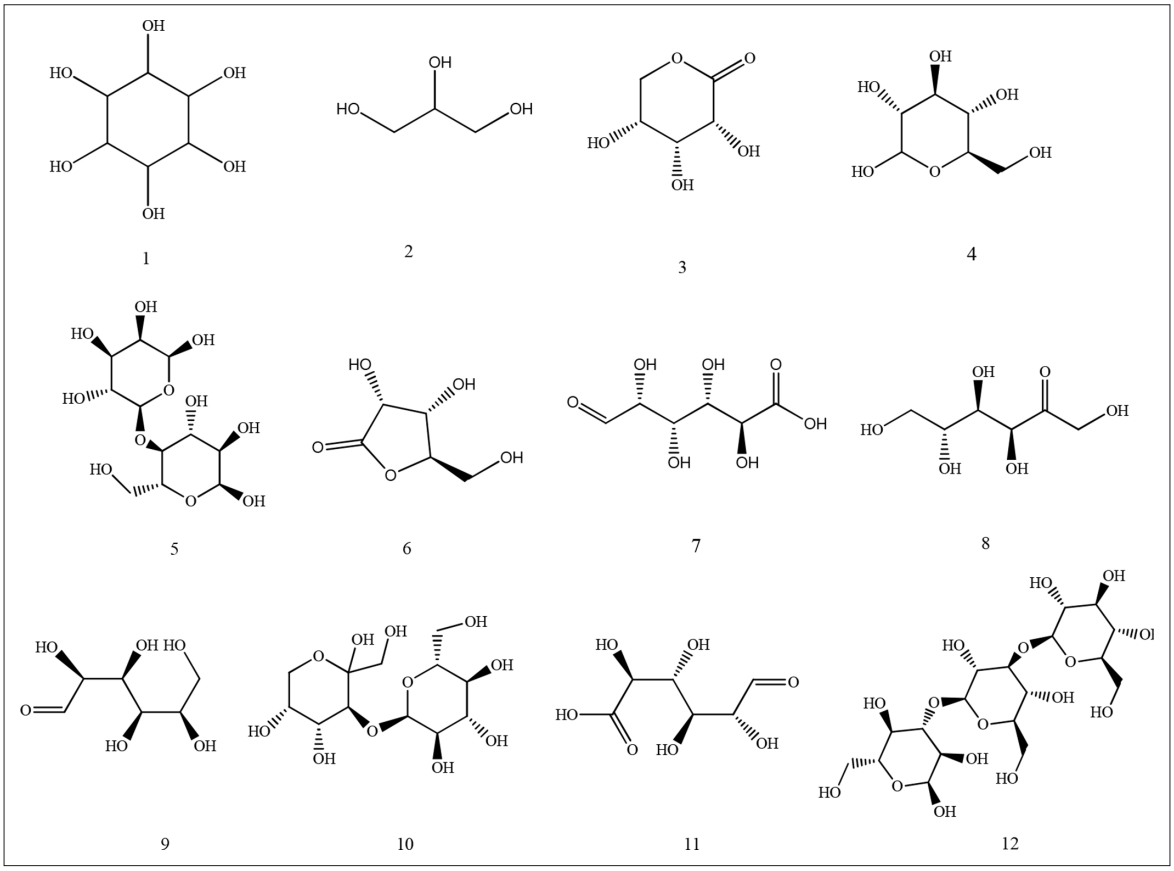



**Figure 5.** Chemical structures of alcohols and sugars in *Corydalis yanhusuo*.

## *Antitumor Activity*

Recently, in vitro studies have elucidated the antitumor effects of *C. yanhusuo*, which are primarily mediated by alkaloids and polysaccharides. Alkaloid extracts of *C. yanhusuo* and berberine markedly inhibit angiogenesis,[79,80] which could have a significant impact on tumor growth and metastasis. The polysaccharide YHPS-1 inhibited the growth of murine sarcoma and lung cancer cell lines.[41] *Corydalis yanhusuo* alkaloids can also inhibit P-glycoprotein activity in tumor cells and reverse multidrug resistance.[81,82] The total alkaloids from *C. yanhusuo* were found to significantly inhibit the proliferation of human liver cells as well as 10 human tumor cell lines derived from different tissues,[83] notably, treatment-resistant gastric cancer cell lines.[84] Liposoluble nonphenolic alkaloids and 13-methyl-palmatrubine from *C. yanhusuo* were also found to have cytotoxic effects against cancer cells and inhibit the growth of A549 and SMMC-7721 cancer cell lines.[85,103] *Corydalis yanhusuo* extract also inhibits the proliferation of MCF-7 and MDA-MB-231 breast cancer cells,[86,87] while it inhibits H22 hepatocellular carcinoma in mice.[88] Tetrahydropalmatine was also shown to inhibit the proliferation and promote apoptosis of U251MG malignant glioma cells in vitro and significantly prevent malignant glioma growth in vivo.[89] It also inhibits a human leukemia cell line.[90]

## *Antibacterial and Anti-Inflammatory Effects*

The chloroform extract of *C. yanhusuo* has high microbiostatic activity against *Fusarium*, *Helminthosporium*, and anthracnose-related fungus, as well as against some bacteria.[91] Palmatine and berberine also inhibit the growth of *Clostridium perfringens*.[92] The 95% ethanol extract of *C. yanhusuo* was shown to have significant anti-inflammatory effects, which were mostly attributed to the activities of coptisine, berberine, palmatine, dihydrosanguinarine, and dehydrocorydaline.[93] *Corydalis yanhusuo* alkaloids also inhibited the activity of human immunodeficiency virus type 1 reverse transcriptase.[94] Furthermore, berberine shows antibacterial and anti-inflammatory effects by inducing the expression of toll-like receptor 2, activating IκB and interferon signaling pathways, and promoting the secretion of tumor necrosis factor.[95]

## *Other Pharmacological Effects*

Besides the above-mentioned properties, tetrahydropalmatine can also prevent the formation of portal hypertension in cirrhosis and significantly reduce glucagon levels.[96] Moreover, it protects against acute radiation-induced lung injury in rats by inhibiting apoptosis and reducing oxidative damage.[97]

**Table 6.** Volatile Oils From *Corydalis yanhusuo*.

| Identifier | Name | Plant part | References |
|---|---|---|---|
| 1 | 2′-Hydroxy-4′-methoxyacetophenone | Roots | [42] |
| 2 | Benzene, 1-(1,5-dimethyl-4-hexen-1-yl)-4-methyl | Roots | [42] |
| 3 | Linoleic alcohol | Roots | [42] |
| 4 | Eicosane | Roots | [42] |
| 5 | Heneicosane | Roots | [42] |
| 6 | Carveol | Roots | [42] |
| 7 | 2,3-Dihydroxypropanal | Roots | [43] |
| 8 | 3,4-Dimethylpentanol | Roots | [43] |
| 9 | 2-Methyl-2-phenylpropane | Roots | [43] |
| 10 | *γ*-Terpinene | Roots | [43] |
| 11 | Verbenone | Roots | [43] |
| 12 | 1-Methoxy-4-(1-propenyl)-benzene | Roots | [43] |
| 13 | Diphenylamine | Roots | [43] |
| 14 | 2-Beta-methoxy-5-alpha-cholestan-19-oic acid | Roots | [43] |
| 15 | *a*-Bisabolol | Roots | [43] |
| 16 | Abietic acid | Roots | [43] |
| 17 | Spiro[2.4]hepta-4,6-diene | Roots | [44] |
| 18 | Heptacosane | Roots | [43] |
| 19 | (Methoxymethyl)trimethylsilane | Roots | [44] |
| 20 | Heptadecane | Roots | [45] |
| 21 | Hexadecane | Roots | [45] |
| 22 | Caryophyllene oxide | Roots | [45] |
| 23 | Pentadecane | Roots | [45] |

**Table 7.** Nucleosides Isolated From *Corydalis yanhusuo*.

| Identifier | Name | Plant part | References |
|---|---|---|---|
| 1 | Cytidine | Roots | [46] |
| 2 | Uridine | Roots | [46] |
| 3 | Adenosine | Roots | [26] |
| 4 | 2′-Deoxyadenosine | Roots | [46] |
| 5 | Thymidine | Roots | [46] |
| 6 | Guanosine | Roots | [46] |
| 7 | Xanthosine | Roots | [21] |

### *Network Pharmacology*

The pharmacological effects of traditional Chinese medicines are complex, with multicomponent and multitarget characteristics. Network pharmacology explains the therapeutic effect of herb pairs.[104] We cross-referenced the chemical compositions of *C. yanhusuo* with the pharmacological functions mentioned in the Chinese Medicine System Pharmacology Database. Using the systems pharmacology analysis platform TCMSP (http://bigd.big.ac.cn/databasecommons/database/id/4096), we designed a compound-target-disease network for *C. yanhusuo* (). The screening conditions were set to oral bioavailability ≥30% and drug-likeness ≥0.18. All TCMSP drug targets were imported into the Uniprot (https://www.uniprot.org/) database, and the target gene name was entered to define the species as *Homo-sapiens*. Overall, 20 chemical components were screened, corresponding to 55 related targets. Based on the information available in the GeneCards (http://www.genecards.org/) database, we identified 6017 pain-related targets, 4479 gastric ulcer-related targets, 3679 cardiac arrhythmia-related targets, and 9921 inflammation-related targets. After analysis of the potential intersections between these identified targets and the chemical components, we found 20 potentially active compounds and 54 corresponding targets (Figure 8). Based on the degree, the most active constituents were leonticine (degree = 31), tetrahydroberberine (degree = 28), and corydalmine (degree = 25), all of which showed properties for treating pain, gastric ulcers, inflammation, and cardiac arrhythmias through the regulation of *PTGS2*, *PTGS1*, *KCNH2*, *SCN5A*, *RXRA*, *CAMKK2*, *NCOA2*, and *ESR1*.

## Pharmacokinetics

To date, few studies have investigated the pharmacokinetics of *C. yanhusuo* extracts and compounds. The pharmacokinetics of intramuscularly injected tetrahydropalmatine sulfate and polycystic liposomes of tetrahydropalmatine sulfate (both at 10 mg/kg) were evaluated in mice. The time taken for the plasma drug concentration to decline to half ($t_{1/2}$) was 3.09 ± 0.37 and 33.97 ± 4.78 hours, respectively, while the peak concentration ($C_{max}$) was 289.05 ± 30.37 and 68.34 ± 8.72 μg/L, respectively. The time taken to reach $C_{max}$ ($T_{max}$) for intramuscularly injected tetrahydropalmatine sulfate and polycystic liposomes of tetrahydropalmatine sulfate was 0.93 ± 0.15 and 3.92 ± 0.43 hours, respectively. These data indicate significant differences in pharmacokinetics depending on the route of administration.[105] Tetrahydropalmatine orally administered to mice at 6.5 mg/kg had a $t_{1/2}$ of 3.13 ± 0.35 hours, $C_{max}$ of 289.05 ± 30.37 μg/L, and $T_{max}$ of 1.16 ± 0.28 hours.[106] These findings suggest that the bioavailability of tetrahydropalmatine can be improved using polycystic liposomes. Moreover, intragastric administration of total alkaloids of *C. yanhusuo* at doses of 125, 250, and 500 mg/kg in rats revealed that the blood concentration of tetrahydropalmatine was positively correlated with its $C_{max}$ and $T_{max}$.[107] Additional studies on rabbits and rats also demonstrated that tetrahydropalmatine and corydaline plasma concentrations were positively correlated with their $C_{max}$ and $T_{max}$.[108,109] Furthermore, the plasma concentration of L-tetrahydropalmatine was shown to always exceed that of D-tetrahydropalmatine in rats treated with 40 mg/kg tetrahydropalmatine.[110,111] The combination of P-glycoprotein and D-tetrahydropalmatine may be responsible for the difference in stereoselective absorption.[111] D-tetrahydropalmatine was found to have no significant inhibitory effect on the CYP450 subtypes of phase I drug-metabolizing enzymes in human liver microsomes. However, L-tetrahydropalmatine had strong inhibitory effects on CYP2D6 (half-maximal inhibitory concentration = 0.46 μmol/L).[112] Rats treated intragastrically

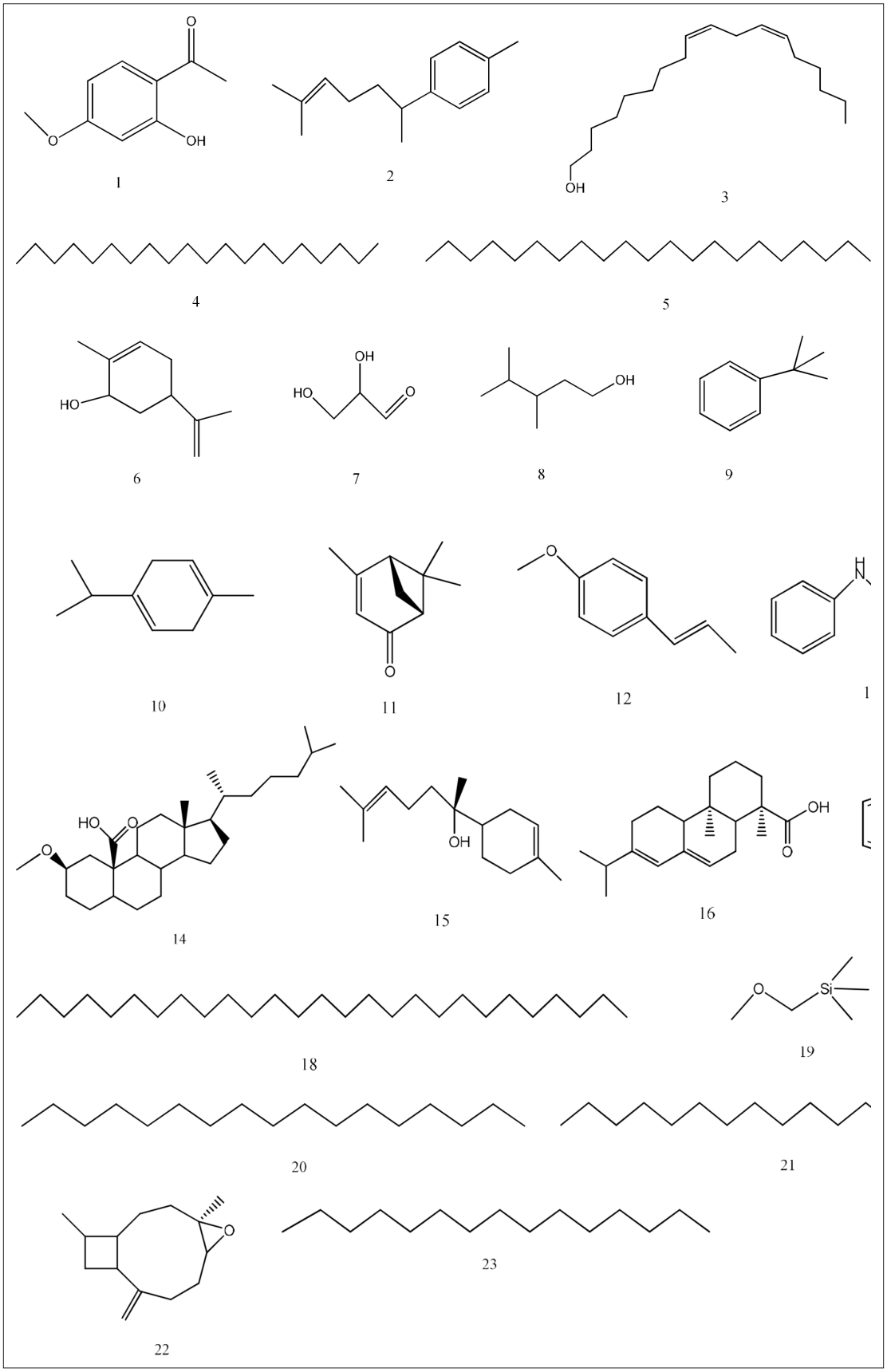



**Figure 6.** Chemical structures of volatile oils in *Corydalis yanhusuo*.

**Table 8.** Pharmacological Effects of *Corydalis yanhusuo*.

| Pharmacological effects | Details | Extracts/compounds | Minimal toxic concentration/dose | Type of experiment | References |
|---|---|---|---|---|---|
| Effect on the nervous system | Analgesic effects | Water extract | 100 mg/kg (i.p.) | In vivo | 9 |
| | | Corydaline | 10 mg/kg (i.p.) | In vivo | 8 |
| | | Tetrahydropalmatine | 10 mg/kg (i.p.) | In vivo | 51 |
| | | Tetrahydropalmatine | 1 mg/kg (i.p.) | In vivo | 9 |
| | | Corydaline | 30 mg/kg (i.v.) | In vivo | 52 |
| | | Tetrahydropalmatine | 15 mg/kg (i.v.) | In vivo | 52 |
| | | Tetrahydrocolumbamine | 10 mg/kg (i.v.) | In vivo | 52 |
| | Sedative and hypnotic effects | Tetrahydropalmatine | 40 mg/kg (i.p.) | In vivo | 53 |
| | | Tetrahydrocolumbamine | 40 mg/kg (i.p.) | In vivo | 53 |
| | | D-Glaucine | 10 mg/kg (i.p.) | In vivo | 53 |
| | Anxiolytic effects | Tetrahydropalmatine | 25 mg/kg (i.p.) | In vivo | 54 |
| | | Total alkaloids | 6 g/kg (i.g.) | In vivo | 55 |
| | Antihypoxia ability | Total alkaloids | 50 mg /kg (i.g.) | In vivo | 56 |
| Effects on the digestive system | Protection of liver function | Tetrahydropalmatine | 20 mg/kg (i.g.) | In vivo | 57 |
| | Inhibiting smooth muscle activity | Tetrahydropalmatine | 20 mg/kg (i.g.) | In vitro | 58 |
| | Promote gastric emptying and small intestinal transit | Corydaline | 0.1 μg/kg (p.o.) | In vivo | 59 |
| Effects on the cardio-cerebrovascular system | Reduced blood pressure | Tetrahydropalmatine | 20 mg/kg (i.v.) | In vivo | 60 |
| | | Tetrahydropalmatine | 5 mg/kg (i.g.) | In vivo | 61 |
| | | Tetrahydropalmatine | 10 μmol/L | In vitro | 62 |
| | Protective effects on myocardium | Total alkaloids | 1 mg/kg (i.g.) | In vivo | 63,64 |
| | | Alcohol extract | 50 mg/kg (p.o.) | In vivo | 65 |
| | | Total alkaloids | 27.9 mg/kg (enteral) | In vivo | 66 |
| | | Tetrahydropalmatine | 5 mg/kg (i.v.) | In vivo | 67 |
| | | Tetrahydropalmatine | 1 μmol/L | In vitro | 68,69 |
| | | Tetrahydropalmatine | 10 mg/kg (i.v.) | In vivo | 70 |
| | | Tetrahydropalmatine | 50 mg/L | In vitro | 71 |
| | | Dehydrocorybulbine | 1.25 mg/L | In vitro | 71 |
| | | Coptisine | 4 mg/L | In vitro | 71 |
| | | Palmatine | 30 mg/L | In vitro | 71 |
| | | Alcohol extract | 100 mg/kg (p.o.) | In vivo | 72 |
| | | Total alkaloids | 0.2 g/kg (i.g.) | In vivo | 73 |
| | Antiarrhythmic effects | Tetrahydropalmatine | 5 mg/kg (i.v.) | In vivo | 67 |
| | | Total alkaloids | 0.5 g/kg (i.g.) | In vivo | 73 |
| | | Tertiary alkaloids | 30 mg/L | In vitro | 74 |
| | | Quaternary alkaloids | 1 mg/L | In vitro | 74 |
| | | Alcohol extract | 0.81 g/kg (i.g.) | In vitro | 75 |
| | Antithrombotic effects | Tetrahydropalmatine | 20 mg/kg (i.g.) | In vivo | 76 |
| | | Water extract | 1.44 g/kg (i.p.) | In vivo | 77 |
| | | Tetrahydropalmatine | 7.5 mg/kg (i.v.) | In vivo | 78 |

(Continued)

**Table 8.** Continued

| Pharmacological effects | Details | Extracts/compounds | Minimal toxic concentration/dose | Type of experiment | References |
|---|---|---|---|---|---|
| Antitumor effects | Angiogenesis-limiting effect | Alkaloid extract | 10 μg/mL | In vitro | [79,80] |
| | Inhibitory effect on the growth of sarcoma 180 and Lewis lung cancer in mice | Polysaccharide | 100 mg/kg (i.p.) | In vivo | [41] |
| | Inhibit P-glycoprotein activity | Tetrahydropalmatine | 2.5 μg/mL | In vitro | [81,82] |
| | Inhibitory effects on 10 human tumor cells | Total alkaloids | $IC_{50}$ = 18.39 μg/mL | In vitro | [83] |
| | Inhibitory effects on the proliferation of 6 human gastric cancer cells | Total alkaloids | 200 mg/mL | In vitro | [84] |
| | Inhibit HepG2 cells | Total alkaloids | 200 mg/mL | In vitro | [84] |
| | Inhibit the growth of A549 cells | 13-methyl-palmatrubine | 3 mg/kg | In vitro | [85] |
| | Inhibit MDA-MB-231 cell line | Alcohol extract | 3 mg/mL | In vitro | [86] |
| | Inhibits MCF-7 cell | Alcohol extract | 50 μg/mL | In vitro | [87] |
| | Antimouse liver cancer H22 | Powder suspension | 1 mg/kg (i.g.) | In vivo | [88] |
| | Inhibit U251MG cell line | Tetrahydropalmatine | 1 mg/kg (i.p.) | In vivo | [89] |
| | Inhibits HL-60 and K562 cell | Tetrahydropalmatine | 0.1 mmol | In vitro | [90] |
| Antibacterial and anti-inflammatory effects | Inhibit white rot fungus and Curvularia leaf spot fungus | Chloroform extract | 125 mg/L | In vitro | [91] |
| | Inhibit *Clostridium perfringens* | Palmatine, berberine | $IC_{50}$ = 18.39 μM | In vitro | [92] |
| | Anti-inflammatory | Alcohol extract | 1μmol/L | In vitro | [93] |
| | Inhibitory effect on human immunodeficiency virus-1 reverse transcriptase | Total alkaloids | 5 mg/mL | In vitro | [94] |
| | Promoting effect on the secretion of anti-inflammatory factors IL-10 and IL-13 | Berberine | 100 mol/L | In vitro | [95] |
| Other pharmacological effects | Portal vein pressure-lowering effect | Tetrahydropalmatine | 1 mg/kg (i.v.) | In vivo | [96] |
| | Protects lung injury | Tetrahydropalmatine | 40 mg/kg (i.p.) | In vivo | [97] |

Abbreviations: $IC_{50}$, half-maximal inhibitory concentration; i.g., intragastric; IL, interleukin; i.p., intraperitoneal; i.v., intravenous; p.o., orally.

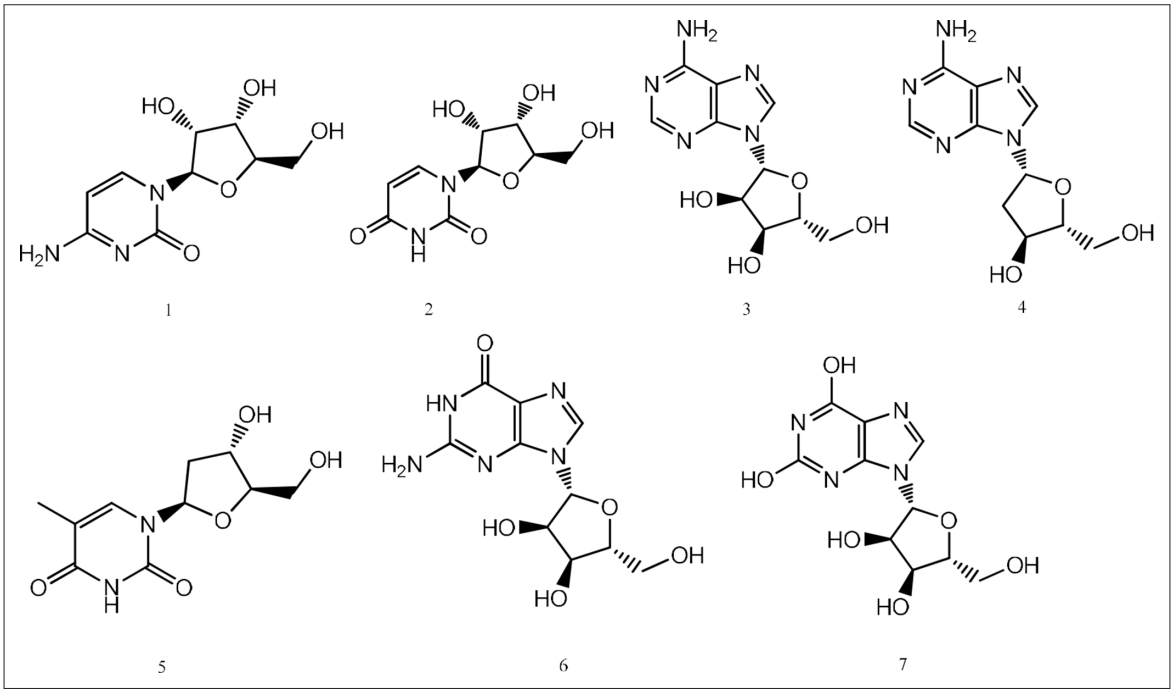



**Figure 7.** Chemical structures of nucleosides in *Corydalis yanhusuo*.

with tetrahydropalmatine at a dose of 40 mg/kg revealed that tetrahydropalmatine is distributed in all tissues, except the lungs, with higher accumulation in the liver.[113] These findings indicate that, in rats, the pharmacokinetics of *C. yanhusuo* extract and tetrahydropalmatine show stereoselectivity.

## Toxicology

The *Chinese Pharmacopeia* provides no information regarding *C. yanhusuo*'s toxicity.[4] However, there are some reports on this matter. One study evaluated the impact of intraperitoneal injection of 150 mg/kg of glaucine in mice. After only 5 minutes following the injection, the mice started to convulse and died quickly of paralysis. The median lethal dose ($LD_{50}$) of glaucine was calculated to be 127 mg/kg.[52] Furthermore, the administration of fumarole extract at 40 g/kg resulted in reduced overall activity, slow breathing, changes in movement and posture, and increased heart and breathing rates in mice, In this study, the mortality rate on the following day was 10%.[114] The $LD_{50}$ of the total alkaloids in *C. yanhusuo* acetic acid extract was 0.86 g/kg in mice, with most mice having died 3 hours following the gastric administration of the extract. This study demonstrated the toxicity and lethality of these alkaloids in mice. Moreover, microscopic examination of tissue samples revealed renal arteriole hemorrhage in some mice.[115] Administration of water extracts of *Rhizoma Corydalis* processed with industrial and edible acetic acid by oral gavage also was found to be toxic to mice, with all animals being reported dead after 72 hours.[116]

To date, the number of studies investigating the toxicity of *C. yanhusuo* remains limited, and most studies have focused on extracts (Table 9). Certain populations should consume this plant cautiously, including pregnant women and women with postpartum blood deficiency and metrorrhagia.[117]

## Future Perspectives and Conclusions

In summary, as traditional Chinese medicine, *C. yanhusuo* is used to treat Qi stagnation and blood stasis. Although various chemical components have been isolated and identified from the plant,

**Table 9.** Toxicologic Effects of *Corydalis yanhusuo*.

| Extracts/compounds | Animal | Minimal toxic concentration/dose | Toxic effect | References |
|---|---|---|---|---|
| Glaucine | Mice | $LD_{50}$ = 127 mg/kg (i.p.) | Death | 52 |
| Alcohol extract | Mice | 40 g/kg (i.g.) | Death | 114 |
| Acetic acid extract | Mice | $LD_{50}$ = 0.86 g/kg (i.g.) | Death | 115 |
| Water extract | Mice | - | Death | 116 |

Abbreviations: i.g., intragastric; i.p., intraperitoneal; $LD_{50}$, median lethal dose.

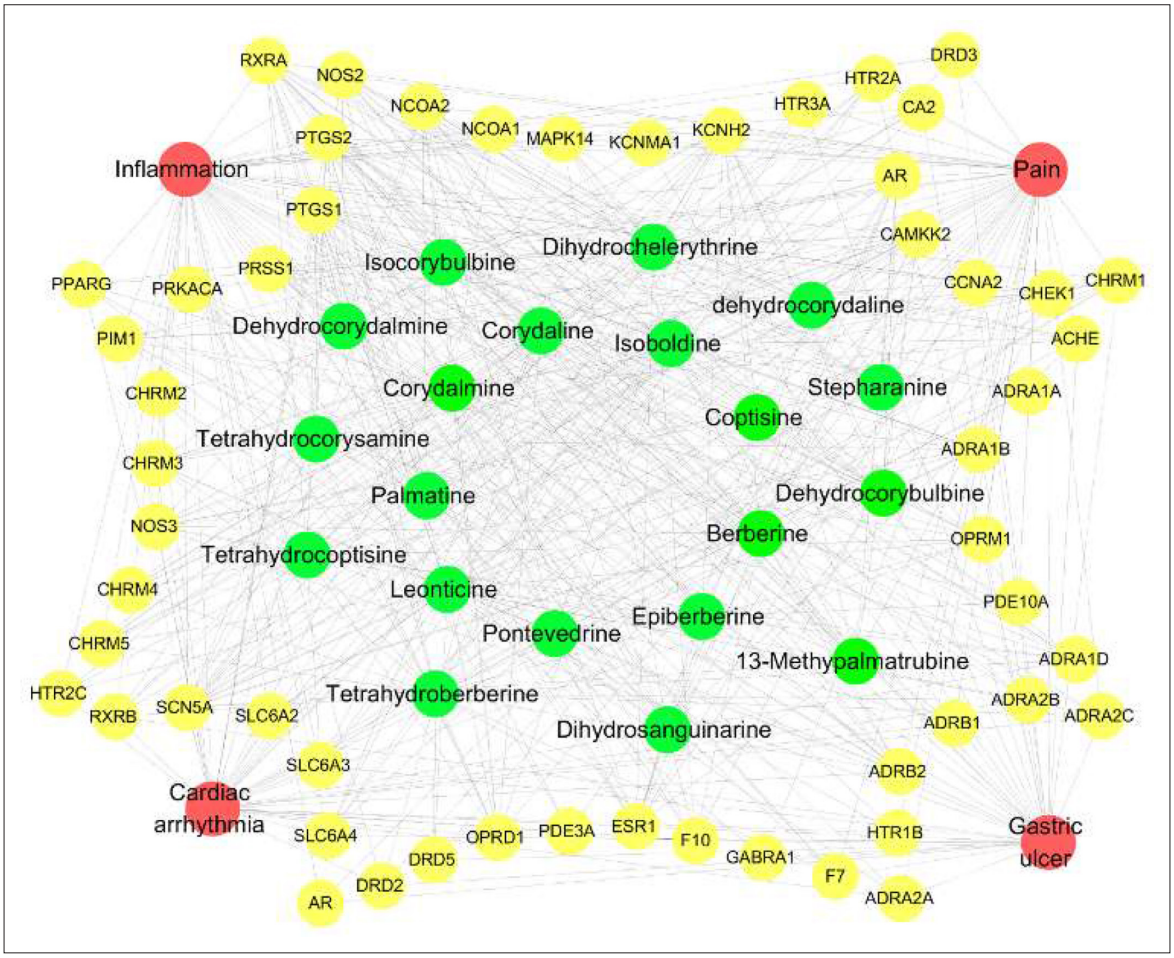



**Figure 8.** Compound-target-disease network associated with *C. yanhusuo*. The underlying network between *C. yanhusuo* components and their targets was designed using Cytoscape 3.7.2 (https://cytoscape.org/). Green circles – chemical compounds of *C. yanhusuo*; yellow circles – potential targets; and red circles – related diseases.

alkaloids are its main active ingredients. Over the past decade, major breakthroughs have been made toward elucidating the active constituents and therapeutic efficacy of *C. yanhusuo*. However, the development of new drugs derived from this plant remains challenging. Thus, it warrants further studies.

Studies have primarily focused on the active components of tetrahydropalmatine, corydaline, berberine, palmatine, and coptisine, among others. For example, *C. yanhusuo* has been reported to contain high glaucine and corydaline content.[118] Glaucine can inhibit breast cancer cell migration and invasion.[119] Therefore, this plant could be a potential source for a novel antitumor drug. In contrast, few studies have evaluated the activity and impact of papaverine and corydaline. Hence, their pharmacodynamics and pharmacokinetics remain unclear.[79]

Evaluation of the medicinal potential of *C. yanhusuo* has mostly focused on its tubers and on the chemical components and pharmacological activities of its stems, leaves, and fibrous roots. Presently, commercially available products labeled to contain *C. yanhusuo* have been found to contain similar *Corydalis* species like *Corydalis turtschaninovii* Bess, *Corydalis repens* Mandl et Kuhldorf, *Corydalis ambigua* Cham. Et Sch. and *Corydalis decumbent* (Thunb.) Pers. Because these species are highly toxic, it is important to identify the actual species in such products to ensure public safety. Researchers have designed a polymerase chain reaction method based on the *ITS2* sequence to distinguish *C. yanhusuo* from its counterfeit products.[120] Authentic *Corydalis* generates a single band of approximately 200-300 bp, whereas counterfeit products do not.[121,122] Therefore, future studies should aim to improve the quality of medicinal materials extracted from *C. yanhusuo*.

Traditional Chinese medicine has multicomponent and multitarget characteristics, and its pharmacological properties cannot be completely attributed to a single component. Quality markers (Q-markers) in Yuanhu Zhitong Dropping Pills include tetrahydropalmatine, corydaline, protopine, imperatorin, and isoimperatorin. Q-markers are the best choice for quality control indicators. It is especially crucial to establish appropriate and feasible Q-markers for Chinese herbal medicines. The Q-marker system can be established from the morphological, chemical, and biological aspects of *C. yanhusuo*. Lastly, the potential cellular targets of

*C. yanhusuo* for the treatment of pain, gastric ulcers, arrhythmias, and inflammation were determined using network pharmacology. However, follow-up studies should aim to verify these targets using in vitro and in vivo experiments.

In conclusion, we provide a comprehensive review of the traditional uses, botany, phytochemistry, pharmacology, pharmacokinetics, and toxicology of *C. yanhusuo*. Altogether, growing evidence paves the way for the development of novel *C. yanhusuo*-based therapeutic agents with broad medicinal applications.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Natural Science Foundation of China [grant number 81803732].

## ORCID ID

Fan Li https://orcid.org/0000-0001-8871-956X

## References

1. He XF, Zhang J, Zhang M. Research progress on chemical constituents, pharmacological activities and toxic side effects of Rhizoma *Corydalis*. *Shanghai J Tradit Chinese Med*. 2017;51(11):97-100.
2. Huang X. Brief introduction of Japan's crude drug resources and imports (continued 4). *Int J Tradit Chinese Med*. 2001:359-361.
3. Luo Y, Wang C-Z, Sawadogo R, Tan T, Yuan C-S. Effects of herbal medicines on pain management. *Am J Chin Med*. 2020;48(1):1-16. doi:10.1142/S0192415X20500019
4. Editorial Committee of Chinese Pharmacopoeia eds. *China Pharmacopoeia*. China Medical Science and Technology Press; 2015.
5. Du WJ, Jin LS, Li LP, et al. Development and validation of a HPLC-ESI-MS/MS method for simultaneous quantification of fourteen alkaloids in mouse plasma after oral administration of the extract of *Corydalis yanhusuo* tuber: application to pharmacokinetic study. *Molecules*. 2018;23(4):714.
6. He K, Gao JL, Zhao GS. Advances in studies on chemistry, pharmacology, and quality control of *Corydalis yanhusuo*. *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 2017;38(12):1909-1912.
7. Yang XB, Yang XW, Liu JX. Study on material base of *Rhizoma Corydalis*. *Zhongguo Zhong Yao Za Zhi* [*China J Chin Mat Med*]. 2014;39(1):20-27.
8. He ZD. *Analgesic Effect of Tetrahydropalmatine A and B onSciatica Rats and its Anti-TRPV-1 Mechanism* [doctoral thesis]. Guangzhou University of Traditional Chinese Medicine; 2012.
9. Wang L, Zhang Y, Wang Z, et al. The antinociceptive properties of the *Corydalis yanhusuo* extract. *PLoS One*. 2016;11(9):e0162875. doi:10.1371/journal.pone.0162875
10. Jiang M. *Study on the Effect of Vinegar on the Content andPharmacodynamics of Main Active Ingredients in Corydalis Yanhusuo* [master's thesis]. Hubei University of Chinese Medicine; 2016.
11. Chen YT, Cao W, Xie YH, et al. Effects of yuanhu zhitong tablet and its main components on experimental dysmenorrhea in rats. *Shaanxi Chin Med*. 2013;34:11-14.
12. State Drug Administration. eds. *Zhongyao Chengfang Zhiji*. Science and Technology Press of Shanghai; 2002.
13. Song MX,Guo WJ, ed. *Guojia Zhongchengyao*. People's Medical Publishing House; 2002.
14. Cai CX. *Chinese Medical Encyclopedia: Korean Medicine*. Shanghai Science and Technology Press; 1992.
15. Xu JZ. *Dong Yi Bao Jian*. People's Medical Publishing House; 1982.
16. Editorial Committee of Flora of China. *Flora of China*. Science Press; 1999.
17. Li YS. Research progress on preparation technology and pharmacological action of tetrahydropalmatine. *Pharm J Chin PLA*. 2013;29:480-483.
18. Chou TQ. The alkaloids of Chinese *Corydalis ambigua*, Cham. Et Sch. (Yen-Hu-So). *Chin J Physiol*. 1928;25(7):544-547.
19. Lu CM. Advances in chemical constituents and pharmacological activities of *Corydalis yanhusuo*. *Chin J Mod Drug App*. 2011;5:126-127.
20. Hu TM, Zhao SX. Alkaloids from the aerial parts of *Corydalis yanhusuo*. *J Nanjing Coll Pharm*. 1985;16:7-11.
21. Zhou Q. *Studies on Chemical Constituents of CorydalisYanhusuo and Chemical Characteristic Expression of Its Herbal Characteristic System* [master's thesis]. Peking Union Medical College; 2012.
22. Fu XY. Identification of compounds in aqueous extract from aerial parts of *Corydalis yanhusuo* WT. Wang by HPLC-ESI-Q-TOF-MS/MS. *Northwest Pharm J*. 2017;32(1):13-17.
23. Hu TT, Zhang X, Ma SZ, Cheng YY, Yao XS. Alkaloids in *Corydalis yanhusuo*. *Zhongguo Zhong Yao Za Zhi* [*China J Chin Mat Med*]. 2009;34:1917-1920.
24. Yang XB, Liu YZ, Yang XW. Study on chemical constituents of *Corydalis yanhusuo* in Pan'an. *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 2013;44(16):2200-2207.
25. Cheng X-Y, Shi Y, Zhen S-L, Sun H, Jin W. HPLC-MS analysis of ethanol extract of *Corydalis yanhusuo* and simultaneous determination of eight protoberberine quaternary alkaloids by HPLC-DAD. *J Chromatogr Sci*. 2010;48(6):441-444. doi:10.1093/chromsci/48.6.441
26. Lv ZM, Sun WX, Duan XH, Yang Z, Liu Y, Tu PF. Chemical constituents from *Corydalis yanhusuo*. *Zhongguo Zhong Yao Za Zhi* [*China J Chin Mat Med*]. 2012;37(2):235-237.
27. Zhou Q, Deng A-J, Qin H-L. Two new quaternary protoberberine alkaloids from *Corydalis yanhusuo*. *J Asian Nat Prod Res*. 2012;14(5):476-481. doi:10.1080/10286020.2012.677038
28. Lu Y, Ma Q, Fu C, Chen C, Zhang D. Quality evaluation of *Corydalis yanhusuo* by high-performance liquid chromatography fingerprinting coupled with multicomponent quantitative analysis. *Sci Rep*. 2020;10(1):4996. doi:10.1038/s41598-020-61951-x

29. Feng ZL, Zhao ZD, Liu JX. Research progress on chemical components and pharmacological effects of *Corydalis yanhusuo*. *Nat Prod Res Dev*. 2018;30(11):2000-2008.
30. Xu XH, Wang ZT, GD Y, Ruan BF, Li J. Study on alkaloids in *Corydalis yanhusuo*. *J China Pharm Univ*. 2002(6):29-32.
31. Hu TT. *Research Progress on Chemical Constituents and Their Bioactivities of Corydalis Yanhusuo W. T. Wang* [master's thesis]. Shenyang Pharmaceutical University; 2009.
32. Zhu M, Chen BZ, Lian WY, et al. Study on *Corydalis yanhusuo*. *Chin Tradit Herb Drugs*. 1986;17(4):150-152.
33. Bao L. *Studies on Chemical Constituents of Ginger and Rhizoma*[master's thesis]. Peking Union Medical College; 2010.
34. Fu XY, Liang WZ, Tu GS. Chemical study of yuanhu alkaloids. VII. alkaloids in yuanhu tubers. *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 1986;17:5-6.
35. Shi JM, Han WL, Ye WC, Chan SK, Wang YT, Zhang QW. Phytochemical investigation of *Corydalis yanhusuo*. *Nat Prod Res Dev*. 2011;23(4):647-651.
36. Qu Y, Liu M, Wu Z. 2,3,9,10-Tetraoxygenated protoberberine alkaloids from *Corydalis yanhusuo* W. T. Wang. *Asian J Tradit Med*. 2007;2(2):61-65.
37. Li FQ, Zhou Q, Ma L, Deng AJ. Isolation and structural elucidation of chemical constituents of *Rhizoma Corydalis*. *Chin J Exp Tradit Med Form*. 2019;24:211-216.
38. Zhang XL, Qu Y, Hou JM, Sun BH, Huang J, Wu LJ. Chemical constituents from the bulb of *Corydalis yanhusuo* W. T. Wang. *J Shenyang Pharm Univ*. 2008:537-540.
39. Liu ZH, Wang RW, He HH, et al. Water-soluble non-alkaloid chemical constituents contained in *Corydalis yanhusuo* by trimethylsilyl derivatization GC-MS. *Zhongguo Zhong Yao Za Zhi* [*China J Chin Mat Med*]. 2012;37(14):2108-2112.
40. Wang PF, Wang QQ, Li XE, Qin MJ. Metabolites research of *Corydalis yanhusuo* tubers with gas chromatography-mass spectrometry. *Chin Bull Bot*. 2012;47:149-154.
41. Tao Y-W, Tian G-Y. Studies on the physicochemical properties, structure and antitumor activity of polysaccharide YhPS-1 from the root *of Cordalis yanhusuo* W. T. Wang. *Chin J Chem*. 2006;24(2):235-239. doi:10.1002/cjoc.200690045
42. Wang M, Shi YJ, Guo DY, Meng F, Liu YY. Analysis of volatile oil of *Corydalis Yanhusuo* by infrared spectrum and gas chromatography-mass spectrometry. *Central South Pharm*. 2017;15:99-102.
43. Su L, Guo XY. Component analysis of volatile oil from *Corydalis yanhusuo* from different origins. *J Anhui Agri Sci*. 2011;39:20418-20420.
44. Bao LP, Su L. Extraction method research of *Corydalis yanhusuo* volatile oil. *Guangdong Chem Ind*. 2014;41(19):10-11.
45. Shi HQ, Chen B, Shao JN, Cheng CG. Analysis and comparison of volatile components of *Corydalis yanhusuo* by headspace solid phase microextraction-GC-MS. *Chin J Pharm*. 2014;45:66-68.
46. Chen DD, Chen YP, Zhou P, Li X, Chen JW. Simultaneous determination of 6 nucleoside components in *Corydalis yanhusuo* W.T. Wang by high performance liquid chromatography. *Nat Prod Res Dev*. 2015;27(9):1571-1575.
47. Wang ZH, Zhang DJ, Du GZ, et al. Determination of 14 inorganic elements in Rhizoma *Corydalis* and its decoction. *Trace Elem Sci*. 1998(11):34-35.
48. Xu H. Determination of trace elements in yuanhu tuber by flame atomic absorption spectrometry. *Chin J Spectrosc Lab*. 2012;29:306-309.
49. Su L. Determination of 5 metal elements in *Corydalis yanhusuo* by ICP-MS. *Guangzhou Chem Indy*. 2012;40(1):94-95.
50. Chen YX, Li F, Zhou ZL. Analysis of liposoluble contents of no-processed and processed Rhizoma *Corydalis* by GC-MS. *J Shandong Univ Tradit Chin Med*. 2010;34(3):251-253.
51. Chang CK, Lin MT. DL-Tetrahydropalmatine may act through inhibition of amygdaloid release of dopamine to inhibit an epileptic attack in rats. *Neurosci Lett*. 2001;307(3):163-166. doi: 10.1016/S0304-3940(01)01962-0
52. Jin GZ, Xun B. Pharmacological studies of *Corydalis yanhusuo* I. analgesic effects of corydaline, tetrahydropalmatine and *Corydalis* L. *Acta Physiolog Sinica*. 1957(2):150-157.
53. Tang XC, Jin GZ, Xun B. Pharmacological studies of *Corydalis yanhusuo* IX. central nervous system effects of *Corydalis* L and D-glaucine. *Acta Physiolog Sinica*. 1962(2):143-148.
54. Henkes H, Franz M, Kendall O, et al. Evaluation of the anxiolytic properties of tetrahydropalmatine, a *Corydalis yanhusuo* compound, in the male Sprague-Dawley rat. *Aana J*. 2011;79(4 Suppl):S75-S80.
55. Wu H, Wang P, Liu M, et al. A 1H-NMR-based metabonomic study on the anti-depressive effect of the total alkaloid of Rhizoma Corydalis. *Molecules*. 2015;20(6):10047-10064. doi:10.3390/molecules200610047
56. Bai X, Xiao HT, Yang J, Zhu J, Hao XY. An experimental study on the anti-stress effects of alkaloids in Rhizoma *Corydalis* to mice. *J Guiyang Med Coll*. 2008;33(2):139-140.
57. Min Q, Bai YT, Shu SJ, Ren P. Protective effect of tetrahydropalmatine on liver injury induced by carbon tetrachloride in mice. *Zhongguo Zhong Yao Za Zhi* [*China J Chin Mat Med*]. 2006;31(6):483-484.
58. Wang GL, Wang WY. Effect of l-tetrahydropalmatine (l-THP) on intestinal smooth muscle. *Pharmacol Clin Chin Mat Med*. 2002;18(3):9-10.
59. Lee TH, Son M, Kim SY. Effects of corydaline from *Corydalis* tuber on gastric motor function in an animal model. *Biol Pharm Bull*. 2010;33(6):958-962.10.1248/bpb.33.958 doi:10.1248/bpb.33.958
60. Ge GQ, Xing SH, Yan M, Bian CP. Effect of tetrahydropalmatine on the peripheral catecholamine content in rats. *Chin Pharmacol Bull*. 1995;11(1):58-61.
61. Luo QM, Yan XB, Liu LC, et al. Effect of tetrahydropalmatine on the ratio of rabbit cardiac diastolic duration to systolic duration. *Chin J Appl Physiol*. 2016;32(3):228-229.
62. Cheng LX, Mao HY, Hu QH. Effects of tetrahydropalmatine on cytoplasm free calcium concentration in pig pulmonary artery smooth muscle cells. *Acta Med Univ Sci Tech Huazhong*. 1997:397-400.
63. Su XY, Li XY, Tian M, et al. Effects of total alkaloids of *Corydalis yanhusuo* on cardiac function decline in rats with acute myocardial ischemia. *Heilongjiang J Tradit Chin Med*. 2013;42:48-49.

64. Yang K, ZZ L, Pan L, et al. Protective effects of total fumaric alkaloids on myocardium of rats with isoproterenol-induced myocardial infarction. *Chin J Clinic Res*. 2016;29(8):1057-1061.
65. Wu L, Ling H, Li L, Jiang L, He M. Beneficial effects of the extract from *Corydalis yanhusuo* in rats with heart failure following myocardial infarction. *J Pharm Pharmacol*. 2007;59(5):695-701. doi:10.1211/jpp.59.5.0010
66. Kang TJ, Jia JL, Tian B, et al. Effect of *yanhusuo* total alkaloid dropping pill on myocardial enzyme spectrum of dog model of acute myocardial ischemia. *Acta Chin Med Pharmacol*. 2019;47:41-44.
67. Wang YX, Zheng YM, Tan YH. Antiarrhythmic effect of tetrahydropalmatine on ischemia-reperfusion arrhythmia and its mechanism. *Chin Pharmacol Bull*. 1993(5):358-361.
68. Liu JL, Liu H. Protective effect of tetrahydropalmatine on cardiac reperfusion injury aggravated by exogenous free radicals in rats. *Chin Pharm J*. 1994;9:462-464.
69. Zhou YG, Su MH, Yang GT. Protective effect of tetrahydropalmatine on calcium overload injury in rat hippocampal neurons. *Chin J Int Med Cardio-Cerebro Dis*. 2010;8:81-82.
70. Liang J, Wang FQ, Zheng PX, Liang JS. Protective effects of tetrahydropalmatine on lipid peroxidation and behavioral and pathological changes in rats with cerebral ischemia-reperfusion injury. *Chin Pharmacoll Bull*. 1999;15:167-169.
71. Li P, Ren JG, Duan CL, Lin CR, Liu JX. Effects of four components of Rhizoma *Corydalis* on anoxia and peroxidation injuries in neonatal cardiomyocytes. *Zhongguo Zhong Yao Za Zhi* [*China J Chin Mat Med*]. 2010;35(1):84-88.
72. Ling H, Wu LM, Li LD. *Corydalis yanhusuo* rhizoma extract reduces infarct size and improves heart function during myocardial ischemia/reperfusion by inhibiting apoptosis in rats. *Phytother Res*. 2006;20(6):448-453. doi:10.1002/ptr.1875
73. Li R. *Research Progress on Chemical Constituents and Their Bioactivities of Corydalis Yanhusuo W. T. Wang* [master's thesis]. Shenyang Pharmaceutical University; 2009.
74. Meng HX, Yao MJ, Ren JG, Liu JY. Effects of tertiary alkaloids and quaternary alkaloids of Rhizoma *Corydalis* on action potential in guinea pig ventricular myocytes and HERG channel currents. *World Chin Med*. 2018;13(1):1-4.
75. Zhang P. *Study on the Mechanism of Corydalis Extract in Treating Coronary Heart Disease with Ventricular Arrhythmia* [doctoral thesis]. Beijing University of Chinese Medicine; 2012.
76. Yang J2013. *Antithrombotic Effect and Mechanism of Tetrahydropalmatine* [master's thesis]. Zhengzhou University; 2013.
77. Li B. *Experimental Study on Antithrombotic Effect of Extract of Corydalis Yanhusuo on Rats* [master's thesis]. Changchun University of Chinese Medicine; 2014
78. Xing JF, Wang MN, Ma XY, Liang WW, Wang YH. Inhibitory effect of tetrahydropalmatine on experimental cerebral thrombosis and platelet aggregation in vitro. *Chin Pharmacol Bull*. 1997:68-70.
79. Wan L, Zhao Y, Zhang Q, et al. Alkaloid extract of *Corydalis yanhusuo* inhibits angiogenesis via targeting vascular endothelial growth factor receptor signaling. *BMC Complement Altern Med*. 2019;19(1):359. doi:10.1186/s12906-019-2739-6
80. Gao J-L, Shi J-M, Lee SM-Y, Zhang Q-W, Wang Y-T. Angiogenic pathway inhibition of *Corydalis yanhusuo* and berberine in human umbilical vein endothelial cells. *Oncol Res*. 2009;17(11-12):519-526. doi:10.3727/096504009789745575
81. Zhang XL, Cao GX, Yu HX, Jin J. Effects of tetrahydropalmatine on uptake of ~99Tc~m-MIBI by human breast cancer cell line MCF-7. *Chin J Nuclear Med*. 2006;313.
82. Lei Y, Tan J, Wink M, Ma Y, Li N, Su G. An isoquinolie alkaloid from the Chinese herbal plant *Corydalis yanhusuo* W. *T. Wang inhibits P-glycoprotein and multidrug resistance-associate protein 1*. *Food Chem*. 2013;136(3-4):1117-1121.
83. Zhang GD, Xie L, Hu WJ, et al. Inhibitory effect of total alkaloids of *Corydalis* on human hepatocellular carcinoma cell line HepG2 and its effect on microRNA expression profile. *J Nanjing Univ Tradit Chin Med*. 2009;25:181-183.
84. Zhang GD, Xie L, Hu WJ, et al. Antiproliferation effect of total alkaloid fraction of *Yanhusuo* on six human gastric cancer cell lines in vitro. *Chin J Integr Tradit West Med Dig*. 2009;17(2):81-85.
85. Chen J, Lu X, Lu C, et al. 13-Methyl-palmatrubine induces apoptosis and cell cycle arrest in A549 cells *in vitro* and *in vivo*. *Oncol Rep*. 2016;36(5):2526-2534. doi:10.3892/or.2016.5093
86. Gao JL, Shi JM, He K. *Yanhusuo* extract inhibits metastasis of breast cancer cells by modulating mitogen-activated protein kinase signaling pathways. *Oncol Rep*. 2008;20(4):819-819.
87. Xu Z, Chen X, Zhang Q, Chen L, Wang Y. Corydalis yanhusuo W.T. Wang extract inhibits MCF-7 cell proliferation by inducing cell cycle G2/M arrest. *Am J Chin Med*. 2011;39(3):579-586. doi:10.1142/S0192415X11009044
88. Mou WS. Inhibitory effect of *Yanhusuo* powder on H22 hepatoma in mice. *Med Information*. 2010;23:1241-1242.
89. Zhao J. *Effects of Simulated Microgravity and Tetrahydropalmatine on Apoptosis of Malignant Glioma U251MG Cells and Its Mechanism* [doctoral thesis]. The Fourth Military Medical University; 2015.
90. Cui L, Wu T. Tetrahydropalmatine enhances the inhibitory effect of vincristine on human leukemia cell line. *Chin Pharm B*. 1995:348-348.
91. Shen XH, Li XG, Liu HF, Quan BW, Tian GL. Antifungal activities of extracts from *Corydalis* and *Pulsatilla in vitro*. *J Agr Sci Yanbian Univ*. 2006;28(1):35-40.
92. Kim JH, Ryu YB, Lee WS, Kim YH. Neuraminidase inhibitory activities of quaternary isoquinoline alkaloids from *Corydalis turtschaninovii* rhizome. *Bioorg Med Chem*. 2014;22(21):6047-6052. doi:10.1016/j.bmc.2014.09.004
93. Ma NN, Li X, Jin H, et al. Spectrum-effect relationship and mechanism of anti-inflammatory effects of different extracts of *Corydalis yanhusuo*. *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 2019;50(10):2413-2419.

94. Wang HX, Ng TB, lectins Eof. Examination of lectins, polysaccharopeptide, polysaccharide, alkaloid, coumarin and trypsin inhibitors for inhibitory activity against human immunodeficiency virus reverse transcriptase and glycohydrolases. *Planta Med*. 2001;67(7):669-672. doi:10.1055/s-2001-17359
95. Li ZQ. Effect of berberine on toll-like receptor 2 signaling pathway and inflammatory cytokines. *China Pharm*. 2010;21(11):980-982.
96. Shao LN, Yan JM. Effect of levo-tetrahydropalmatine on portal venous pressure and its mechanism. *Chin Pharmacol Bull*. 1995:248-250.
97. Yu J, Liu L, Zhang Y, Yang F, Cao BW. Tetrahydropalmatine protects against acute radiation-induced lung injury in rats. *J Clinic Pathologic Res*. 2017;37(1):62-68.
98. Xie M. Determination of total alkaloids in Rhizoma *Corydalis* vinegar and comparison of analgesic effects on mice. *Strait Pharm J*. 2014:33-34.
99. Li R, Cai QQ, Niu YB, SC D, Dou ZY. Comparative study between crude *Rhizoma Corydalis* and vinegar *Rhizoma Corydalis* in pharmacological action. *Chin J Exp Tradit Med Form*. 2014;20(19):133-137.
100. Xu JY, Bai WF, Qiu CK, Tu P, Yu SY, Luo SY. Effect of *Corydalis yanhusuo* and L-THP on gastrointestinal dopamine system in morphine-dependent rats. *Zhong Yao Ca*. 2015;38(12):2568-2572.
101. Lei HQ, YX X, Ju M, Zhao GS. Effects of tetrahydropalmatine and sinomenine on the activity of rabbit oviduct smooth muscle. *J Xi'an Jiaotong Univ*. 1993(3):219-222.
102. Zhang Q, Gao W, Wang WY, Yang SY, Qi L. Effects of tetrahydropalmatine on cerebral ischemia-reperfusion injury. *J Jilin Med Univ*. 2016;37:146-148.
103. Sang XY, Zhang L, Liu L. A study on extraction and anti-hepatocarcinoma effect of the alkaloids in *Corydalis Yanhusuo*. *J Zhejiang Sci Tech Univ*. 2009;26(5):754-756.
104. Li C, Du X, Liu Y, et al. A systems pharmacology approach for identifying the multiple mechanisms of action for the Rougui-Fuzi herb pair in the treatment of cardiocerebral vascular diseases. *Evid Based Complement Alternat Med*. 2020;2020(7):1-17. doi:10.1155/2020/5196302
105. Liu JM, Wang F, Ye YJ, et al. Preparation and pharmacokinetics in rats of tetrahydropalmatine multivesicular liposomes. *Chin J Exp Tradit Med Form*. 2014;20:124-127.
106. Liu XY. Pharmacokinetics of tetrahydropalmatine in rats. *J Nanjing Univ Tradit Chin Med*. 2012;28:555-557.
107. Lin L, Liu JY, Zhang Y, Lin CR, Duan CL. Pharmacokinetic studies of tetrahydropalmatine and dehydrocorydaline in rat after oral administration of *Yanhusuo* extraction by LCMS/MS method. *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 2008;43(11):1123-1127.
108. Hu N, Liang RX, Wang L, et al. Pharmacokinetics study of *Corydalis* extracts in rat plasma. *Chin J Exp Tradit Med Form*. 2011;17(4):186-189.
109. Pang ZG, Wang BQ, Wang CY, Huang H. Study on pharmacokinetics of tetrahydropalmatine in rabbit plasma. *Chin J Pharm Anal*. 1995;15:13-16.
110. Hong ZY, Fan GR, Chai YF, Wen J, Yin XP, YT W. Stereoselective pharmacokinetics of tetrahydropalmatine in rats. *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 2005;40(8):746-749.
111. Wu P-S, Huang S-D, Ye Y-J, Sun S-Y, Jiang H-D. Difference absorption of l-tetrahydropalmatine and dl-tetrahydropalmatine in intestine of rats. *Yao Xue Xue Bao*. 2007;42(5):534-534.
112. Yan JJ, Feng S, He LN, He X. Inhibitory mechanism of tetrahydropalmatine enantiomers on cytochrome P450 in human liver microsomes. *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 2015;46(4):534-540.
113. Du WJ. *Pharmacokinetics of Corydalis Yanhusuo Extract in Mice* [master's thesis]. Zhejiang University; 2017.
114. Wang SC, Liu MY, Hu YW. Toxicity of angelica, curcuma, *Corydalis yanhusuo* and their compatibility in mice. *Li Shi Zhen Med Mater Med Res*. 2004;15:211-213.
115. Jiao YH, Jiang B, Yu M, et al. Acute toxicity test of total alkaloids of *Corydalis yanhusuo* acetate (LD50 determination). *Presented at the 2010 National Academic Conference on Pharmacotoxicology*; August 12, 2010, 2010; Qinghai Province, China.
116. Cheng LP, Gu XY, Mao SJ. Acute toxicity of different types of vinegar in mice and analgesic effect of processed *Corydalis*. *Chin J Exp Tradit Med Form*. 2010;16:71-72.
117. Liao XY. *BenCao JingShu*. Shanxi Science and Technology Press; 1980.
118. Zhang D, Wang CL, Pu DD, Song X. Simultaneous determination of 5 alkaloids in *Rhizoma Corydalis* by HPLC. *Central South Pharm*. 2018;16(12):1759-1762.
119. Kang H, Jang S-W, Pak JH, Shim S. Glaucine inhibits breast cancer cell migration and invasion by inhibiting MMP-9 gene expression through the suppression of NF-κB activation. *Mol Cell Biochem*. 2015;403(1-2):85-94. doi:10.1007/s11010-015-2339-9
120. Xu CX. *Identification of Corydalis Yanhusuo and Its Counterfeits* [master's thesis]. Guangzhou University of Traditional Chinese Medicine; 2016.
121. Chan Q-Y, Jiang L, Cheng M-E, et al. Identification of *Corydalis yanhusuo*,*C. turtschaninovii*,*C. decumbens* by allele-specific PCR. *Zhongguo Zhong Yao Za Zhi*. 2019;44(15):3261-3267. doi:10.19540/j.cnki.cjcmm.20190527.108
122. Zhang TJ, Xu J, Shen XP, et al. Relation of "property-response-component" and action mechanism of Yuanhu Zhitong Dropping Pills based on quality marker (Q-Marker). *Yao Xue Xue Bao* [*Chin Tradit Herb Drugs*]. 2016;47(13):2199-2211.