Review article

*Agrimonia pilosa* Ledeb.: A review of its traditional uses, botany, phytochemistry, pharmacology, and toxicology

Sihua Wen¹, Xiaofei Zhang¹, Yanan Wu, Shangshang Yu, Wei Zhang, Ding Liu, Kai Yang, Jing Sun

School of Pharmacy, Shaanxi University of Chinese Medicine, Xianyang, China

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**ABSTRACT**

**Ethnopharmacological relevance:** *Agrimonia pilosa* Ledeb. is the dried above-ground part of dragon's tooth grass, a plant of the Rosaceae family, which is widely distributed in China, Korea, and Japan. *Agrimonia pilosa* Ledeb. is a herbal medicine with great scope for development and use. It is astringent and hemostatic, and it is used for treating malaria, preventing dysentery, detoxification, and as a tonic for deficiency.

**Aim of the review:** We summarize the traditional uses, botanical and chemical composition, extraction methods, and pharmacological and toxicological progress of *Agrimonia pilosa* Ledeb. and discuss the future research trends and development prospects of this plant.

**Materials and methods:** Information on *Agrimonia pilosa* Ledeb. was gathered via the Internet (China National Knowledge Infrastructure, Google Scholar, PubMed, Web of Science, SpringerLink, Wiley, Wanfang Data, and Baidu Academic). Additional information was obtained from books (Ben Cao Tu Jing, A Textual Research on the Name and Reality of Plants, Modern Practical Chinese Medicine, Zhen Nan Ben Cao) and PhD and MS dissertations.

**Results:** Phytochemical studies have identified more than 252 compounds from *Agrimonia pilosa* Ledeb., including flavonoids, volatile oils, tannins, phenols, m-benzotrienols, pentacyclic triterpenoids, isocoumarins, lignans, organic acids, and other chemical constituents. The compounds and extracts isolated from *Agrimonia pilosa* Ledeb. show various pharmacological activities, including anti-inflammatory, anticancer, antitumor effects, antioxidant, analgesic effects, and other pharmacological effects.

**Conclusion:** This review highlights the botany, phytochemistry, pharmacology, toxicology, and traditional uses of *Agrimonia pilosa* Ledeb., providing a basis for future research and clinical applications. *Agrimonia pilosa* Ledeb. has shown remarkable effectiveness in the treatment of various diseases, especially enteritis, gastric ulcers, and gastrointestinal bleeding. Most prescriptions for *Agrimonia pilosa* Ledeb. are empirical and lack rigorous clinical observation. For these reasons, the toxicology, standardized clinical studies, nature of active ingredients, pharmacokinetics, mechanism, and metabolism of *Agrimonia pilosa* Ledeb. should be deepened, especially through clinical trials, to ensure the clinical safety of its use for further research.

1. Introduction

*Agrimonia pilosa* Ledeb. (APL), also known as desiccated grass, dragon's tooth grass, melon herb, and others, is the dried above-ground part of dragon's tooth grass of the Rosaceae family. There are about 124 genera and 3300 species in the Rosaceae family, distributed worldwide, with more in the northern temperate zone. Among them, APL is distributed in China, Korea and Japan, it is distributed in Jiangsu Province, Zhejiang Province, Hubei Province and other places in China. APL is bitter, astringent, and flat and belongs to the heart and liver meridians. APL can be used to stop bleeding, intercept malaria, prevent dysentery, for detoxification, as a tonic for deficiency, and for the treatment of hemoptysis, vomiting blood, massive bleeding, malaria, bloody dysentery, carbuncle, sore and poison, itching and banding, dehydration, and strain. APL is the main herb in the Compound Agrimonia Enteritis Capsule, which is used to treat urgent diarrhea, loose

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¹ Corresponding author.

E-mail address: sunjing202203@126.com (J. Sun).

¹ These authors contributed equally to this work.

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stools, loss of appetite, tiredness, abdominal distension and pain, and acute and chronic enteritis. APL contains numerous flavonoids, volatile oils, tannins, phenols, m-benzotrienols, pentacyclic triterpenoids, isocoumarins, ligans, organic acids, and other chemical components and has anti-inflammatory, anti-cancer, anti-tumor, antioxidant and analgesic effects.

Many studies have been conducted to confirm the traditional uses of APL, but there are almost no studies on the toxicology and pharmacokinetics of APL. Therefore, we review the research progress on the traditional use, botany, chemical composition, extraction methods, pharmacology, and toxicology of APL and provide an outlook on the future development of the plant with the aim to highlight the importance of APL and provide some guidance on its use (Figure 1).

2. Materials and methods

To cultivate a comprehensive understanding of the current research status of APL, we performed a no language restrictions the use of data-base search, including China National Knowledge Infrastructure (CNKI), Google Scholar, PubMed, Web of Science, SpringerLink, Wiley, Wanfang Data and Baidu Academic to retrieve articles on the botany, phytocchemistry, extraction methods, and pharmacology of APL, for information about APL. We also searched for articles on the botany and traditional uses of APL from PhD and MS dissertations and books such as Ben Cao Tu Jing, A Textual Research on the Name and Reality of Plants and Modern Practical Chinese Medicine. By summarizing and organizing this review, This review covers extraction methods as well as botanical, phytocchemical, pharmacological, and toxicological research on APL from 1978 to 2022. Publications on unrelated topics and non-SCI indexed journal issues were excluded. In total, we found more than 300 articles, as well as books. We here cite a total of 117 sources, mostly phytocchemical and pharmacological studies.

3. Traditional use

The name Xianhecao is thought to have originated from two scholars who went to ancient Beijing for an examination; on the way, one suffered from epistaxis. Although his companion used every emergency method possible to stop the bleeding, his efforts were unsuccessful. When they were at their wits’ end, a crane flew from the sky. The men asked the crane for help, and it dropped the grass it was holding in its mouth. The man who was bleeding put the grass in his mouth and chewed it; after swallowing the juice, the nosebleed stopped. To commemorate the help of the crane, the herb was named Xianhecao [1]. APL was first recorded in the book of Ben Cao Tu Jing for the treatment of white dysentery and its leaves are used to treat sores and ringworm in Lv Chan Yan Ben Cao; it is described as being used to treat menstruation, either before or after, cold face and abdominal pain, and red and white bloody dysentery in Zhen Nan Ben Cao. It is described in the book Shengcao Yaoxing Beiyao for treating falls and injuries, stopping bleeding and dispelling pathogenic toxins; it is described as being used to lower the qi and invigorate the blood, disperse rheumatism, treat fall and vomit with blood, hemorrhage, dysentery, and blood from intestinal wind in Hundred Herbs Mirror; it is described as being used to treat the wind and phlegm lumbar in A Textual Research on the Name and Reality of Plants; it is described as being used for treating scrofula in the book Weiyao Tiaobian; and it is described as being a strong astringent and hemostatic agent with cardiac effects in Modern Practical Chinese Medicine, treating hemoptysis in lung disease, intestinal bleeding, gastric ulcer bleeding, uterine bleeding, dental bleeding, hemorrhoid bleeding, and liver abscess. APL has antioxidant, analgesic, anti-inflammatory, anti-cancer, anti-tumor, and gastrointestinal protective effects. In addition, APL has other pharmacological effects, including anti-coagulant and anti-fatigue effects [2].

One of the traditional uses of APL is to reduce inflammation. The anti-inflammatory effects of APL are of great interest and are well supported by the literature [3, 4, 5]. APL has a long history of treating enteritis and has achieved good results. Recently, the Chinese medicinal preparations that use APL as the main application in clinical practice include Compound Agrimonia Enteritis Capsule, Abdominal Security Granules, and Nourishing Blood and Tranquilizing Capsules. APL has astringent functions and is used to stop bleeding, intercept malaria, prevent dysentery, in detoxification, and Tonifying deficiency. Moreover, APL is known to have good therapeutic effects on acute and chronic enteritis. Among

Figure 1. Flow chart.
them, the Compound Agrimonia Enteritis Capsule is a secret formula of the chief physician Lai Chunmao, a famous old ethnic herbalist in Yunnan. The compound is a natural agent, which has antibacterial and anti-inflammatory effects, and functions to strengthen the spleen, improve functioning of the intestines, clearing heat and drying dampness, stopping diarrhea and regulating qi [6]. The Compound Agrimonia Enteritis Capsule is also used for treating acute and unpleasant diarrhea due to spleen deficiency and dampness and heat, or loose stools and diarrhea, fatigue, abdominal distension, abdominal pain, and acute and chronic enteritis. Table 1 lists the traditional use of APL in China.

4. Botany

APL is Agrimonia L. plant, Agrimonia L. is a genus under the Rosaceae family, with more than 10 species worldwide, distributed in the north temperate and tropical alpine and Latin America, including four species in China, distributed in the north and south provinces. Including Agrimonia coreana Nakai, Agrimonia eupatoria Linn. subsp. asiatica (Juzep.) Sk., Agrimonia nipponica var. occidentalis, Agrimonia pilosa Ldb. var. nepalensis (D.Don) Nakai et al, all of them are perennial herbs. Rhizomes inclined, often with underground buds, odd-pinnate leaves, with stipules. Flowers small, bisexual, in terminal spike-like racemes; sepal tube turbinate, angular, with several layers of bars at the tip, connivent, spreading or reflexed after flowering; sepal 5, imbricate arrangement; petals 5, yellow; disc margin thickened, encircling the mouth of the calyx tube; stamens 5–15 or more, inserted in a row outside the disc; pistils usually 2, enclosed in the calyx tube, style terminal, filiform, projecting outside the calyx tube, stigma slightly enlarged; ovules 1 per carpel, pendulous. Ovules 1 per carpel, pendulous. Achesens 1–2, enclosed in a barbed calyx crown. Seeds 1. Chromosome base x = 7.

APL is a perennial herb, which can grow up to 50–120 cm tall, with long white hairs throughout the plant. The rootstock is short, often with one or more root buds. The stems of APL stand erect and are sparingly pilose and glandular hairy. Leaves alternate between pinnate, leaflets unequal in size, interval arrangement, ovoid to obovate-orbicular, 2.5–7 cm long, 1.5–3.5 cm wide, serrated margins, both surfaces pilose; stipules subovate, Racemes terminal; calyx obconic, 5-lobed, lobes basally bearing numerous hooked bristles, persistent; five yellow petals; stamens 5–15; ovary semi-inferior, style prominent. The calyx tube thickens at fruit ripening and is pendulous, with a round of erect bars at the tip and a deeper longitudinal groove outside, Flowering June or fruit ripening and is pendulous, with a round of erect barbs at the tip and APL using a powder-strongly resembles the head of a red-crowned crane, hence the name fl-

5. Chemical composition

Over the last few decades, approximately 252 compounds (Table 2) (see Figure 3), have been separated from APL, including flavonoids, volatile oils, tannins, phenols, phloroglucinol, pentacyclic triterpenoids, isocoumarins, lignans, organic acids, and others. Flavonoids, phenols, and tannins have many pharmacological activities and are considered to be the main active constituents of APL.

5.1. Flavonoids

Flavonoids are one of the most prevalent and important active substances in APL [8]. At present, 49 flavonoids have been isolated from APL, mainly flavonoids, flavonols, and dihydroflavonol. Including Rutin (1), Luteolin-7-O-glucoside (2), Luteolin-7-O-glucuronic acid (3), Quercitrin (4), Apigenin-7-O-glucoside (5), Apigenin-7-O-glucuronide (6), Vexitin (7), Isovexitin (8), (2R,3S)-Dihydrocannabinol 3-O-β-D-glucoside (9), (2S,3R)-Dihydrocannabinol 3-O-β-D-glucoside (10), Agriflavone (11), Kaempferol-3-O-[(S)-3-hydroxy-3-methylbutyl] (1–6)-β-D-Glucoside (12), Trilisoide (13), Catechin (14), Hyperoside (15), Quercitin (16), 3-methoxy quercitin (17), Apigenin-7-O-β-D-glucoside-600-methyl ester (18), Quercitin-7-O-β-D-glucoside (19), Quercitin-3-O-β-D-glucoside (20), Kaempferol (21), Kaempferol-3-O-α-L-rhamnoside (22), Isocatechin (23), Kaempferolide (24), Kaempferide-3-O-α-L-rhamnopyranoside (25), Apigenin (26), Apigenin-7-O-β-D-glucopyranoside (27), Apigenin-7-O-methylglucuronate (28), Apigenin-7-O-butylglucuronate (29), Luteolin-7-O-sophoroside (30), Luteolin-7-O-(6-acetyl)-D-glucopyranoside (31), Luteolin (32), Luteolin-7-O-β-D-glucopyranoside (33), Wogonin (34), (–)-Catechin (35), Pinosolane A (36), Pinosolane B (37), Pinosolane C (38), (2R,3R,4R)-Taxifolin (39), (2R,3R,4S)-Taxifolin-3-O-β-D-glucopyranoside (40), (25S,35S)-Taxifolin (41), Dehydrodicatechin A (42), Kaempferol-3-O-nutioside (43), 3-O-kaempferol 2,3-di-O-β-acyl-D-glucopyranose-600-methyl ester (44), Quercetin-3-O-α-ara-binofuranosyl-β-D-glucopyranoside (45), Kaempferol-3-glucoside (46), Catechin (47), (2S,3S,4S)-Taxifolin-3-O-β-D-glucopyranoside (48), (–)-Aromadendrin-3-O-β-D-glucopyranoside (49) [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22].

5.2. Volatile oil compounds

The main components of the olitative oil from APL are ketones, alcohols, acids, esters, and many hydrocarbon compounds. Quantitative analysis of volatile oil APL oil found that it is predominantly comprised of alcohols. There are 127 kinds of volatile oil compounds, including 3-Hydroxybutyric acid (50), 6-diacetyle-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-Dibenzoferandione(9bH)-dibenzoferandione (51), 2,6-Di-tert-butylphenol (52), 2,5-Dimethyl-3-butylyphrazine (53), Lauric acid (54), Nerolidol (55), 1-Dodecanol methyl ether (56), 1,1-dimethoxyhexadecane (57), Decahydro-1,1,7-trimethyl-1-hydro-cyclopolyprop-4-methylene-7-ol (58), 4-Methyl-2-tert-oktylphenol (59), 1,2,3,5,6,8-hexahydroxyphthalalene (60), Hornitol (61), α-Myrtholhol (62), Penta-tricontane (63), 3,7,11-Trimethyl-2,6-dodecatrien-1-ol (64), 7-Tetradecene (65), Thi-(2-aminoethyl) thiosulfate (66), 6-Hexacosone (67), Tetradecatrace (68), 1-Vinilhexyhexadecane (69), 6,10,14-trimethyl-2-pentadecanone (70), α-Pinene (71), Camphene (72), β-Pinene (73), 3-Octanol (74), Cymene (75), D-limonene (76), Eucalyptol (77), α-Trans-octocene (78), α-Campholenol (79), Camphor (80), Bornol (81), 4, terpineol (82), α-Terpineol (83), Pulegone (84), 1-(2-Furyl)-1-hexane (85), Bergamot oil (86), 2-Methyl-4-hydroxycetophenone (87), Thymol (88), Carvacrol (89), Neryl acetate (90), Eugenol methyl ether...
Table 1. The traditional and clinical uses of *Agrimonia pilosa* Ledebei China.

| Preparation name       | Main compositions                                                                 | Preparation method       | Part used        | Traditional and clinical uses                                                                 | References |
|------------------------|----------------------------------------------------------------------------------|--------------------------|------------------|-----------------------------------------------------------------------------------------------|------------|
| Fufang Xianhecao       | Agrimoniae Herba 1250 g, Coptidis Rhizoma 375 g, Aucklandiae Radix 375 g, Cicadae Periostracum 375 g, Acori Tatarinowii Rhizoma 375 g, Platycodonis Radix 250 g | Water decocting          | Whole grass      | Clearing heat and drying dampness, strengthening the spleen and stopping diarrhea.             | [85]       |
| Changyan Jiaonang      | Agrimoniae Herba 80 mg, Polygonum chinense 0.12 g, Acalypha australis L. 0.12 g, Bidensplosa L. 0.24 g, Chenopodium ambrosioides L. 0.24 g | Water decocting          | Whole grass      | Clearing heat and removing toxins, drying dampness and stopping dysentery.                     | [86]       |
| Fuan Keli              | Agrimoniae Herba 167 g, Rehmanniae Radix Praeparata 100 g, Polygoni Multiflori Caulis 100 g, Ecliptae Herba 100 g, Rehmanniae Radix 100 g, Spatholobi Caulis 100 g, Albiziae Cortex 100 g, | Water decocting          | Whole grass      | Nourishing Yin and nourishing Blood, calming the mind and tranquilizing the spirit.            | [87]       |
| Yangxue Anshen Keli    | Agrimoniae Herba 167 g, Rehmanniae Radix Praeparata 100 g, Polygoni Multiflori Caulis 100 g, Ecliptae Herba 100 g, Rehmanniae Radix 100 g, Spatholobi Caulis 100 g, Albiziae Cortex 100 g, | Water decocting          | Whole grass      | Clearing heat and detoxifying toxins, relieving dampness and promoting drenching.             | [87]       |
| Ningmitai Jiaonang     | Polygonum capitatum 450 g, Imperatae Rhizoma 263 g, Cocculus orbicularis (L.) DC. 224 g, Berberidis Radix 169 g, Agrimoniae Herba 169 g, Hibiscus Mutabilis Foliol 18g, Forsythiae Fructus 226 g | Water decocting          | Whole grass      | Clearing heat and detoxifying toxins, relieving dampness and promoting drenching.             | [87]       |
| Milingqing Jiaonang    | Polygonum capitatum 420 g, Phellodendri Chinensis Cortex 300 g, Osmalis corniculata L. 300 g, Agrimoniae Herba 160 g, Imperatae Rhizoma 240 g, Plantaginis Herba 200 g | Water decocting          | Whole grass      | Clearing heat and detoxifying toxins, relieving dampness and promoting drenching.             | [87]       |
| Changchun Hongyao Jiaonang | Notoginseng Radix Et Rhizoma 121.2 g, Aconit Kusnezoffii Radix 12.12 g, Aconiti Radix Cocta 12.12 g, Nelumbinis Pluma 12.12 g, Angelicae Sinensis Radix 20.22 g, Drynariae Rhizoma 40.4 g, Acori Tatarinowii Rhizoma 8.1 g, Taraxaci Herba 60.6 g, Diosii Herba 6.7 g, Olibanum 20.2 g, Myrrha 20.2 g, Agrimoniae Herba 60.6 g, Bornoeum Syntheticum 24.2 g, Carthami Flos 40.4 g, Chrysanthemi Flos 40.4 g, Gardeniae Fructus 40.4 g, Foenulis Ricini 12.12 g, Corydalis Ricini 20.2 g | Water decocting          | Whole grass      | Promoting blood circulation and removing blood stasis, relieving swelling and pain.          | [87]       |
| Xianchun Pian           | Strychni Semen Pulveratum 50 g, Buchonis Venenum 10 g, Psoraleae Fructus 165 g, Pinelliae Rhizoma 50 g, Curcumae Radix 50 g, Gelsemii Radix 50 g, Angelicae Sinensis Radix 20 g, Agrimoniae Herba 50 g | Water decocting          | Whole grass      | Removing blood stasis and dispersing nodules, benefiting Qi and relieving pain.              | [87]       |
| Gorgliuxiao Jiaonang   | Ostraeae Concha 210 g, Cypere Rhizoma 128 g, Sanguini Rhizoma 64 g, Curcumae Rhizoma 64 g, Eupolypol Bulbas 64 g, Agrimoniae Herba 126 g, Codonopisradix 64 g, Atractylodis Macrocephalae Rhizoma 64 g, Hedorigis diffusa Wild 210 g, Moutan Cortex 128 g, Euodiae Fructus 64 g | Water decocting          | Whole grass      | Activating blood circulation and resolving blood stasis, softening hardness and dispersing knobs | [87]       |
| Shuangji Weiyang Jiaonang | Semen Ephedrae 32 g, Ephedri Dihydroxy Rhizoma 32 g, Paederiae Radix 32 g, Callicarpa nudiflora Hook. ex Arn. 21 g, Corydalis Rhizoma 32 g, Aconiti Radix Cocta 32 g, Bletillae Radix 63 g, Coptidis Rhizoma 375 g, Cuscutae Radix 375 g, Cicadae Periostracum 375 g, Angelicae Sinensis Radix 20 g, Corydalis Radix 375 g, Stemonae Radix Cortex 300 g, Oxalis corniculata L. 300 g, Agrimoniae Herba 169 g, Hibiscus Mutabilis Foliol 18g, Forsythiae Fructus 226 g | Water decocting          | Whole grass      | Promoting blood circulation and resolving blood stasis, relieving swelling and pain.          | [87]       |
| Litemin Jiaonang       | Agrimoniae Herba 150 g, Potentillae Discoloris Herba 150 g, Gelsemii Radix 50 g, Angelicae Sinensis Radix 20 g, Eupolypol Bulbas 64 g, Agrimoniae Herba 60.6 g, Sanguini Rhizoma 64 g, Sphenantherae Radix 64 g, Hedorigis diffusa Wild 210 g, Moutan Cortex 128 g, Euodiae Fructus 64 g | Water decocting          | Whole grass      | Clearing heat and detoxifying, antibacterial and anti-dysentery.                             | [87]       |
| Shengxuesioban Jiaonang | Indigo Naturalis 167 g, Forsythiae Fructus 500 g, Agrimoniae Herba 500 g, Moutan Cortex 833 g, Glycyrrhize Radix Et Rhizoma 250 g | Water decocting          | Whole grass      | Clearing heat and removing toxins, cooling the blood to stop bleeding, dispersing blood stasis and eliminating blemishes | [87]       |
| Pingxuan Jiaonang      | Cephalisphoenix 360 g, Aralia chinensis L. 360 g, Polygonati Rhizoma 48 g, Gastrodiae Rhizoma 60 g, Notoginseng Radix Et Rhizoma 60 g, Galium sparium L. 240 g, Agrimoniae Herba 360 g, Aristolochiae Fructus 60 g | Water decocting          | Whole grass      | Nourishing the liver and kidney, calming the liver and submerging the yang.                   | [87]       |
| Quyu Sanjie Jiaonang   | Prunellae Spica, Cremastrae Pseudobulbus Pleione Pseudobulbus, Hedyotis diffusa, Solanum lyramum Thunb., Eupolypol Bulbas, Notoginseng Radix Et Rhizoma, Crataegi Fructus, Agrimoniae Herba, Astragali Radix, Scopolandra, Auranti Fructus, Meliae Cortex | Water decocting          | Whole grass      | Removing blood stasis, subduing swelling, dispersing nodules and relieving pain.              | [87]       |
| Baixian Fuyan Qingshuan | Sophorae Flavescentis Radix 640 g, Stemonae Radix 320 g, Cnidii Fructus 320 g, Agrimoniae Herba 320 g, Callicarpae Formosaneae Foliol 320 g, Alumen 10 g, Bornoeum Syntheticum 5 g, Camphor 10 g | Water decocting          | Whole grass      | Clearing heat and removing toxins, killing insects and relieving itching, removing blood stasis and astringency | [87]       |
| Baogong Zhixue Keli    | Ostraeae Concha 667 g, Paenaeae Radix Alba 333 g, Platycladi Cacumen 400 g, Rehmanniae Radix 333 g, Rosae Laevigatae Fructus 400 g, Bupleuri Radix 167 g | Water decocting          | Whole grass      | Strengthening menstruation and stopping bleeding, nourishing Yin and clearing heat.          | [88]       |
| Preparation name | Main compositions | Preparation method | Part used | Traditional and clinical uses | References |
|------------------|-------------------|--------------------|-----------|-------------------------------|------------|
| Xinfuman Ruangao | Hydrocarpus anthelmintica Pierre 20 g, Stemoneae Radix 5 g, Gnidii Fructus 2.5 g, Agrimoniae Herba 0.25 g, Angelicae Dahuriae Radix 5 g | Water decocting | Whole grass | Anti-mite and anti-itch | [87] |
| Yangxue Anshen Wan | Polypodi Multiflori Caulis 150 g, Spaltholobii Caulis 150 g, Rehmanniae Radix Praeparata 150 g, Rehmanniae Radix 150 g, Albiziae Cortex 150 g, Ecliptae Herba 150 g, Agrimoniae Herba 250 g | Crushing and mixing | Whole grass | Nourishing Yin and nourishing Blood, calming the mind and tranquilizing the spirit | [89] |
| Fuan Chongji | Agrimoniae Herba 160 g, Polygonum chinense 240 g, Acalypha australis L 240 g, Bidentispilosa L 480 g, Chenspodium ambrosioides L 480 g | Water decocting | Whole grass | Clearing heat and removing toxins, drying dampness and stopping dysentery | [89] |
| Shenlu Bugao | Spaltholobii Caulis 160 g, Ligustri Lucidi Fructus 120 g, Ecliptae Herba 80 g, Agrimoniae Herba 80 g, Rehmanniae Radix Praeparata 80 g, Epimedi Folium 60 g, Cibotii Rhizoma 60 g, Atractyloidis Macrocephalae Rhizoma 60 g, Cynomorii Herba 40 g, Codonopsisradix 40 g, Dipsaci Radix 20 g, Polygonati Odorati Rhizoma 20 g, Ginseng Radix Et Rhizoma 16 g | Water decocting | Whole grass | Benefiting Qi and nourishing Blood, tonifying the Kidney and strengthening Yang | [89] |
| Jianhenpian | Ecliptae Herba 72 g, Spaltholobii Caulis 108 g, Rosae Laevigateae Fructus 72 g, Artemisiae Argyi Folium 72 g, Mox Fructus 54 g, Cuscutae semen 36 g, Agrimoniae Herba 72 g, Ostreae Concha 108 g, Cibotii Rhizoma 54 g, Ligustri Lucidi Fructus 108 g, Glycyrrhizae Radix Et Rhizoma 18 g, Albiziae Cortex 36 g, Polygoni Multiflori Caulis 54 g, Spatholobi Caulis Fructus 54 g | Water decocting | Whole grass | strengthen the kidney and astringent essence | [89] |
| Weixuening | Polypodi Cuspidati Rhizoma Et Radix 115 g, Paoniae Radix Alba 71.8 g, Agrimoniae Herba 143.8 g, Rehmanniae Radix 115 g, Spaltholobii Caulis 143.8 g, Rehmanniae Radix Praeparata 115 g, Ecliptae Herba 43.8 g, Pseudostellariae Radix 57.6 g | Water extraction and alcohol precipitation | Whole grass | Tonifying the Blood and invigorating the Blood, clearing heat and cooling the Blood | [89] |
| Daifeicao | Armeniaceae semen Amurum 12 g, Ephedrae Herba 12 g, Terminalia chebula Retz. 12 g, Gardeniae Fructus 12 g, indigo naturalis 12 g, bletillae rhizoma 12 g, phytoplaccae radix 12 g, Pumex 12 g, Meretricis Concha 12 g, Cyclinae Concha 12 g, Agrimoniae Herba 90 g, Ardiae Japonicae Herba 150 g, Stemoneae Radix 12 g, Semen Trichosanthis 12 g | Crushing and mixing | Whole grass | Stops bleeding, dissolves phlegm, smooths the flow of Qi, settles asthma, stops sweating, and reduces fever | [89] |
| Zhierling Chongji | Codonopsisradix 90 g, Pseudostellariae Radix 90 g, Polygoni Multiflori Radix Praeparata 60 g, Atractyloidis Macrocephalae Rhizoma 90 g, Sinensis Radix 90 g, Paoniae Radix Alba 60 g, Sojae Semen 54 g, Mahoniae 90 g, Poria 60 g, Schisandraceae Chinensis Fructus 15 g, Acorii Tatarinowii Rhizoma 30 g, Triticum Cotyledon album 60 g, Poria 40 g, Dipsaci Radix 20 g, Polygonati Odorati Rhizoma 15 g, Ginseng Radix Et Rhizoma 16 g | Water decocting | Whole grass | Benefiting Qi and strengthening the spleen, tonifying the brain and strengthening the body | [89] |
| Xingnao Zaizaowan | Astragali Radix 60 g, Epimedi Foliolatum 35 g, Acorii Tatarinowii Rhizoma 15 g, Ginseng Radix Et Rhizoma 12.5 g, Angelicae Sinensis Radix 12.5 g, Phormitina 10 g, Notoginseng Radix Et Rhizoma 10 g, Carthami Flos 10 g, Stephaniae Tetrandrae Radix 10 g, Paoniae Radix Rubra 10 g, Puerariae Radix 10 g, Halotrichidii Concha 10 g, Gastrodiae Rhizoma 10 g, Agrimoniae Herba 10 g, Sophorae Flos 10 g, Atractyloidis Macrocephalae Rhizoma 10 g, Arisaema Cum Bile 10 g, Puerariae Lobae Radix 10 g, Scrophulariae Radix 10 g, Coptidis Radix 10 g, Forsythiae Fructus 10 g, Alismatis Rhizoma 10 g, Chaenxiong Rhizoma 10 g, Lycii Fructus 10 g, Scrophulariae Radix 2.5 g, Polypodi Multiflori Radix Praeparata 15 g, Campanulaceae semen 10 g, Aquilariae Lignum Resinatum 5 g, Typhoni Rhizoma 5 g, Asari Radix Et Rhizoma 5 g, Ecliptae Herba 5 g, Ecliptae Herba 2.5 g, Gleditsiae Fructus Abnormalis 5 g, Borneolum Syntheticum 5 g, Margarita 7.5 g, Rhei Radix Et Rhizoma 5 g | Crushing and mixing | Whole grass | Clearing phlegm and awakening the brain, dispelling wind and activating energy | [89] |
| Anshen Tangjiang | Ganoderma 50 g, Atractyloidis Macrocephalae Rhizoma 100 g, Ligustri Lucidi Fructus 100 g, Albiziae Cortex 100 g | Water decocting | Whole grass | invigorate blood circulation and calm the mind | [89] |
### Table 1 (continued)

| Preparation name | Main compositions | Preparation method | Part used | Traditional and clinical uses | References |
|------------------|-------------------|--------------------|-----------|-------------------------------|------------|
| **Zhier Linggao Zi Codonopsis radix 90 g, Pseudostellariae Radix 90 g, Pian Zaizhang Shengxue Kuiyang Jiaonang Arcae Concha 32 g, eggshell 48 g, Citri Reticulatae Lidan Zhitong Pian Bupleuri Radix 60 g, Paeoniae Radix Rubra 60 g, Zhichuang Zhixue Xuebao Jiaonang Rehmanniae Radix Praeparata 62 g, Angelicae Sinensis Liteminpian Agrimoniae Herba 150 g, Potentillae Discoloris Herba Yangxue Anshenpian Agrimoniae Herba 100 g, Ecliptae Herba 60 g, Prepartion name Main compositions Preparation** | **| **| **| **| **|
| **Weixuening Chongji Polygoni Cuspidati Rhizoma Et Radix 100 g, Paeoniae Radix Alba 62.5 g, Agrimoniae Herba 125 g, Rehmanniae Radix 100 g, Spatholobi Caulis 125 g, Rehmanniae Radix Praeparata 100 g, Ecliptae Herba 37.5 g, Pseudostellariae Radix 50 g** | Water extraction and alcohol precipitation | Whole grass | invigorate blood circulation and calm the mind | ![References](http://example.com) |
| **Yangxue Anshenpian Agrimoniae Herba 100 g, Ecliptae Herba 60 g, Spatholobi Caulis 60 g, Rehmanniae Radix Praeparata 60 g, Rehmanniae Radix 60 g, Albiziae Cortex 60 g, Polygoni Multiflori Radix 60 g** | Water decocting | Whole grass | Nourishing Yin and nourishing Blood, calming the mind and tranquilizing the spirit | ![References](http://example.com) |
| **Liteminpian Agrimoniae Herba 150 g, Potentillae Discoloris Herba 150 g** | Alcohol extraction | Whole grass | Clearing heat and detoxifying, antibacterial and anti-dysentery | ![References](http://example.com) |
| **Xuebao Jiaonang Rehmanniae Radix Praeparata 62 g, Angelicae Sinensis Radix 46 g, Rhamnodi Radix 61 g, Salviae Milliroturhize Radix Et Rhizoma 46 g, Codonopsisradix 77 g, Spatholobi Caulis 30 g, Aconiti Lateralis Radix Praeparata 2 g, Cinnamomi Ramulus 4 g, Lycii Fructus 62 g, Agrimoniae Herba 47 g, Chaunxiang Rhizoma 15 g, Polgony Cuspidati Rhizoma Et Radix 31 g, Rumex patientia L. 46 g, Forsythiae Fructus 30 g, Paeoniae Radix Rubra 16 g, Psoraleae Fructus 30 g, Polygony Multiflori Radix Praeparata 47 g, Aastragal Radix 46 g, Acanthopanacis Senticosi Radix Et Rhizoma 76 g, Cervi Cornu Pantotrichum 3.5 g, Plecta Hominis 31 g, Ligustri Lucidi Fructus 46 g, Moutan Cortex 18 g, Cibotii Rhizoma 15 g, Asini Corii Colla 15 g, Atractylodis Macrocephalae Radix 90 g, Angelicae Sinensis Radix 90 g, Rehmanniae Radix 90 g, Albaapaeoniae Radix Alba, Polygoni Multi Iherba, Rehmanniae Radix Praeparata, Epimedii Folium, Polygoniti Rhizoma, Cervi Cornu Pantotrichum, Codonopsisradix, Ophiopogonis Radix, Agrimoniae Herba, Atractylodis Macrocephalae Rhizoma, Lycii Fructus, Ecliptae Herba, Psoraleae Fructus** | Water decocting | Whole grass | Tonifying Yin and cultivating Yang, benefiting the kidney and strengthening the spleen | ![References](http://example.com) |
| **Yangxue Anshen Tangjiang Polygoni Multiflori Caulis 90 g, Spatholobi Caulis 90 g, Rehmanniae Radix Praeparata 90 g, Rehmanniae Radix 90 g, Albiziae Cortex 90 g, Ecliptae Herba 90 g, Agrimoniae Herba 150 g** | Water decocting | Whole grass | Nourishing Yin and nourishing Blood, calming the mind and tranquilizing the spirit | ![References](http://example.com) |
| **Zhichuang Zhixue Wan Sophorae Flos 100 g, Schizonepetae Herba 100 g, Citri Reticulatae Pericarpium 100 g, Platycladi Cacumen 100 g, Sanguisorbae Radix 100 g, Spatholobi Caulis 100 g, Zizyphi Fructus 100 g, Atractylodis Rhizoma 60 g, Toosendan Fructus 30 g, Artemisiae Scopariae Herba 100 g, Corydalis Rhizoma 100 g, Ecliptae Herba 100 g, Gynostemma Plicatum 100 g, Dioscoreae Radix 90 g, Schisandrae Chinensis Radix 46 g, Manihot Utilis 46 g, Taraxaci Herba 150 g, Curcumae Longae Fructus 100 g, Agrimoniae Herba 150 g** | Crushing and honey addition | Whole grass | Clearing damp-heat from intestinal wind, cooling the blood and stopping bleeding | ![References](http://example.com) |
| **Lidan Zhitong Pian Bupleuri Radix 60 g, Paeoniae Radix Rubra 60 g, Aurantii Fructus 60 g, Glycyrrhizae Radix Et Rhizoma 30 g, Artemisiae Scopariae Herba 100 g, Corydalis Rhizoma 100 g, Atractylodis Rhizoma 60 g, Toosendan Fructus 60 g, Agrimoniae Herba 150 g, Isatidis Radix 100 g, Taraxaci Herba 150 g, Curcumae Longae Radix 100 g** | Water decocting | Whole grass | Clearing heat and removing gall bladder, regulating Qi and relieving pain | ![References](http://example.com) |
| **Kuiyang Jiaonang Arcae Concha 32 g, eggshell 48 g, Citri Reticulatae Pericarpium 16 g, Alumen 32 g, Polygony Orientalis Fructus 32 g, Margarita 0.5 g, Agrimoniae Herba 112 g** | Water decocting | Whole grass | Stopping acidity and pain, producing muscle and astringency | ![References](http://example.com) |
| **Zaiizhang Shengxue Pian Cucurbitae Semen, Ginseng Radix Et Rhizoma Rubra, Spatholobi Caulis, Asini Corii Colla, Angelicae Sinensis Radix, Ligustri Lucidi Fructus, Astragal Radix, Leonur Iherba, Rehmanniae Radix Praeparata, Paeoniae Radix Albapaeoniae Radix Alba, Polygony Multiflori Radix Praeparata, Epimedii Foliun, Polygoniti Rhizoma, Cervi Cornu Pantotrichum, Codonopsisradix, Ophiopogonis Radix, Agrimoniae Herba, Atractylodis Macrocephalae Rhizoma, Lycii Fructus, Ecliptae Herba, Psoraleae Fructus** | Water decocting | Whole grass | Tonifying the liver, strengthening the spleen, benefiting the Qi and nourishing the blood | ![References](http://example.com) |
| **Zhier Linggao Zi Codonopsisradix 90 g, Pseudostellariae Radix 90 g, Adenophorae Radix 90 g, Rehmanniae Radix 90 g, Polygoni Multiflori Radix Praeparata 60 g, Atractylodis Macrocephalae Rhizoma 90 g, Angelicae Sinensis Radix 60 g, Paeoniae Radix Alba 90 g, Sojae Semen Nigrum 90 g, Aucklandiae Radix 15 g, Lablab Semen Album 90 g, Dioscoreae Rhizoma 90 g, Agrimoniae Herba 90 g, Mahonia 90 g, Poria 60 g, Schisandrae Chinensis Radix 90 g, Aconiti Tatarinowii Rhizoma 30 g, Tricosum aestivum L. 150 g, Glycyrrhiza Radix Et Rhizoma 15 g, Ostreae Concha 150 g, Ostreae Concha 150 g, Citri** | Water decocting | Whole grass | Benefiting Qi and strengthening the spleen, tonifying the brain and strengthening the body | ![References](http://example.com) |
| Preparation name | Main compositions | Preparation method | Part used | Traditional and clinical uses | References |
|------------------|-------------------|--------------------|-----------|------------------------------|------------|
| **Table 1**      |                   |                    |           |                              | (continued) |
| **Yuyejin Wan**  | Eucommiae Cortex, Rehmanniae Radix, Scutellariae Radix, Astragali Complanati semen, Angelicae Sinensis Radix, Armeriae Agugi Foliium, Nelumbinis semen, Dioscoreae rhizoma, Ophiopogonis Radix, Fritillariae Thunbergii Bulbus, Salviae Milii Herbae | Crushing and mixing | Whole grass | Benefiting Qi, soothing the liver, regulating menstruation and stopping dysmenorrhea. | [89] |
| **Xianhe Jiaonang** | Agrimoniae Herba 1250 g, Codonopsis radix 375 g, Atractylodis macrocephalae rhizoma 375 g, Acori tatarinowii rhizoma 375 g, Platycodonis radix 250 g | Water extraction and alcohol precipitation | Whole grass | Strengthening the spleen, benefiting the intestines and stopping diarrhea, clearing heat and dampness, resolving dampness and harmonizing the middle, dispelling wind and draining pus | [89] |
| **Shenlu Bupian** | Ginseng Radix Et Rhizoma Rubra 20 g, Venison 30 g, Epimedi Foliolum 75 g, Cibotii Rhizoma 75 g, Ecliptae Herba 100 g, Polygonati Odorati Rhizoma 25 g, Ligustri flos 201 g | Water decocting | Whole grass | Benefiting Qi and nourishing blood, tonifying the kidney and strengthening Yang | [89] |
| **Fuyanding Jiaonang** | Calliarciae formosae folium, Sophora flavescens radix, Camphor, Agrimoniae Herba, Alumen, Stemona Radix, Borneolum syntheticum, Caudii fructus, Benzalkonium bromide | Water decocting | Whole grass | Clearing heat and drying dampness, killing worms and relieving itching | [89] |
| **Fufang Tiersian Zhixue Fen** | Acalypha australis L. 100 g, Puerariae Fritii 100 g, Euphorbiae humifusae herbae 100 g, Herbae Acori tatarinowii 900 g, Gelatini 120 g | Water decocting | Whole grass | Cooling the blood, collecting astringency and stopping bleeding | [89] |
| **hangyangning Wan** | Atractylodis Macrocephalae Rhizoma 360 g, Linderae Radix 360 g, Dioscoreae Rhizoma 360 g, Bletillae Rhizoma 360 g, Citri reticulatae pericarpium viride 180 g, Alpiniae officinarum rhizoma 90 g, Paeoniae Radix Rubra 600 g, Agrimoniae Herba 600 g, Glycyrrhizae Radix Et Rhizoma 360 g, Mucuna Pruriens 90 g, Cyperi Rhizoma 180 g, Flos gossypii 600 g | Crushing and mixing | Whole grass | Warming the middle and dispersing cold, regulating Qi and relieving pain, controlling acidity and stopping bleeding | [85] |
| **Yifei Qinghua Gao** | ononis radix 125 g, Glehniae Radix 100 g, Ophiopogonis Radix 75 g, Agrimoniae Herba 125 g, Bistortae Rhizoma 100 g, Patriniae parvifoliae 83 g, Hedyotis diffusa 167 g, Fritillariae Cirrhosae Bulbus 75 g, Astersis Radix Et Rhizoma 75 g, Platycodonis Radix 75 g, Armeniaceae semen amarum 100 g, Glycyrrhizae Radix Et Rhizoma 50 g | Water decocting | Whole grass | Benefiting Qi and nourishing Yin, clearing heat and removing toxins, resolving phlegm and relieving cough | [85] |
| **Pingxiao pian** | Curcumae Radix 54 g, Agrimoniae Herba 54 g, Faecees Trogopteri 45 g, Alumen 54 g, Natrii Sulphatae 54 g, Toxiodendri Resinae 18 g, Aurantii Fructus 90 g, Strychni semen pulpereatamen 36 g | Water decocting | Whole grass | Promoting blood circulation and resolving blood stasis, dispersing nodules and subsiding swelling, detoxifying and relieving pain | [85] |
| **Pingxiao Jiaonang** | Curcumae Radix 54 g, Agrimoniae Herba 54 g, Faecees Trogopteri 45 g, Alumen 54 g, Natrii Sulphatae 54 g, Toxiodendri Resinae 18 g, Aurantii Fructus 90 g, Strychni semen pulpereatamen 36 g | Water decocting | Whole grass | Promoting blood circulation and resolving blood stasis, dispersing nodules and subsiding swelling, detoxifying and relieving pain | [85] |
| **Pingxiao Jiaonang** | Curcumae Radix 54 g, Agrimoniae Herba 54 g, Faecees Trogopteri 45 g, Alumen 54 g, Natrii Sulphatae 54 g, Toxiodendri Resinae 18 g, Aurantii Fructus 90 g, Strychni semen pulpereatamen 36 g | Water decocting | Whole grass | Promoting blood circulation and resolving blood stasis, dispersing nodules and subsiding swelling, detoxifying and relieving pain | [85] |
| Preparation name | Main compositions | Preparation method | Part used | Traditional and clinical uses | References |
|------------------|------------------|-------------------|-----------|-----------------------------|------------|
| Jiaonang Zaizao Shengxue | Polygoni Cuspidati Rhizoma Et Radix, Paeoniae Radix Alba, Agrimoniae Herba, Rehmanniae Radix, Spatholobi Caulis, Rehmanniae Radix Praeparata, Ecliptae Herba, Pseudostellariae Radix | Water extraction and alcohol precipitation | Whole grass | Nourishing Yin and nourishing Blood, clearing heat and cooling the Blood | [85] |
| Xingnao Zaizao Jiaonang | Astragalii Radix 162.2 g, Epimedi Folium 94.6 g, Acori Tatarinowii Rhizoma 40.5 g, Ginseng Radix Et Rhizoma Rubra 33.8 g, Notoginseng Radix Et Rhizoma 27 g, Pheretima 27 g, Angelicae Sinensis Radix 33.8 g, Carthami Flos 27 g, Stephaniae Tetraptera Radix 27 g, Paeoniae Radix Rubra 27 g, Persicae Semen 27 g, Hallotidis Concha 27 g, Gastrodiae Rhizoma 27 g, Agrimoniae Herba 27 g, Sophorae Flos 27 g, Atractylodis Macrocephalae Rhizoma 27 g, Ariaema Cum Bile 27 g, Paeriaes Lobatae Radix 27 g, Scrophulariae Radix 27 g, Coptidis Rhizoma 27 g, Forsythiae Fructus 27 g, Alismatis Rhizoma 27 g, Chuanxiong Rhizoma 27 g, Lycii Fructus 27 g, Scorpio 6.8 g, Polygoni Multiflori Radix Praeparata 40.5 g, Cassiae Semen 27 g, Aquilariae Lignum Resinatm 13.5 g, Typhonii Rhizoma 13.5 g, Asari Radix Et Rhizoma 13.5 g, Acori Tatarinowii Radix 13.5 g, Bombyx Batryticatus 6.8 g, Gleditsiae Fructus Abnormalis 13.5 g, Borneol Synthetico 13.5 g, Boric Acid 20.3 g, Rhei Radix Et Rhizoma 13.5 g | Water decocting | Whole grass | Clearing phlegm and awakening the brain, dispelling wind and activating energy | [85] |
| Baicai Puyan Qingshuan | Sophorae Flavescentis Radix 640 g, Stemona Radix 320 g, Cinodi Fructus 320 g, Agrimoniae Herba 320 g, Callicarpae Formosanae Foliim 320 g, Alumen 10 g, Borneol Synthetico 5 g, Camphor 10 g, Glycerol 2600 g, Gelatin 950 g | Water decocting | Whole grass | Clearing heat and removing toxins, killing insects and relieving itching, removing blood stasis and astringency | [87] |
| Fuxuean Flan | Angelicae Sinensis Radix, Leonur Iherba, Ligustri Lucidi Fructus, Ecliptae Herba, Notogingseng Radix Et Rhizoma, Salviae Miltiorrhizae Radix Et Rhizoma, Agrimoniae Herba, Cypers Rhizoma, Typhi Pollen, Platycladi Cacumen, Codonopissradix, Atractylodis Macrocephalae Rhizoma | Water decocting | Whole grass | Invigorating blood circulation, stopping bleeding and regulating menstruation | [90] |
| Fuyinmang Xiji | Frxini Cortex, Iastidis Foliim, Houttuyniae Herba, Sophorae Flavescentis Radix, Agrimoniae Herba, Violae Herba | Water decocting | Whole grass | Clearing heat and drying dampness, removing itching and relieving bandages | [91] |
| Gongning Keli | Rubiae Radix Et Rhizoma 195 g, Typhi Pollen 156 g, Notogingseng Radix Et Rhizoma 78 g, Sanguisorbae Radix 390 g, Scutellariae Radix 117 g, Rehmanniae Radix 195 g, Agrimoniae Herba 390 g, Sepiae Endococha 390 g, Codonopissradix 234 g, Paeoniae Radix Alba 195 g, Glycyrrhiza Radix Et Rhizoma 78 g | Water decocting | Whole grass | Removing blood stasis and clearing heat, consolidating menstruation and stopping bleeding | [85] |
| Shiling Qingsue Keli | Hallotidis Concha, Agrimoniae Herba, Ostreeea Concha, Achyranthis Bidentatae Radix, Sophorae Flos, Prunellae Spica, Curcumae Rhizoma, Acuminatus Cum Uncis, Haemenitis, Alismatis Rhizoma, Gastrodiae Rhizoma, Corni Fructus | Water decocting | Whole grass | Nourishing Yin and submerging Yang, calming the liver and quelling wind, resolving blood stasis and stopping bleeding | [92] |
| Xiangui Jiaonang | Ginseng Radix Et Rhizoma Rubra, Auranti Fructus Immaturus, Ephedrae Herba, Cinnamomum Pseudochinensis, Rehmanniae Radix Praeparata, Ophiopogonis Radix, Trachelospermum Caulisellotum, Agrimoniae Herba, Asii Corii Colla, Gastrodiae Rhizoma | Water decocting | Whole grass | Benefiting Qi and nourishing Yin, warming the meridians and opening the veins | [93] |
| Zaizao Shengue Jiaonang | Ginseng Radix Et Rhizoma Rubra 25.5 g, Spatholobi Caulis 59.5 g, Asii Corii Colla 25.5 g, Angelicae Sinensis Radix 42.5 g, Ligustri Lucidi Fructus 25.5 g, Astragalii Radix 42.5 g, Leonur Iherba 25.5 g, Rehmanniae Radix Praeparata 42.5 g, Paeoniae Radix Alba 25.5 g, Polygoni Multiflori Radix Praeparata 42.5 g, Epimedi Foliim 25.5 g, Polygorni Rhizoma 34 g, Cervi Corni Pustocirrhim 2.55 g, Codonopissradix 34 g, Ophiopogonis Radix 25.5 g, Agrimoniae Herba 34 g, Atractylodis Macrocephalae Rhizoma 25.5 g, Paeoriae Fructus 25.5 g, Lycii Fructus 34 g, Ecliptae Herba 25.5 g | Water decocting | Whole grass | Tonifies the liver and kidney, nourishes the qi and blood | [85] |
| Zhiling Jiaonang | Astragalii Radix, Glehniae Radix, Atractylodis Macrocephalae Rhizoma, Solanum lyrumtum Thunb., Ciri Reticulatae Pericarpium, Glycyrrhizae Radix Et Rhizoma, Indometacin, Ligustri Lucidi Fructus, Ophiopogonis Radix, Poria, Agrimoniae Herba, | Water decocting | Whole grass | Benefiting Qi, strengthening the spleen, nourishing Yin and moistening dryness | [94] |
Table 1 (continued)

| Preparation name | Main compositions | Preparation method | Part used | Traditional and clinical uses | References |
|------------------|-------------------|--------------------|----------|-------------------------------|------------|
| Fuyanling Shuan  | Benzalkonium Bromide, Cnidii Fructus, Alumine, Sophorae Flavescentis Radix, Borreolum Syntheticum, Agrimoniae Herba, Sterones Radix, Camphor, Callicarpeae Formosanae, Fumus, Boric Acid | Water decocting Whole | grass    | Clearing heat and drying dampness, killing worms and relieving itching | [95]       |
| Yiqi Hewei Jiaonang | Glycyrrhiza Radix Et Rhizoma, Agrimoniae Herba, Atractylodis Macrocephalae Rhizoma, Paeniae Radix Alba, Aurantii Fructus, Scutellariae Radix, Codonopsisradix, Salviae Miltiorrhizae Radix Et Rhizoma, Asagral Radix, Santali Albi Lignum | Water decocting Whole | grass    | Strengthening the spleen, harmonizing the stomach, clearing ligaments and relieving pain | [95]       |
| Yiqi Xiaohe Keli  | Anemarrhenae Rhizoma, Trichosanthis Radix, Scrophulariae Radix, Agrimoniae Herba, Polygoni Multiflori Radix, Corni Fructus, Dioscoreae Rhizoma, Astragali Radix, Atractylodis Rhizoma | Water decocting Whole | grass    | Benefit Qi and nourish Yin, increase body fluid and quench thirst | [95]       |
| Xuebao Pian       | Powdered Buffalo Horn Extract, Atractylodis Macrocephalae Rhizoma, Astini Cori Colla, Cibotii Rhizoma, Moutan Cortex, Ligustri Lucidi Fructus, Placenta Hominis, Cervi Cornu Pantotrichium, Acanthopanacis Senticosis Radix Et Rhizoma Seu Caulis, Astragali Radix, Polygoni Multiflori Radix Praeparata, Psoraleae Fructus, Paeniae Radix Rubra, Forsythiae Fructus, Rumex patientia L, Polygoni Cuspidati Rhizoma Et Radix, Chuanxiong Rhizoma, Agrimoniae Herba, Lyci Fructus, Cinnamonamomum Ramulus, Aconiti Lateralis Radix Praeparata, Stapholobi Caulis, Codonopsisradix, Salviae Miltiorrhizae Radix Et Rhizoma, Rhapontici Radix, Angelicae Sinensis Radix, Rehmanniae Radix Praeparata, Ginseng Radix Et Rhizoma, Citri Reticulatae Pericarpium, Ox spinal cord | Water decocting Whole | grass    | Benefit Qi and nourish Yin, increase body fluid and quench thirst | [95]       |
| Shangkeling Penwuji | Valeriana officinalis L. 18.3, Gualapimia cucullata 12.2 g, Chimonanthi Radix 12.2 g, Betelice Rhizoma 12.2 g, Verbenae Herba 12.2 g, Aconiti Kuinnzezoffi Radix 12.2 g, Agrimoniae Herba 12.2 g, Sophorae Tonkinensis Radix Et Rhizoma 12.2 g, Curcuma Rhizoma 18.3 g, Sparganii Rhizoma 18.3 g | Water decocting Whole | grass    | Clearing heat and cooling the blood, activating blood circulation, resolving fetishes, subduing swelling and relieving pain | [96]       |
| Weixuening Tangjiang | Polygoni Cuspidati Rhizoma Et Radix 0.15 g, Paeniae Radix Alba 94 mg, Agrimoniae Herba 0.19 g, Rehmanniae Radix 0.15 g, Spatholobi Caulis 0.19 g, Rehmanniae Radix Praeparata 0.15 g, Ecliptae Herba 57 mg, Pseudostellariae Radix 76 mg | Water decocting Whole | grass    | Tonifying the Blood and invigorating the Blood, clearing heat and cooling the Blood | [86]       |
| Zhierling Keli    | Codonopsisradix, Pseudostellariae Radix, Adenophorae Radix, Rehmanniae Radix, Polygoni Multiflori Radix Praeparata, Atractylodis Macrocephalae Rhizoma, Angelicae Sinensis Radix, Paeniae Radix Alba, Sojae Semen Nigrum, Aucklandiae Radix, Lablab Semen Album, Dioscoreae Rhizoma, Agrimoniae Herba, Mahonia, Portia, Schisandraceae Chinensis Fructus, Acorni Tatarinowii Rhizoma, Trichicum aestivum L, Glycyrrhizae Radix Et Rhizoma, Ostelea Concha, Citri Reticulatae Pericarpium, Polygaeae Radix, Jujubae Fructus | Water decocting Whole | grass    | Benefiting Qi and strengthening the spleen, tonifying the brain and strengthening the body | [86]       |
| Zaihao Shengxue Pian | Ginseng Radix Et Rhizoma Rubra 25.5 g, Spatholobi Caulis 59.5 g, Astini Cori Colla 25.5 g, Angelicae Sinensis Radix 42.5 g, Ligustri Lucidi Fructus 25.5 g, Astragali Radix 42.5 g, Leunur Ibera 25.5 g, Rehmanniae Radix Praeparata 42.5 g, Paeniae Radix Alba 25.5 g, Polygoni Multiflori Radix Praeparata 42.5 g, Epimedi Folium 25.5 g, Polygonati Rhizoma 34 g, Cervi Cornu Pantotrichium 2.55 g, Codonopsisradix 34 g, Ophiopogonis Radix 25.5 g, Agrimoniae Herba 34 g, Atractylodis Macrocephalae Rhizoma 25.5 g, Paeniae Fructus 25.5 g, Lyci Fructus 34 g, Ecliptae Herba 25.5 g | Water decocting Whole | grass    | Tonifies the liver and kidney, nourishes the qi and blood | [85]       |
| Longjing Pian     | Atractylodis Rhizoma 174 g, Plantaginis Semen 35 g, Pattrinia villosa 348 g, Lonicerae Japonicae Flos 174 g, Moutan Cortex 174 g, Hedvotis diffusa 348 g, Paeniae Radix Rubra 174 g, Agrimoniae Herba 174 g, Capsidi Radix 174 g, Phellodendri Chinensis Cortex 174 g | Water decocting Whole | grass    | Clearing heat and removing toxins, cooling the blood and promoting drainage | [85]       |
| Longjing Jiaonang | Atractylodis Rhizoma 261 g, Plantaginis Semen 52.5 g, Pattrinia villosa 522 g, Lonicerae Japonicae Flos 261 g, Moutan Cortex 261 g, Hedvotis diffusa 522 g, Paeniae | Water decocting Whole | grass    | Clearing heat and removing toxins, cooling the blood and promoting drainage | [85]       |
(91), Caryophyllene (92), Geraniol acetate (93), β-Cedrene (94), α-Cedrene (95), Geranyl acetone (96), Aromadendrene (97), Curcumene (98), β-Selinene (99), α-Selinene (100), δ-Guaiene (101), α-Bisabolene (102), Cuparene (103), Myristicin (104), e-Cadinene (105), Transnerolidol (106), Caryophyllene oxide (107), Cedrol (108), (-)-Cedrol (109), Muurolol (110), α-cadinol (111), Patchoulol (112), Cedryl acetate (113), Farnesyl acetate (114), Hexahydrofarnesyl acetone (115), Hexanal (116), Anethole (117), Limonene (118), Bomyl acetate (119), Butyrylfuran (120), Linalool (121), Decanoic acid (122), L-camphor (123), α-longipinene (124), Caryophyllene (125), Copaene (126), Longifolene (127), 3,4-dimethylbenzaldehyde (128), 2,4-dimethylbenzaldehyde (129), Fenchol (130), Aromadendrene (131), Nonanoic acid (132), α-himachalene (133), Acoradiene (134), α-guaiene (135), Dibutyl phthalate (136), Phytol (137), Linoleic acid (138), Epiglobulol (139), Elemicin (140), Torreyol (141), Farnesyl acetate (142), α-eudesmol (143), Dimethyl phthalate (144), 5,6,7,7a-tetrahydro-4,4,7a-trimethyl-2(4H)-benzofuranone (145), 3-pentadecyl-phenol (146), 3,8-dimethyldecane (147), Geranyllinalool (148), (E,E,E)-squalene (149), 3,4-dimethylbenzaldehyde (150), 9-butyl-9H-fluoren-9-ol, 3,8-dimethylidecane (151), (Z, Z, Z)-9, 12, 15-octadecatrienoic acid (152), Ethyllinoleate (153), (Z,Z,Z)-9,12,15-octadecatrienoic acid, ethyl ester (154), Ethyl steareate (155), bis (2-ethylhexyl) adipate (156), 3-pentadecyl-phenol (157), 3,8-dimethyldecane (158), Geranylinalool (159), (E,E,E)-squalene (160), Henriciacontane (161), Vitamin (162), γ-sitosterol (163), Cineole (164), 1-(2-furyl)-1-hexanone (165), Bergamot oil (166), 2-methyl-4-pyrimidinyl (167), Bornyl acetate (168), Thymol (169), Carvacrol (170), Nerolidol acetate (171), 3,3,5,5-tetramethylcyclohexanol (172), Geranyl acetate (173), (+)-Cedrol (174), Patchouli alcohol (175), Cedryl acetate (176) [23, 24, 25, 26, 27].

5.3. Phenolic compounds

Five phenolic compounds have been isolated and identified from APL, which include pilosanol N (177), Agrimophol (178), B3 Proanthocyanidins (179), Ellagic acid (180), Ellagic acid 4-O-D-xylopyranoside (181) [16, 28, 29, 30].

5.4. Phloroglucinol derivatives

The phloroglucinol derivatives are a less polar class of compounds and comprise the main active ingredients of APL. Fourteen phloroglucinol compounds have been isolated and identified from APL, including Aripinol A (182), Aripinol B (183), Aripinol C (184), Peudoaspidin (185), α-kosin (186), Agrimol A (187), Agrimol B (188), Agrimol C (189), Agrimol D (190), Agrimol E (191), Agrimol F (192), Agrimol G (193), Agrimophol (194), Psudoaspidin (195) [15, 30, 31, 32].
| Classification | No. | Chemical component | Reference |
|----------------|-----|-------------------|-----------|
| **Flavonoids** |     |                   |           |
| 1              |     | Rutin             | [8]       |
| 2              |     | Luteolin-7-O-glucoside | [8]     |
| 3              |     | Luteolin-7-O-glucuronide | [8]     |
| 4              |     | Quercitin         | [8]       |
| 5              |     | Apigenin-7-O-glucoside | [8]     |
| 6              |     | Apigenin-7-O-glucuronide | [8]     |
| 7              |     | Vitexin           | [9]       |
| 8              |     | Isovitexin        | [9]       |
| 9              |     | (2R,3S)-dihydrokaempferol 3-O-β-D-glucoside | [21] |
| 10             |     | (2S,3R)-dihydrokaempferol 3-O-β-D-glucoside | [21] |
| 11             |     | Agrifavone        | [10]      |
| 12             |     | Kaempferol-3-O-[(S)-3-hydroxy-3-methylglutaryl (1→6)]-β-D-Glucoside | [10] |
| 13             |     | Trilirside        | [11]      |
| 14             |     | Catechin          | [12]      |
| 15             |     | Hyperoside        | [12]      |
| 16             |     | Quercitin         | [12]      |
| 17             |     | 3-methoxy quercetin | [13]    |
| 18             |     | Apigenin-7-O-β-D-glucuronide-600-methyl ester | [14] |
| 19             |     | Quercetin-7-O-β-D-glycoside | [14] |
| 20             |     | Quercetin-3-O-β-D-glycoside | [14] |
| 21             |     | Kaempferol        | [14]      |
| 22             |     | Kaempferol-3-O-α-L-rhamnoside | [14] |
| 23             |     | Isoquercitri      | [15]      |
| 24             |     | Kaempferide       | [16]      |
| 25             |     | Kaempferide-3-O-α-L-rhamnopyranoside | [16] |
| 26             |     | Apigenin          | [17]      |
| 27             |     | Apigenin-7-O-β-D-glucopyranoside | [16] |
| 28             |     | Apigenin-7-o-methylglucuronate | [18] |
| 29             |     | Apigenin-7-0-butylglucuronate | [18] |
| 30             |     | Luteolin-7-O-soforside | [8]    |
| 31             |     | Luteolin-7-O-(6-O-acetyl)-D-glucopyranoside | [8] |
| 32             |     | Luteolin          | [16]      |
| 33             |     | Luteolin-7-O-β-D-glucopyranoside | [16] |
| 34             |     | Wogonin           | [17]      |
| 35             |     | (→)-catechin      | [19]      |
| 36             |     | PilosanoA         | [16]      |
| 37             |     | PilosanoB         | [16]      |
| 38             |     | PilosanoC         | [16]      |
| 39             |     | (2R, 3R)(→)-Taxifolin | [15]   |
| 40             |     | (2R, 3R)(→)-Taxifolin-3-O-β-D-glucopyranoside | [16] |
| 41             |     | (2S, 3S)-(-)-Taxifolin | [20]  |
| 42             |     | Dehydrodicatechin A | [19] |
| 43             |     | Kaempferol-3-O-rutinoside | [8]  |
| 44             |     | 3-O-kaempferol 2,3-di-O-acetyl-4-O-(cis-p-coumaroyl)-6-O-(trans-p-coumaroyl)β-D-glucosopyranoside | [22] |
| 45             |     | Quercetin-3-O-α-arabinofuranosyl-β-D-galactopyranoside | [22] |
| 46             |     | Kaempferol-3-glycoside | [22] |
| 47             |     | Catechin          | [22]      |
| 48             |     | (2S, 3S)(→)-Taxifolin-3-O-β-D-glucopyranoside | [20] |
| 49             |     | (→)-Aromadendrin-3-O-β-D-glucopyranoside | [8] |
| **Volatile oil** | 50 | 3-Hydroxybutyric Acid | [23] |
| 51             |     | 2,6-diaceetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-Dibenzo furandione9b)-dibenzo furandione | [23] |

(continued on next page)
Table 2 (continued)

| Classification | No. | Chemical component | Reference |
|----------------|-----|--------------------|-----------|
| Phenolic       | 167 | 2-methyl-4-pyrimidinyl | [27]      |
|                | 168 | Bornyl acetate     | [27]      |
|                | 169 | Thymol             | [27]      |
|                | 170 | Carvacrol          | [27]      |
|                | 171 | Neryl acetate      | [27]      |
|                | 172 | 3,3,5,5-tetramethylcyclohexanol | [27] |
|                | 173 | Geranyl acetate    | [27]      |
|                | 174 | (+)-Cedrol         | [27]      |
|                | 175 | Patchouli alcohol  | [27]      |
|                | 176 | Cedryl acetate     | [27]      |
| Tannins        | 177 | Pilosan N          | [38]      |
|                | 178 | Agrimophol         | [16]      |
|                | 179 | B3 Proanthocyanidins | [30]  |
|                | 180 | Ellagic acid       | [29]      |
|                | 181 | Ellagic acid 4-O-D-xylopyranoside | [29] |
| Tannins        | 196 | Agritannin        | [10]      |
|                | 197 | Potentillin        | [16]      |
|                | 198 | Pedunculagin       | [16]      |
|                | 199 | Casuarinin         | [16]      |
|                | 200 | Agrimonin          | [16]      |
|                | 201 | Alagrimonic A      | [16]      |
|                | 202 | Alagrimonic B      | [16]      |
| Isocoumarins   | 203 | Arimonolide        | [34]      |
|                | 204 | Dmethylagrimonolide | [34]    |
|                | 205 | (35)-Agrimonolide-6-O-β-D-glucopyranoside | [34] |
|                | 206 | (35)-Desmethylagrimonolide-6-O-β-D-glucopyranoside | [34] |
|                | 207 | (35)-Desmethylagrimonolide-4’-O-β-D-glucopyranoside | [34] |
|                | 208 | (35)-Agrimonolide-6-O-α-L-Arabino furanoside-(1→6)-β-D-side | [34] |
|                | 209 | (35,4R)-4-Hydroxyagrimonolide-6-O-β-D-glucopyranoside | [34] |
|                | 210 | Penylethylisoumarin glycoside | [35] |
|                | 211 | Agrimolinol-6-O-β-D-glucosid | [35] |
|                | 212 | (35)-esmethylagrimonolide-4’-O-β-D-glucopyranoside | [37] |
| Pentacyclic    | 213 | 1S,3R,17R,18R,19R,20R(1,3,19,22-tetrahydroxy-28-norurs-12-ene-2-one | [38] |
| triterpenoids  |     | Corosolic acid     | [38]      |
|                |     | Pomolic acid       | [38]      |
|                |     | Tormentic acid     | [38]      |
|                |     | epi-tormentic acid | [38]      |
|                |     | 1,2,3,4,5,6,7,8-tetrahydroxyxyres-12-en-28-oic acid | [38] |
|                | 219 | Ursolic acid       | [39]      |

(continued on next page)
Table 2 (continued)

| Classification | No. | Chemical component | Reference |
|----------------|-----|--------------------|-----------|
| 220 | Eusophoric acid | [16] |
| 221 | Pomolic acid | [16] |
| 222 | Rosamulin | [16] |
| 223 | Tormentic acid | [16] |
| 224 | 1,2,3,19,22-tetrahydroxy-12-en-28-oic acid | [16] |
| 225 | 27-hydroxy-a-amyrin | [16] |
| Organic acids | 226 | Methyl 2-hydroxyl tricosanoate | [40] |
| 227 | Palmitic acid | [40] |
| 228 | Gallic acid | [42] |
| 229 | Isovanillic acid | [42] |
| 230 | Protocatechuic | [42] |
| 231 | Chlorogenic acid | [30] |
| 232 | Protocatechuic aldehyde | [44] |
| 233 | Palmitic acid | [40] |
| 234 | 27-hydroxy-a-amyrin | [16, 38, 39] |

5.5. Tannins

Seven tannin compounds have been isolated and identified from APL, including Agritannin (196), Potentilltin (197), Pedunculagin (198), Casuarinin (199), Agrimoniin (200), Alagrimonic A (201), Alagrimonic B (202) [10, 16].

5.6. Isocoumarins

Ten isocoumarins have been isolated and identified from APL, including Arizomolide (203), Dimethylarizomolide (204), (3S)-Agrimonolide-6-O-β-D-glucopyranoside (205), (3S)-Desmethylarimولide-6-O-β-D-glucopyranoside (206), (3S)-Desmethylyarimolide-4’-O-β-D-glucopyranosyl (207), (3S)-Agrimonolide-6-O-α-L-Arabinofuranose (1→6)-β-D-side (208), (3S,4R)-4-Hydroxyarimonolide-6-O-β-D-glucopyranoside (209), Penylethylisocoumarin glycoside (210), Agravimolide-6-O-β-D-glucosid (211), (3S)-esmethylyarimolide-4’-O-β-D-glucopyranoside (212) [34, 35, 36, 37].

5.7. Pentacyclic triterpenoids

Thirteen pentacyclic triterpenoid compounds have been isolated and identified from APL, including 1S,3R,17R,18R,19R,20R,22R,1,3,19,22-tetrahydroxy-28-norurs-12-en-2-one (213), Corosolic acid (214), Pomolic acid (215), Tormentic acid (216), epi-tormentic acid (217), 1,2,3,19,22-tetrahydroxy-12-en-28-oic acid (218), Ursolic acid (219), Eusophoric acid (220), Pomolic acid (221), Rosamulin (222), Tormentic acid (223), 1,2,3,19,22-tetrahydroxy-12-en-28-oic acid (224), 27-hydroxy-a-amyrin (225) [16, 38, 39].

5.8. Organic acids

Nine organic acid compounds have been isolated and identified from APL, including Methyl 2-hydroxyl tricosanoate (226), Palmitic acid (227), Gallic acid (228), Isovanillic acid (229), Protocatechuic (230), Chlorogenic acid (231), Neochlorogenic acid (232), Cryptochlorogenic acid (233), p-Coumaric acid (234) [30, 33, 40, 41, 42].

5.9. Lignans

Ten lignans have been isolated and identified from APL, including Pilosaneolignan ester (235), Pilosaneolignanside A (236), Picraquassioside C (237), Longifloroside B (238) [43], 214, 38, 39], (27S,8S)-3-methoxy-8,4,7-oxynolignan-3’-4’,7,9,9’-pentol (240), Rourioside (241), 7S,8R)-1-[4-O-(β-D-glucopyranosyl)-3-methoxynaphthyl-1-2-[4-(3-hydroxy-propyl)-2,6-methoxyphenoxyl]-1,3-propanediol (242), Densipsicoside (243), Icariol A2 (244) [43].

5.10. Others

Other compounds have also been found in APL, including Nnaut-thracene (245), β-sitosterol (246), Dihydrodihydrodiconiferyl alcohol 9’-O-β-D-glucose (247), 5,7-Dihydroxy-2-propylchromone 7-O-beta-D-glucopyranoside (248), Takehancrome C (249), (24R)-24-ethyl-5a-cholestan-3β,5,6β-triol (250), Protocatechuic aldehyde (251), β-daucosterol (252) [44, 45].

6. Extraction methods

At present, APL extraction is mainly performed to extract flavonoids, phenols, polysaccharides, tannins, and other effective components. Most of the extraction processes were optimized using response surface methodology, but extraction times varied widely and extraction rates of other active parts were not adequately considered when one of the active parts was extracted. The extraction components are relatively single, and the optimization process for volatile oils, terpenoids, and other components is less. In the future, more consideration can be given to the integrated extraction of multiple components and the optimization of extraction processes for volatile oils as well as terpenoids, and in-depth studies on extraction methods [46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56]. The APL extraction methods are summarized in Table 3.

7. Pharmacological potential (see Figure 4)

7.1. Anti-inflammatory potential

Choon Young Kim [57] et al. evaluated the inhibitory effects of APL on lipopolysaccharide (LPS)-induced oxidative stress and inflammation in HepG2 hepatocytes. In hepatocytes exposed to LPS, where inflammatory responses were accompanied by elevated oxidative stress leading to hepatic dysfunction and injury, APL treatment significantly reduced the LPS-induced intracellular levels of reactive oxygen species (ROS) and eliminated the expression of significantly downregulated genes and proteins encoding glutathione peroxidase. It was also shown that APL has
antioxidant and anti-inflammatory activities and helps to protect hepatocytes from LPS.

Chang Hwa Jung [58] et al. investigated the ability of APL to attenuate inflammation, using in vitro assays to examine the release of ROS from nitric oxide (NO), which plays a key role in inflammation and immune responses. It was shown that 80% of APL ethanolic extracts significantly inhibited NO release and ROS production. Among them, n-butanol extract showed the most potent anti-inflammatory effect based on the results of in vitro assays, in which it significantly reduced NO in LPS-activated RAW 264.7 macrophages and inhibited nitric oxide synthase (iNOS) expression. However, the extract did not inhibit cyclooxygenase-2 (COX-2) expression, indicating that n-butanol extract can reduce NO production by inhibiting iNOS but not COX-2. The results suggest that the n-butanol extract of APL has potential anti-inflammatory activity. Junsei Taira [59] et al. isolated Pilosanol N, a catechin, from APL, which was found to inhibit LPS/IFN-γ-induced NO production and iNOS gene and protein expression in RAW264.7 macrophages. It was also shown that Pilosanol N reduced NO levels by a mechanism that reduces NO production and NO scavenging, i.e., Pilosanol N has anti-inflammatory activity. Xin Jin [60] et al. isolated and purified Tiliroside, the main component of APL extract, by high performance liquid chromatography and found that Tiliroside could exert its anti-inflammatory effects through the downregulation of iNOS and COX-2 protein expression levels and the inactivation of mitogen-activated protein kinase.

Da-Sol Kim [61] et al. examined the anti-inflammatory effect of APL extract (APL-E) on Porphyromonas gingivalis LPS-induced RAW 264.7 cells. It was shown that APL extract inhibited the expression of pro-inflammatory cytokines and decreased the nitrite concentration, including interleukin-1β (IL-1β), interleukin 6 (IL-6), and tumor necrosis factor α (TNF-α), in Porphyromonas gingivalis LPS-induced RAW 264.7 cells. Additionally, the protein expression of COX-2 and iNOS was dose-dependently inhibited by APL extracts. The results show that APL extract had an anti-inflammatory effect on LPS-induced RAW 264.7 cells of Bacillus gingivalis. Jae-Jin Kim [62] et al. determined the effect of methanolic APL extract on LPS-induced inflammatory mediator production using RAW 264.7 murine macrophages. In LPS-induced RAW 264.7 cells, APL attenuated the production of inflammatory mediators,
including NO, PGE2, and pro-inflammatory cytokines. The results suggest that APL has potent anti-inflammatory effects through modulation of TRIF-dependent and Syk-PLC/AKT signaling pathways (see Figure 5).

7.2. Anti-cancer potential

Zhang Tingting [63] et al. examined the inhibitory effect of APL aqueous extract and 5-FU culture solution on Hep G2 growth, the apoptosis rate, the Bax mRNA expression level, and Caspase-3 protein expression in hepatocellular carcinoma cells. To this end, different concentrations of APL aqueous extract and 5-FU culture solution were added to human hepatocellular carcinoma HepG2 cells to study the effects on proliferation and apoptosis. The results showed that the aqueous extract of APL induced apoptosis by up-regulating the gene expression of Bax and the protein expression of Caspase-3 to promote HepG2 apoptosis and inhibit its proliferation [64]; therefore, APL has anti-cancer activity.

Cai Tiantian [65] et al. detected the proliferation inhibition effect of APL aqueous extract on pancreatic cancer cells BXPC-3 and PANC-1 by SRB assay. The effect of APL aqueous extract on the cycle distribution of BXPC-3 pancreatic cancer cells was detected by flow cytometry. The results showed that the aqueous extract of APL significantly inhibited the proliferation of BXPC-3 and PANC-1 cells in a time- and concentration-dependent manner. Annexin V-FITC/PI double staining assay was used to detect the effect of APL aqueous extract on the apoptosis of BXPC-3 cells. The aqueous extract of APL inhibited the proliferation of pancreatic cancer cells by inducing apoptosis of BXPC-3 and PANC-1 apoptosis, inhibit the proliferation of pancreatic cancer cells, and play an anti-pancreatic cancer role.

Su Thae Hnit [66] et al. analyzed the DNA and RNA of cancer cells stained with Hoechst 33342 and pyronin Y, respectively, by flow cytometry. It was shown that the anti-cancer effect could be attributed to the polyphenol Agrimol B derived from APL. The effect of Agrimol B on cancer cells may originate from its effect on c-MYC, SKP2, and p27, as observed by immunoblotting and immunofluorescence. Agrimol B enriches prostate and lung cancer cells in the G0 phase (a reversible quiescent state outside the cell cycle) and affects key regulators that control the G0 state. Oral administration of APL or Agrimol B has also been shown to reduce the growth of xenografts in animal prostate cancer cells, thereby demonstrating anti-cancer effects (see Figure 6).

Table 3. Method for extracting of Agrimonia pilosa Ledeb.

| Active ingredients | Extraction method | Extraction reagent | Extraction temperature (°C) | Extraction time (h) | Material to liquid ratio (mL/g) | Number of extractions | Extraction rate (%) | References |
|-------------------|-------------------|--------------------|-----------------------------|--------------------|-------------------------------|----------------------|-------------------|------------|
| flavonoid         | Ethanol reflux extraction method | 60% ethanol        | /                           | 1.5                | 15.69                         | 2                    | 10.68             | [46]       |
| tannin            | reflux            | 90% ethanol        | 45–50 °C                    | 2                  | 5                             | /                    | /                | [47]       |
| flavonoid         | ultrasonic extraction | 64% ethanol       | 40 °C                       | 1.23               | 10.5                          | 3                    | 10.628            | [48]       |
| flavonoid         | Ethanol reflux extraction method | 30% ethanol      | 100 ºC                      | 1.67               | 15                            | 3                    | 9.92              | [49]       |
| polyphenol        | ultrasonic extraction | 60% methanol     | 35 ºC                       | 0.417              | 20                            | /                    | 1.46              | [50]       |
| polyphenol        | ultrasonic extraction | 71% ethanol      | 60 ºC                       | 0.333              | 24                            | /                    | 3.56              | [51]       |
| flavonoid         | ultrasonic extraction | 72% ethanol      | 60 ºC                       | 0.333              | 25                            | /                    | 9.02              | [52]       |
| flavonoid         | Ethanol reflux method | 70% ethanol      | 80 ºC                       | 1                  | 10                            | 3                    | 10.52             | [53]       |
| polysaccharide    | leaching          | /                  | 80 ºC                       | 12                 | 15                            | /                    | 2.15              | [54]       |
| polysaccharide    | ultrasonic extraction | /             | /                           | 0.333              | 80                            | /                    | 8.04              | [55]       |
| flavonoid         | leaching          | 40% ethanol        | 70 ºC                       | 0.5                | 10                            | 3                    | /                 | [56]       |
7.3. Anti-tumor potential

Kenichi Miyamoto [67] et al. investigated the effect of a tannin, Agrimoniin, from APL on antitumor effects in ascites and solid rodents. Agrimoniin almost completely inhibited tumor growth and prolonged the lifespan of mice bearing MM2 cells when administered intraperitoneally, intravenously, or orally at doses exceeding 10 mg/kg before or after MM2 cell inoculation. Agrimoniin also inhibited the growth of MH1 34 and meth-A solid-type tumors. Agrimoniin was found to enhance the immune response of the host animal by acting on tumor cells and some immune cells to achieve anti-tumor effects.

Tian Lulu [68] used microfluidic microarray technology and flow cytometry to study the cell cycle, apoptosis, necrosis, migration, and invasion of hepatocellular carcinoma HepG2 cells following treatment with medicinal substance fractions of APL to comprehensively evaluate its anti-hepatic tumor efficacy. The results showed that the total flavonoid fraction of APL has a significant apoptosis and necrosis-promoting effect on HepG2 cells, a significant G2/M blocking effect on the cell cycle, and a significant inhibition effect on cell migration and invasion. The efficacy of the drug gradually increased with increasing dose, showing strong anti-liver tumor effects. Cheng YG [69] et al. used the CCK-8 colorimetric assay to detect cell proliferation. The results showed
that total flavonoid extracts inhibited the proliferation of gastric cancer MKN-45 cells, liver cancer Hep G2 cells, myeloma U266 cells, breast cancer MCF-7 cells, lung cancer A549 cells, and cervical cancer He La cells and showed an obvious concentration-dependent effect. The inhibitory effect was particularly strong on Hep G2 and A549 cells. Meanwhile, Tian Lulu [70] et al. used the MTT colorimetric method to study the effects of different medicinal components of APL on the proliferation of human liver cancer HepG2 cells, human gastric cancer HGC-27 cells, and human colon cancer Caco-2 cells. The results showed that the proliferation of HepG2, HGC-27, and Caco-2 cells was strongly inhibited by the APL stem.

Meng Qi [71] et al. used a mouse H22 tumor model to observe the effect of APL on tumor growth. The results showed that the tumor inhibition rate of APL was 51.3%, which met the screening criteria for anti-tumor activity and confirmed its exact anti-tumor effect. The study also showed that its anti-tumor effect was associated with 16 active components of APL, which interfered with the PI3K-Akt signaling pathway, the cancer pathway, proteoglycans in cancer, the NF-kB signaling pathway, and the Jak-STAT signaling pathway, among others. Zhu Yuan [72] suggested that ellagic acid is the main material basis of the anti-tumor effect of APL, which can be divided into APL A, B, C, D, E, and Hexin. The anti-tumor active ingredients of APL induce tumor cell cycle blocking, apoptosis, and enhance immunity against tumor cells. Ryozo Koshiura [73] et al. investigated the effect of the roots of APL on several transplantable rodent tumors, and APL extract significantly prolonged the lifespan of S180- , methyl-A fibrosarcoma and MM-2 mammary carcinoma-bearing mice after intraperitoneal injection. APL extract also inhibited the growth of 5–180 solid-type tumors. These results suggest that the roots of APL contain anti-tumor components and that the mechanism of anti-tumor activity (see Figure 7).

7.4. Antioxidant potential

Xi Liu [74] et al. investigated the antioxidant activity of flavonoid and triterpenoid compounds in APL using three free radical scavenging assays α-diphenyl-β-picrylhydrazyl (DPPH) radical, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical, and hydroxyl radical and a β-carotene-linoleic acid assay for evaluation. The results showed that the flavonoid compound was rich in quercetin and hyperoside, and the triterpenoid compound was rich in 1β, 2β, 3β, 19α-tetrahydroxy-12-en-28-oic acid and corosolic acid; the flavonoid compound showed significant free radical scavenging activity. Liancai Zhu [75] et al. also investigated the antioxidant activity of the water extract of APL by assessing the free radical scavenging and anti-lipid peroxidation capacity. It was found that the water extract of APL showed moderate antioxidant activity to scavenge free radicals, indicating that APL has good antioxidant activity.

Cheng Yangang [76] et al. extracted the total flavonoids from APL and evaluated their antioxidant activity. The results showed that the antioxidant activity of the total flavonoids increased with the increase in mass concentration, resulting in a strong antioxidant capacity.

Dae-Sik Hah [77] et al. evaluated the antioxidant activity of APL leaves on non-lipid oxidative damage. Studies investigating the antioxidant activity of methanol extracts from APL leaves against non-lipid oxidation, including liposome oxidation, deoxyribose oxidation, protein oxidation, chelating activity against metal ions, scavenging activity against hydrogen peroxide, scavenging activity against hydroxyl radicals, and 2′-deoxyguanosine oxidation, demonstrated significant effects. It was concluded that the methanolic extract of APL leaves is effective in protecting non-lipids from various oxidative model systems; thus, APL has antioxidant activity.

7.5. Analgesic potential

Soo-Hyun Park [78] et al. measured the analgesic effect of APL by tail-flick and hot plate tests and showed that oral administration of APL extract (200 mg/kg) reduced the number of twists in the acetic acid-induced twist test, in addition to reducing the cumulative nociceptive response time, showing an analgesic effect. The results suggest that the analgesic effect of APL extract may be mediated by α2-adrenergic receptors.

Meng Qingting [79] et al. used acetic acid to induce twisting in mice, xylene to induce ear swelling, and histamine phosphate to increase capillary permeability to investigate the anti-inflammatory effects of different APL extracts. The results showed that the n-butanol components of APL achieved analgesic effects by inhibiting acute inflammation.
### Table 4. Pharmacological effects of Agrimonia pilosa Ledeb.

| Pharmacological action | Details | Result | in vitro/in vivo | Ref. |
|------------------------|---------|--------|-----------------|-----|
| **Antioxidant effect**  | APL extract treatment of LPS induced oxidative stress in HepG2 cells | APL extract treatment significantly reduced the level of intracellular reactive oxygen species induced by LPS, and the phenolic compounds in APL extract had antioxidant activity | in vitro | [97] |
|                        | assessed inhibitory effect of APL-E on expression of melanogenic enzyme proteins including tyrosinase, tyrosinase-related protein 1 and tyrosinase-related protein 2 in B16BL6 cells, at the same time, the inhibitory effect of APL on free radical was determined by measuring DPH and hydroxyl radical scavenging activity. | APL water extract effectively inhibited free radical generation, in DPHH and hydroxy radical scavenging activity, Agrimonia pilosa Ledeb water extract had a potent anti-oxidant activity in a dose-dependent manner. | in vitro | [98] |
| **Anti-inflammatory effects** | The effect of APL extracted with 80% ethanol on induced nitric oxide synthase and raw 264.7 cells in macrophage line was observed | the various solvent extracts of APL, n-butanol fraction showed the most powerful inhibitory ability against nitric oxide (NO) production in LPS-induced RAW 264.7 cells without affecting cell viability. | in vitro | [99] |
|                        | Using Raw 264.7 murine macrophages the effects of methanol extract of APL in LPS-induced production of inflammatory mediators were measured. | APL attenuated the production of inflammatory mediators such as NO, PGE2 and pro-inflammatory cytokines in LPS -induced Raw 264.7 cells. | in vitro | [100] |
|                        | The anti-inflammatory mechanism of tiliroside was examined using LPS -activated RAW 264.7 macrophage cells. | Tiliroside significantly downregulated the elevated expression levels of iNOS and COX-2 induced by lipopolysaccharide, the phosphorylation of JNK and p38 proteins were also significantly inhibited. | in vitro | [101] |
|                        | APL (100<sub>±</sub>500mg/kg) evaluated the effects of the water extract of APL using HCl/EtOH-induced gastritis rat models, the rats in each group were orally administered with two doses of APL (100 and 500 mg/kg). | The treatment with 500 mg/kg APL reduced the gastric ulcer area, prevented a decreased in PGE2 concentration induced by HCl/EtOH in rats, could be used to prevent the gastritis caused by the HCl/EtOH-induced damage to stomach lining. | in vitro | [102] |
|                        | Anti-inflammatory activity of agrimoniolutein isolated from APL was evaluated using LPS stimulated RAW 264.7 cell models. | The pre-treatment with agrimoniolutein significantly reduced the levels of pro-inflammatory cytokines (IL-1β, IL-6, and TNF-α), as well as attenuated the expression of iNOS and COX-2 in LPS-stimulated macrophages. | in vitro | [103] |
|                        | The effect of 80% ethanol extract of APL on NO release and ROS production, which play a key role in inflammatory and immune responses. | APL n-butanol extract displayed the most potent anti-inflammatory effects based on in vitro assay. The extract also significantly reduced nitric oxide in LPS-activated RAW 264.7 macrophage cells (p < 0.05), and suppressed the nitric oxide synthase (iNOS) expression. | in vitro | [104] |
|                        | To study the inhibitory effect of APL extract on the expression of Pro-inflammatory cytokine-related genes and protein altered by LPS examine the anti-inflammatory effects of APL root extracts in Porphyromonas gingivalis LPS-induced RAW 264.7 cells. | APL extract treatment significantly reduced the gene level of proinflammatory cytokines | in vitro | [105] |
|                        | APL was extracted by 30% ethanol Raw264.7 cells were treated with APL was extracted by 30% ethanol extract at different concentrations for 30 min and then stimulated with lipopolysaccharide (1μg/ml) or without for indicated times.Cel viability was measured by MTT assay, and nitric oxide production was measured by Griess assay. The expression of inflammatory mediators, iNOS and COX-2 and inflammatory cytokines, TNF-α, IL-1β, and IL-6 was detected by RT-PCR, and the phosphorylation of ERK1/2, p38 and JNK MAP kinases was analyzed by Western blot.Also, the expression of NF-κB in nuclear and cytosol was detected by Western blot. | APL root extracts suppressed nitrite concentrations, pro-inflammatory cytokines such as IL-1β, IL-6 and TNF-α in P. gingivalis LPS induced RAW 264.7 cells. APL root extracts has anti-inflammatory effects in P. gingivalis LPS induced RAW 264.7 cells. | in vitro | [106] |
|                        | Anti-cancer effect | To observe that APL hinders cell cycle progression in prostate cancer and lung cancer cells in G0 stage | It was determined that the most effective herb was APL and further established that agrimol B was a novel compound that possessed anti-cancer properties of APL. | in vitro | [108] |
|                        | different concentrations of APL aqueous extract and 5-FU culture solution were added to human hepatocellular carcinoma HepG2 cells to study the effects on proliferation and apoptosis. | the aqueous extract of APL induced apoptosis by up-regulating the gene expression of Bax and the protein expression of Caspase-3 to promote HepG2 apoptosis and inhibit its proliferation. | in vitro | [67] |
|                        | detected the proliferation inhibition effect of APL aqueous extract on pancreatic cancer cells BXPC-3 and PANC-1 by SRB assay. The effect of APL aqueous extract on the cycle distribution of BXPC-3 pancreatic cancer cells was detected by flow cytometry. | the aqueous extract of APL significantly inhibited the proliferation of BXPC-3 and PANC-1 cells in a time- and concentration-dependent manner. Annexin V-FITC/PI double staining assay was used to detect the effect of APL aqueous extract on the apoptosis of BXPC-3 cells. The aqueous extract of APL inhibited the proliferation of pancreatic cancer cells by inducing apoptosis of BXPC-3 and PANC-1 apoptosis, inhibit the proliferation of pancreatic cancer cells, and play an anti-pancreatic cancer role. | in vitro | [69] |
|                        | APL water extract effectively inhibited free radical generation, in DPHH and hydroxy radical scavenging activity, Agrimonia pilosa Ledeb water extract had a potent anti-oxidant activity in a dose-dependent manner. | APL significantly prolonged the life span of S180-, Meth A fibrosarcoma and MM-2 mammary carcinoma-bearing mice by intraperitoneal pre- or postmedication. Also, inhibited the growth of 5-180 solid type tumor | in vivo | [110] |
|                        | Anti-tumor effects | The effect of agrimoinin, a tannin contained in APL, on ascites type and solid type rodent tumors was investigated. | Agrimoinin almost completely rejected the tumor growth in the mice also inhibited the growth of MH1 34 and Meth-A solid type tumors. | in vivo | [109] |
|                        | the effects of the methanol extract from roots of the APL on several transplantable rodent tumors caused by cyclophosphamide were investigated | APL significantly prolonged the life span of S180-, Meth A fibrosarcoma and MM-2 mammary carcinoma-bearing mice by intraperitoneal pre- or postmedication. Also, inhibited the growth of 5-180 solid type tumor | in vivo | [110] |
|                        | Each extract was given intraperitoneally to mice once at 4d before the intraperitoneal inoculation of mouse mammary carcinoma MM2 cells, various extracts from the roots of APL. | non-sugar fractions with median polarity showed antitumor activity, Agrimoinin itself showed antitumor activity when given | in vitro | [111] |
Analgesic effects APL extract administered orally (200 mg/kg) showed an anti-inflammatory effect as measured by the tail-flick and hot-plate tests. APL extract attenuated the writhing numbers in the acetic acid-induced writhing test, furthermore, the cumulative nociceptive response time for intrathecal (L5) injection of substance P (0.7 μg) was diminished by APL extract. APL extract shows an anti-inflammatory property in various pain models.

Inhibitory effect of Agrimonia pilosa on in vitro-cultured S180 cell proliferation was measured by MTT assay. The inhibition rate gradually increases with the increase of extract concentration and the extension of time, with IC50 175.64, 90.59, and 71.74 μg/ml at 24 h, 4 h, and 72 h respectively indicating that the water extract of Agrimonia pilosa has inhibitory effect on S180 tumor cells.

Inhibitory effect of Agrimonia pilosa on gastric mucosal injury was evaluated. APL100, APL150 inhibited tumor growth after medicine injected. APL did not only induced caspase-dependent apoptosis in LLC-bearing mouse tumor. In APL100, it was decreased 72% in CYP3A11. In APL150, it were decreased 62%, 75% in CYP3A11 and MRP1a respectively.

Preventive and therapeutic effects of APL on gastric mucosal injury were observed. The n-butanol and ethyl acetate extracts of Agrimonia may be the main effective parts of its anti-fatigue.

Other pharmacological effects EM mice in the experiment were regularly trained in batches for 2 weeks. The n-butanol and ethyl acetate extracts of Agrimonia may be the main effective parts of its anti-fatigue.

7.6. Other pharmacological potential

Studies have shown that APL has gastroprotective effects. Zeng Xinping [80] found that APL reduces the area of gastric mucosal damage and maintains gastric mucosal integrity by increasing the expression of tight junction proteins (Claudin-1, Occludin, ZO-1), adhesion junction proteins (E-cadherin, α-catenin), and the transcription factor SOX2. APL also has anti-coagulant effects. Tian Lulu [81] et al. found that APL stems and leaves have a strong ability to reduce plasma prothrombin levels in mice. Moreover, APL is known to have anti-glycemic effects. Huang Shuangshuang [82] et al. found that high doses of APL and metformin hydrochloride lowered the blood glucose of streptozotocin-induced diabetic mice. APL also has anti-fatigue effects. Kang Linzhi [83] et al. found that APL n-butanol and ethyl acetate extract combated exercise fatigue by...
interfering with the body's energy metabolism and protecting hypoxic tissues. Table 4 lists the pharmacological effects of APL.

8. Toxicology

At present, there are relatively few studies on the toxicology of APL. The Compound Agrimonia Enteritis Capsule, which is based on APL, is used for treating acute and unpleasant diarrhea caused by spleen deficiency and damp heat, loose stools and diarrhea, malnutrition and tiredness, abdominal distension and abdominal pain, and acute and chronic enteritis. It has been clinically observed that the drug has a rapid effect on the above symptoms without adverse reactions. Lu Ying [84] et al. used an acute toxicity test and mouse bone marrow micronucleus test to systematically evaluate the safety of APL. The results showed that APL is a nontoxic substance and has no chromosomal aberration effect under the test conditions. Therefore, APL is tentatively deemed a relatively safe Chinese medicine.

9. Discussion

This review systematically summarizes and organizes the botany, chemical composition, extraction methods, pharmacology, toxicology, and traditional uses of APL to lay a foundation for future research on APL. Although APL preparations have been used in both traditional and local medicine to treat various diseases, only anti-inflammatory, anti-cancer, anti-tumor, and analgesic properties are supported by pharmacological studies. There is also no clinical evidence suitable to elucidate the effects of APL in its traditional uses. Comprehensive and systematic preclinical studies and clinical trials are needed. The pure compounds Agrimol B and Agrimonin of APL have in vitro anticancer and antitumor activity, which inhibits the growth of cancer and tumor cells. The oral bioavailability of Agrimol B is 3.01, and the oral bioavailability of Agrimonin is 19.38. In addition, there is no literature support for integrate the data on activity of extracts and pure compounds. Further trials are needed to combine the activity data of the extracts and pure compounds of APL with traditional use and the data on the chemistry.

A total of 252 APL compounds were collected in this review. These mainly included flavonoids, volatile oils, phenols, pentacyclic triterpenes, isocoumarins, lignans, organic acids, m-benzotriols, and tannins, most of which are flavonoids or phenols. They have a wide range of activities that may contribute directly or indirectly to the pharmacological effects of APL. However, only a few compounds have been studied for their pharmacological activity. Most of the pharmacological studies were performed in vitro. The chemical characterization of extracts and active fractions of APL plants using modern instrumental analysis has only rarely been performed in pharmacological studies. Identification of the components in the extracts and active fractions is necessary to assess the mechanism of action, quality control, and clinical application.

There are several problems in APL scientific research; we here summarize several topics that should be prioritized in a detailed investigation. First, flavonoids are the main bioactive compounds in APL plants and exhibit a wide range of pharmacological activities. However, the study of other compounds such as volatile oils, phenolics, pentacyclic triterpenes, isocoumarins, lignans, organic acids, m-triols, and tannins isolated from APL has been neglected, which severely limits the limits the range of APL research and applications. Second, so far, most studies on the pharmacological activities of APL have assessed single components such as flavonoids and phenols, while the pharmacological activities of the plant such as antitumor, antioxidant, and anti-inflammatory properties have only been available in animal experiments and in vitro studies without clinical trial support. More time should be devoted to systematic clinical trial studies of APL. Third, there have not been enough toxicological and pharmacokinetic studies. Although APL is traditionally considered a safe herbal drug, its safety in clinical applications still requires evidence for factors such as common adverse reactions and unsuitable populations. These should be the focus of future studies. Studies on toxicity are necessary. Fourth, most APL prescriptions are empirical and lack strict clinical observations, uniform diagnoses, and treatment criteria. Systematic and standardized clinical studies of APL should be conducted in the future to expand research on the pathogenesis of APL.

In conclusion, APL is a valuable medicinal resource with a wide range of pharmacological effects, as shown in experimental studies; however, a more comprehensive study of its mechanism of action, pharmacokinetics, toxicity, and clinical trials is essential to establishing its safety. We also hope to discover new structures and new active molecules from APL plants and provide comprehensive information on the chemical composition, biological effects, and clinical applications of the APL plant to facilitate further usage of the plant and drug discovery.

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Additional information

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