



Review article

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

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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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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, lignans, 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 database 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, phytochemistry, 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, phytochemical, 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 phytochemical 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 lumbago 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

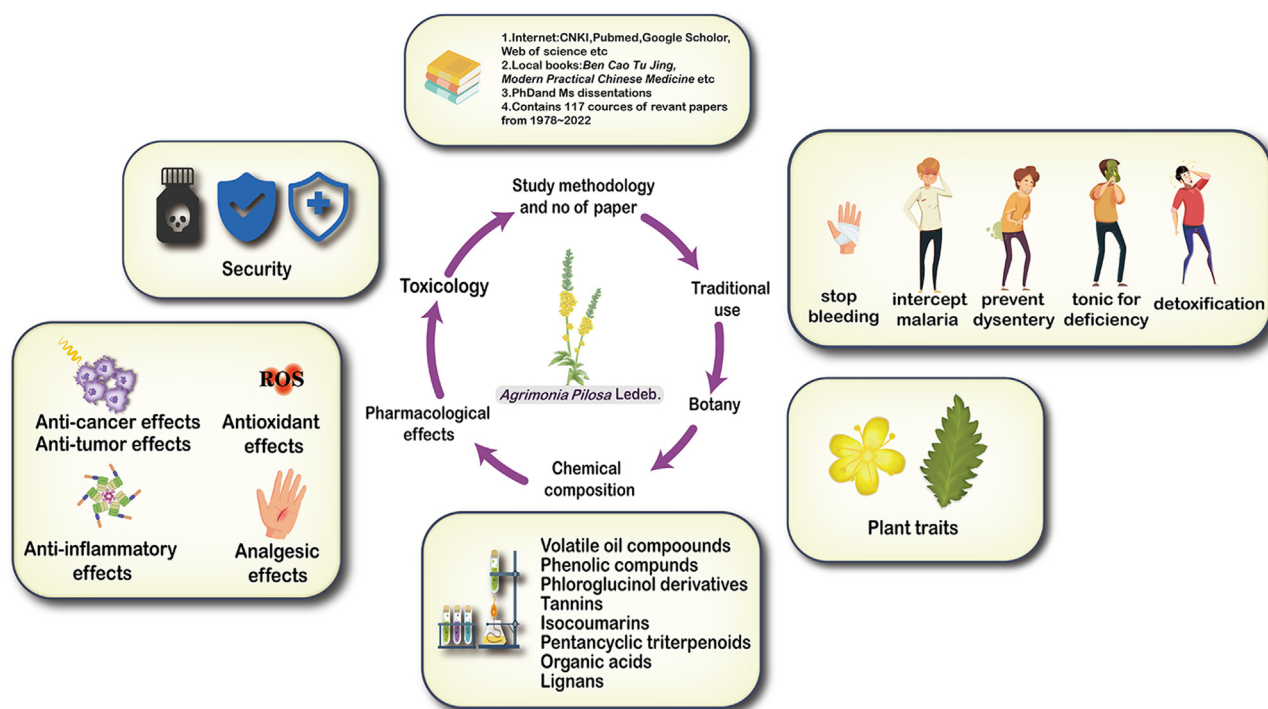


Figure 1. Flow chart.

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 barbs at the tip, connivent, spreading or reflexed after flowering; sepals 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. Achenes 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 sparsely 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 barbs at the tip and a deeper longitudinal groove outside, Flowering June–July. This plant strongly resembles the head of a red-crowned crane, hence the name *Xianhecao* (see Figure 2 A B C).

Some studies have examined the raw and microscopic characteristics of APL using a powder-filming method and a physicochemical identification method. The results showed that APL is a dry whole grass with a woody stem base, light brown to purple-red, 4–6 mm in diameter, smooth and glabrous, with distinct stem nodes, and is sparse above and dense below, sometimes with remnant stipules (see Figure 2 D). Moreover, the upper stem is greenish-brown, yellowish-brown, covered with white pilose, with gray-green, crinkled, and curled leaves and occasional flowering or fruiting branches have a slight odor and tastes slightly bitter and astringent. Good quality APL has purple-red stems, tender branches, and intact leaves. Microscopic observations of APL has purple-red stems, tender branches, and intact leaves. Microscopic observations of APL have shown that the powder of the above-ground unwooded part of APL is dark green with polygonal upper epidermal cells, while the lower epidermal cell walls are undulatory curved and the stomata are indeterminate or unequal. APL also has non-glandular single cells, which are variable in length, thick-walled, lignified, and with warty projections have a spiral shape. with small glandular hairs 1- to 4-celled at the head, an ovoid, stalk 1- to 2-celled, a few other glandular scales with head single cell, up to 68 μm in diameter, containing oil droplets, and with a unicellular stalk. Calcium oxalate cluster crystals are common, which range from 9 to 50 μm in diameter. Physicochemical identification of APL

has shown that APL extract reacts with 5% vanillin concentrated sulfuric acid solution to form a reddish-brown ring at the interface; it reacts with 3% ferric chloride test solution to form a dirty green color; and it reacts with magnesium powder and concentrated hydrochloric acid to form a cherry red color [7].

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-glucuronide (3), Quercitrin (4), Apigenin-7-O-glucoside (5), Apigenin-7-O-glucuronide (6), Vitexin (7), Isovitexin (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-methylglutaryl (1 \rightarrow 6)]- β -D-Glucoside (12), Trlrioxide (13), Catechin (14), Hyperoside (15), Quercetin (16), 3-methoxy quercetin (17), Apigenin-7-O- β -D-glucuronide-600-methylester (18), Quercetin-7-O- β -D-glycoside (19), Quercetin-3-O- β -D-glycoside (20), Kaempferol (21), Kaempferol-3-O- α -L-rhamnoside (22), Isoquercitrin (23), Kaempferide (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-O-acetyl)-D-glucopyranoside (31), Luteolin (32), Luteolin-7-O- β -D-glucopyranoside (33), Wogonin (34), (+)-Catechin (35), Pilosanol A (36), Pilosanol B (37), Pilosanol C (38), (2R,3R)-(+)-Taxifolin (39), (2R,3R)-(-)-Taxifolin-3-O- β -D-glucopyranoside (40), (2S,3S)-(-)-Taxifolin (41), Dehydrodicatichin A (42), Kaempferol-3-O-rutinoside (43), 3-O-kaempferol 2,3-di-O-acetyl-4-O-(cis-p-coumaroyl)-6-O-(trans-p-coumaroyl)- β -D-glucosopyranoside (44), Quercetin-3-O- α -arabinofuranosyl- β -D-galactopyranoside (45), Kaempferol-3-glycoside (46), Catechin (47), (2S,3S)-(-)-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 volatile oil from APL are ketones, alcohols, acids, esters, and many hydrocarbon compounds. Quantitative analysis of volatile APL oil found that it is predominantly comprised of alcohols. There are 127 kinds of volatile oil compounds, including 3-Hydroxybutyric Acid (50), 6-diacetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-Dibenzofurandione9bh)-dibenzofurandione (51), 2,6-Di-tert-butylphenol (52), 2,5-Dimethyl-3-butylpyrazine (53), Lauric acid (54), Nerolidol (55), 1-Dodecatriene methyl ether (56), 1,1-dimethoxyhexadecane (57), Decahydro-1,1,7-trimethyl-1-hydro-cyclopropyl-4-methylene-7-ol (58), 4-Methyl-2-tert-octylphenol (59), 1,2,3,5,6,8-hexahydroxynaphthalene (60), Hornitol (61), α -Myrrholol (62), Pentatriacontane (63), 3,7,11-Trimethyl-2,6,10-dodecatrien-1-ol (64), 7-Tetradecene (65), Thi-(2-aminoethyl) thiosulfate (66), Heptacosane (67), Tetratriacontane (68), 1-Vinyloxyhexadecane (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 -Transocimene (78), α -Campholenal (79), Camphor (80), Borneol (81), 4-terpineol (82), α -Terpineol (83), Pulegone (84), 1-(2-Furyl)-1-hexanone (85), Bergamot oil (86), 2-Methyl-4-hydroxyacetophenone (87), Thymol (88), Carvacrol (89), Neryl acetate (90), Eugenol methyl ether

Table 1. The traditional and clinical uses of *Agrimonia pilosa* Ledeb. in China.

Preparation name	Main compositions	Preparation method	Part used	Traditional and clinical uses	References
Fufang Xianhecao Changyan Jiaonang	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]
Fuan Keli	Agrimoniae Herba 80 mg, Polygonum chinense 0.12 g, Acalypha australis L. 0.12 g, Bidenspilosa 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]
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	Nourishing Yin and nourishing Blood, calming the mind and tranquilizing the spirit.	[87]
Ningmitai Jiaonang	Polygonum capitatum 450 g, Imperatae Rhizoma 263 g, Cocculus orbiculatus (L.) DC. 224 g, Berberidis Radix 169 g, Agrimoniae Herba 169 g, Hibisci Mutabilis Folium 18g, Forsythiae Fructus 226 g	Water decocting	Whole grass	Clearing heat and detoxifying toxins, relieving dampness and promoting diuresis	[87]
Milingqing Jiaonang	Polygonum capitatum 420 g, Phellodendri Chinensis Cortex 300 g, Oxalis 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 diuresis	[87]
Changchun Hongyao Jiaonang	Notoginseng Radix Et Rhizoma 121.2 g, Aconiti Kusnezoffii Radix 12.12 g, Aconiti Radix Cocta 12.12 g, Nelumbinis Plumula 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, Cirsii Herba 6.7 g, Olibanum 20.2 g, Myrrha 20.2 g, Agrimoniae Herba 60.6 g, Borneolum Syntheticum 24.2 g, Carthami Flos 40.4 g, Chrysanthemi Flos 40.4 g, Gardeniae Fructus 40.4 g, Paridis Rhizoma 13.5 g, Cinnabaris 12.1 g, Corydalis Rhizoma 20.2 g	Water decocting	Whole grass	Promoting blood circulation and removing blood stasis, relieving swelling and pain.	[87]
Xianchan Pian	Strychni Semen Pulveratum 50 g, Bufonis Venenum 10 g, Psoraleae Fructus 165 g, Pinelliae Rhizoma 50 g, Curcumae Radix 50 g, Ginseng Radix Et Rhizoma 30 g, Astragali Radix 20 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]
Gongliuxiao Jiaonang	Ostreae Concha 210 g, Cyperi Rhizoma 128 g, Sparganii Rhizoma 64 g, Curcumae Rhizoma 64 g, Eupolyphaga Steleophaga 64 g, Agrimoniae Herba 126 g, Codonopsisradix 64 g, Atractylodis Macrocephalae Rhizoma 64 g, Hedyotis diffusa Willd 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 knots	[87]
Shuangjin Weiyang Jiaonang	Hemsleya Amabilis 42 g, Fagopyri Dibotryis Rhizoma 32 g, Sargentodoxae Caulis 32 g, Callicarpa nudiflora Hook. ex Arn. 21 g, Corydalis Rhizoma 32 g, Agrimoniae Herba 32 g, Bletillae Rhizoma 63 g, Phoenix dress 42 g, Aristolochia debilis Sieb. et Zucc. 32 g, Juglans regia 40 g	Water decocting	Whole grass	Soothing the liver and regulating Qi, strengthening the stomach and relieving pain, astringent and stopping bleeding	[87]
Litemin Jiaonang	Agrimoniae Herba 150 g, Potentillae Discoloris Herba 150 g	Water decocting	Whole grass	Clearing heat and detoxifying, antibacterial and anti-dysentery	[87]
Shengxuexiaoban Jiaonang	Indigo Naturalis 167 g, Forsythiae Fructus 500 g, Agrimoniae Herba 500 g, Moutan Cortex 833 g, Glycyrrhizae 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	Crepisphoenix 360 g, Aralia chinensis L. 360 g, Polygonati Rhizoma 48 g, Gastrodiae Rhizoma 60 g, Notoginseng Radix Et Rhizoma 60 g, Galium spurium L. 240 g, Agrimoniae Herba 360 g	Water decocting	Whole grass	Nourishing the liver and kidney, calming the liver and submerging the yang	[87]
Quyuan Sanjie Jiaonang	Prunellae Spica, Cremastrae Pseudobulbus Pleiones Pseudobulbus, Hedyotis diffusa, Solanum lyratum Thunb., Eupolyphaga Steleophaga, Notoginseng Radix Et Rhizoma, Crataegi Fructus, Agrimoniae Herba, Astragali Radix, Scolopendra, Aurantii 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 Formosanae Folium 320 g, Alumen 10 g, Borneolum 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	Ostreae Concha 667 g, Paeoniae 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]

(continued on next page)

Table 1 (continued)

Preparation name	Main compositions	Preparation method	Part used	Traditional and clinical uses	References
	Notoginseng Radix Et Rhizoma 67 g, Agrimoniae Herba 400 g, Ailanthi Cortex 333 g, Isatidis Folium 333 g				
Xinfuman Ruangao	Hydrocarpus anthelmintica Pierre 20 g, Stemonae Radix 5 g, Cnidii Fructus 2.5 g, Agrimoniae Herba 0.25 g, Angelicae Dahuricae Radix 5 g	Water decocting	Whole grass	Anti-mite and anti-itch	[87]
Yangxue Anshen Wan	Polygoni Multiflori Caulis 150 g, Spatholobi 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, Bidenspilosa L. 480 g, Chenopodium ambrosioides L. 480 g	Water decocting	Whole grass	Clearing heat and removing toxins, drying dampness and stopping dysentery	[89]
Shenlu Bugao	Spatholobi Caulis 160g, Ligustri Lucidi Fructus 120g, Ecliptae Herba 80 g, Agrimoniae Herba 80 g, Rehmanniae Radix Praeparata 80 g, Epimedii Folium 60 g, Cibotii Rhizoma 60 g, Atractylodis 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]
Jianshenpian	Ecliptae Herba 72 g, Spatholobi Caulis 108 g, Rosae Laevigatae Fructus 72 g, Artemisiae Argyi Folium 72 g, Mori 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, Schisandrae Chinensis Fructus 54 g	Water decocting	Whole grass	strengthen the kidney and astringent essence	[89]
Weixuening	Polygoni Cuspidati Rhizoma Et Radix 115 g, Paeoniae Radix Alba 71.8 g, Agrimoniae Herba 143.8 g, Rehmanniae Radix 115 g, Spatholobi Caulis 143.8 g, Rehmanniae Radix Praeparata 115 g, Ecliptae Herba 43.2 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]
Dafeicao	Armeniacae Semen Amarum 12 g, Ephedrae Herba 12 g, Terminalia chebula Retz. 12 g, Gardeniae Fructus 12 g, indigo naturalis 12 g, bletillae rhizoma 12 g, phytolaccae radix 12 g, Pumex 12 g, Meretricis Concha Cyclinae Concha 12 g, Agrimoniae Herba 90 g, Ardisiae Japonicae Herba 150 g, Stemonae 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, Adenophorae Radix 90 g, Rehmanniae Radix 90 g, Polygoni Multiflori Radix Praeparata 60 g, Atractylodis Macrocephalae Rhizoma Angelicae 90 g, Sinensis Radix 90 g, Paeoniae Radix Alba 60 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 Fructus 15 g, Acori Tatarinowii Rhizoma 30 g, Triticum aestivum L. 150 g, Glycyrrhizae Radix Et Rhizoma 15 g, Ostreae Concha 150 g, Ostreae Concha 150 g, Citri Reticulatae Pericarpium 45 g, Polygalae Radix 45 g, Jujubae Fructus 300 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, Epimedii Folium 35 g, Acori Tatarinowii Rhizoma 15 g, Ginseng Radix Et Rhizoma Rubra 12.5 g, Angelicae Sinensis Radix 12.5 g, Pheretima 10 g, Notoginseng Radix Et Rhizoma 10 g, Carthami Flos 10 g, Stephaniae Tetrandrae Radix 10 g, Paeoniae Radix Rubra 10 g, Persicae Semen 10 g, Haliotidis Concha 10 g, Gastrodiae Rhizoma 10 g, Agrimoniae Herba 10 g, Sophorae Flos 10 g, Atractylodis Macrocephalae Rhizoma 10 g, Arisaema Cum Bile 10 g, Puerariae Lobatae Radix 10 g, Scrophulariae Radix 10 g, Coptidis Rhizoma 10 g, Forsythiae Fructus 10 g, Alismatis Rhizoma 10 g, Chuanxiong Rhizoma 10 g, Lycii Fructus 10 g, Scorpio 2.5 g, Polygoni Multiflori Radix Praeparata 15 g, Cassiae Semen 10 g, Aquilariae Lignum Resinatum 5 g, Typhonii Rhizoma 5 g, Asari Radix Et Rhizoma 5 g, Aucklandiae Radix 5 g, Bombyx Batryticatus 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, Atractylodis Macrocephalae Rhizoma 100 g, Ligustri Lucidi Fructus 100 g, Albiziae Cortex	Water decocting	Whole grass	invigorate blood circulation and calm the mind	[89]

(continued on next page)

Table 1 (continued)

Preparation name	Main compositions	Preparation method	Part used	Traditional and clinical uses	References
	150 g, Polygoni Multiflori Caulis 150 g, Agrimoniae Herba 250 g, Ecliptae Herba 100 g, Glycyrrhizae Radix Et Rhizoma 50 g				
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	[89]
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	[89]
Liteminjian	Agrimoniae Herba 150 g, Potentillae Discoloris Herba 150 g	Alcohol extraction	Whole grass	Clearing heat and detoxifying, antibacterial and anti-dysentery	[89]
Xuebao Jiaonang	Rehmanniae Radix Praeparata 62 g, Angelicae Sinensis Radix 46 g, Rhapontici Radix 61 g, Salviae Miltiorrhizae 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, Chuanxiong Rhizoma 15 g, Polygoni Cuspidati Rhizoma Et Radix 31 g, Rumex patientia L. 46 g, Forsythiae Fructus 30 g, Paeoniae Radix Rubra 16 g, Psoraleae Fructus 30 g, Polygoni Multiflori Radix Praeparata 47 g, Astragali Radix 46 g, Acanthopanax Senticosi Radix Et Rhizoma Seu Caulis 76 g, Cervi Cornu Pantotrichum 3.5 g, Placenta Hominis 31 g, Ligustri Lucidi Fructus 46 g, Moutan Cortex 18 g, Cibotii Rhizoma 15 g, Asini Corii Colla 15 g, Atractylodis Macrocephalae Rhizoma 31 g, Citri Reticulatae Pericarpium 15 g, Ginseng Radix Et Rhizoma 15.5 g, Bubali Cornu 18.5 g, Ox spinal cord 4.5 g	Water decocting	Whole grass	Tonifying Yin and cultivating Yang, benefiting the kidney and strengthening the spleen	[89]
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	[89]
Zhichuang Zhixue Wan	Sophorae Flos 100 g, Schizonepetae Herba 100 g, Citri Reticulatae Pericarpium 100 g, Platycladi Cacumen 100 g, Sanguisorbae Radix 100 g, Agrimoniae Herba 100 g	Crushing and honey addition	Whole grass	Clearing damp-heat from intestinal wind, cooling the blood and stopping bleeding	[89]
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 100 g, Agrimoniae Herba 150 g, Isatidis Radix 100 g, Taraxaci Herba 150 g, Curcumae Longae Rhizoma 100 g	Water decocting	Whole grass	Clearing heat and removing gall bladder, regulating Qi and relieving pain	[89]
Kuiyang Jiaonang	Arcae Concha 32 g, eggshell 48 g, Citri Reticulatae Pericarpium 16 g, Alumen 32 g, Polygoni Orientalis Fructus 32 g, Margarita 0.5 g, Agrimoniae Herba 112 g	Water decocting	Whole grass	Stopping acidity and pain, producing muscle and astringency	[89]
Zaizhang Shengxue Pian	Cuscutae Semen, Ginseng Radix Et Rhizoma Rubra, Spatholobi Caulis, Asini Corii Colla, Angelicae Sinensis Radix, Ligustri Lucidi Fructus, Astragali Radix, Leonur Iherba, Rehmanniae Radix Praeparata, Paeoniae Radix Albapaeoniae Radix Alba, Polygoni Multiflori Radix Praeparata, Epimedii Folium, Polygonati 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	[89]
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 Fructus 15 g, Acori Tatarinowii Rhizoma 30 g, Triticum aestivum L 150 g, Glycyrrhizae 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	[89]

(continued on next page)

Table 1 (continued)

Preparation name	Main compositions	Preparation method	Part used	Traditional and clinical uses	References
	Reticulatae Pericarpium 45 g, Polygalae Radix 45 g, Jujubae Fructus 300 g				
Yuyejin Wan	Eucommiae Cortex, Rehmanniae Radix, Scutellariae Radix, Astragali Complanati Semen, Angelicae Sinensis Radix, Artemisiae Argyi Folium, Nelumbinis Semen, Dioscoreae Rhizoma, Cistanches Herba, Amomi Fructus, Polygalae Radixglycyrrhizae Radix Et Rhizoma, Crataegi Fructus, Leonur Iherba, Glycyrrhizae Radix Et Rhizoma, Paeoniae Radix Alba, Notopterygii Rhizoma Et Radix, Ophiopogonis Radix, Fritillariae Thunbergii Bulbus, Salviae Miltiorrhizae Radix Et Rhizoma, Crinis Carbonisatus, Cuscutae Semen, Dipsaci Radix, Aurantii Fructus, Amomi Fructus Rotundus, Cyperi Rhizoma, Chuanxiong Rhizoma, Pinelliae Rhizoma, Poria, Farfarae Flos, Inula japonica Thunb., Piperislongifrutus, Codonopsisradix, Toosendan Fructus, Gardeniae Fructus, Coptidis Rhizoma, Astragali Radix, Atractylodis Macrocephalae Rhizoma, Croci Stigma, Magnoliae Officinalis Cortex, Amber, Cinnamomi Cortex, Ginseng Radix Et Rhizoma, Jujubae Fructus, Corni Fructus, Cervi Cornus Colla, Rubi Fructus, Mantidis Oothea, Galla Chinensis, Morindae Officinalis Radixglycyrrhizae Radix Et Rhizoma, Spatholobi Caulis, Agrimoniae Herba, Testudinis Carapacis Et Platri Colla, Sepiae Endoconcha, Ecliptae Herba, Rosae Chinensis Flos, Asini Corii Colla	Crushing and mixing	Whole grass	Benefiting Qi, soothing the liver, regulating menstruation and stopping dysmenorrhea.	[89]
Xianhe Jiaonang	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 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, Epimedii Folium 75 g, Cibotii Rhizoma 75 g, Ecliptae Herba 100 g, Polygonati Odorati Rhizoma 25 g, Ligustri Lucidi Fructus 151 g, Rehmanniae Radix Praeparata 100 g, Cynomorii Herba 51 g, Dipsaci Radix 50 g, Atractylodis Macrocephalae Rhizoma 75 g, Agrimoniae Herba 100 g, Codonopsisradix 50 g, Spatholobi Caulis 201 g	Water decocting	Whole grass	Benefiting Qi and nourishing blood, tonifying the kidney and strengthening Yang	[89]
Fuyanling Jiaonang	Callicarpae Formosanae Folium, Sophorae Flavescens Radix, Camphor, Agrimoniae Herba, Alumen, Stemonae Radix, Borneolum Syntheticum, Cnidii Fructus, Benzalkonium Bromide	Water decocting	Whole grass	Clearing heat and drying dampness, killing worms and relieving itching	[89]
Fufang Tiexian Zhixue Fen	Acalypha australis L. 100 g, Psoraleae Fructu 100 g, Euphorbiae Humifusae Herba 100 g, Agrimoniae Herba 100 g, Petiolus Trachycarpi 100 g, Bletillae Rhizoma 900 g, Gelatin 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, Margarita 90 g, Cyperi Rhizoma 180 g, Five-finger fig 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	onopsisradix 125 g, Glehniae Radix 100 g, Ophiopogonis Radix 75 g, Agrimoniae Herba 125 g, Bistortae Rhizoma 100 g, Patrinia villosa 83 g, Hedyotis diffusa 167 g, Fritillariae Cirrhosae Bulbus 75 g, Asteris Radix Et Rhizoma 75 g, Platycodonis Radix 75 g, Armeniaca 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, Faeces Trogopterori 45 g, Alumen 54 g, Natrii Sulfas 54 g, Toxicodendri Resina 18 g, Aurantii Fructus 90 g, Strychni Semen Pulveratum 36 g	Water decocting	Whole grass	Promoting blood circulation and resolving blood stasis, dispersing nodules and subduing swelling, detoxifying and relieving pain	[85]
Pingxiao Jiaonang	Curcumae Radix 54 g, Agrimoniae Herba 54 g, Faeces Trogopterori 45 g, Alumen 54 g, Natrii Sulfas 54 g, Toxicodendri Resina 18 g, Aurantii Fructus 90 g, Strychni Semen Pulveratum 36 g	Water decocting	Whole grass	Promoting blood circulation and resolving blood stasis, dispersing nodules and subduing swelling, detoxifying and relieving pain	[85]
Pingxiao Jiaonang	Curcumae Radix 54 g, Agrimoniae Herba 54 g, Faeces Trogopterori 45 g, Alumen 54 g, Natrii Sulfas 54 g,	Water decocting	Whole grass	Promoting blood circulation and resolving blood stasis, dispersing nodules and subduing swelling, detoxifying and relieving pain	[85]

(continued on next page)

Table 1 (continued)

Preparation name	Main compositions	Preparation method	Part used	Traditional and clinical uses	References
	Toxicodendri Resina 18 g, Aurantii Fructus 90 g, Strychni Semen Pulveratum 36 g				
Weixuening Heji	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	Astragali Radix 162.2 g, Epimedii 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 Tetrandrae Radix 27 g, Paeoniae Radix Rubra 27 g, Persicae Semen 27 g, Haliotidis Concha 27 g, Gastrodiae Rhizoma 27 g, Agrimoniae Herba 27 g, Sophorae Flos 27 g, Atractylodis Macrocephalae Rhizoma 27 g, Arisaema Cum Bile 27 g, Puerariae 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 Resinatum 13.5 g, Typhonii Rhizoma 13.5 g, Asari Radix Et Rhizoma 13.5 g, Aucklandiae Radix 13.5 g, Bombyx Batryticatus 6.8 g, Gleditsiae Fructus Abnormalis 13.5 g, Borneolum Syntheticum 13.5 g, Margarita 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]
Baicao Fuyan Qingshuan	Sophorae Flavescens Radix 640 g, Stemonae Radix 320 g, Cnidii Fructus 320 g, Agrimoniae Herba 320 g, Callicarpae Formosanae Folium 320 g, Alumen 10 g, Borneolum Syntheticum 5 g, Camphor 10 g, Boric Acid 60 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 Pian	Angelicae Sinensis Radix, Leonur Iherba, Ligustri Lucidi Fructus, Ecliptae Herba, Notoginseng Radix Et Rhizoma, Salviae Miltiorrhizae Radix Et Rhizoma, Agrimoniae Herba, Cyperi Rhizoma, Typhae Pollen, Platycladi Cacumen, Codonopsisradix, Atractylodis Macrocephalae Rhizoma	Water decocting	Whole grass	Invigorating blood circulation, stopping bleeding and regulating menstruation	[90]
Fuyinkang Xiji	Fraxini Cortex, Isatidis Folium, Houuttuyniae Herba, Sophorae Flavescens Radix, Agrimoniae Herba, Viola Herba	Water decocting	Whole grass	Clearing heat and drying dampness, removing itching and relieving bandages	[91]
Gongning Keli	Rubiae Radix Et Rhizoma 195 g, Typhae Pollen 156 g, Notoginseng Radix Et Rhizoma 78 g, Sanguisorbae Radix 390 g, Scutellariae Radix 117 g, Rehmanniae Radix 195 g, Agrimoniae Herba 390 g, Sepiae Endoconcha 390 g, Codonopsisradix 234 g, Paeoniae Radix Alba 195 g, Glycyrrhizae Radix Et Rhizoma 78 g	Water decocting	Whole grass	Removing blood stasis and clearing heat, consolidating menstruation and stopping bleeding	[85]
Shilong Qingxue Keli	Haliotidis Concha, Agrimoniae Herba, Ostreae Concha, Achyranthis Bidentatae Radix, Sophorae Flos, Prunellae Spica, Curcumae Rhizoma, keel, Uncariae Ramulus Cum Uncis, Haematitum, 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, Aurantii Fructus Immaturus, Ephedrae Herba, Cinnamomi Ramulus, Rehmanniae Radix Praeparata, Ophiopogonis Radix, Trachelospermi Caulisetfolium, Agrimoniae Herba, Asini Corii Colla, Gastrodiae Rhizoma	Water decocting	Whole grass	Benefiting Qi and nourishing Yin, warming the meridians and opening the veins	[93]
Zaizao Shengxue Jiaonang	Ginseng Radix Et Rhizoma Rubra 25.5 g, Spatholobi Caulis 59.5 g, Asini Corii Colla 25.5 g, Angelicae Sinensis Radix 42.5 g, Ligustri Lucidi Fructus 25.5 g, Astragali 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, Epimedii Folium 25.5 g, Polygonati Rhizoma 34 g, Cervi Cornu Pantotrichum 2.55 g, Codonopsisradix 34 g, Ophiopogonis Radix 25.5 g, Agrimoniae Herba 34 g, Atractylodis Macrocephalae Rhizoma 25.5 g, Psoraleae 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	Astragali Radix, Glehniae Radix, Atractylodis Macrocephalae Rhizoma, Solanum lyratum Thunb., Citri 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]

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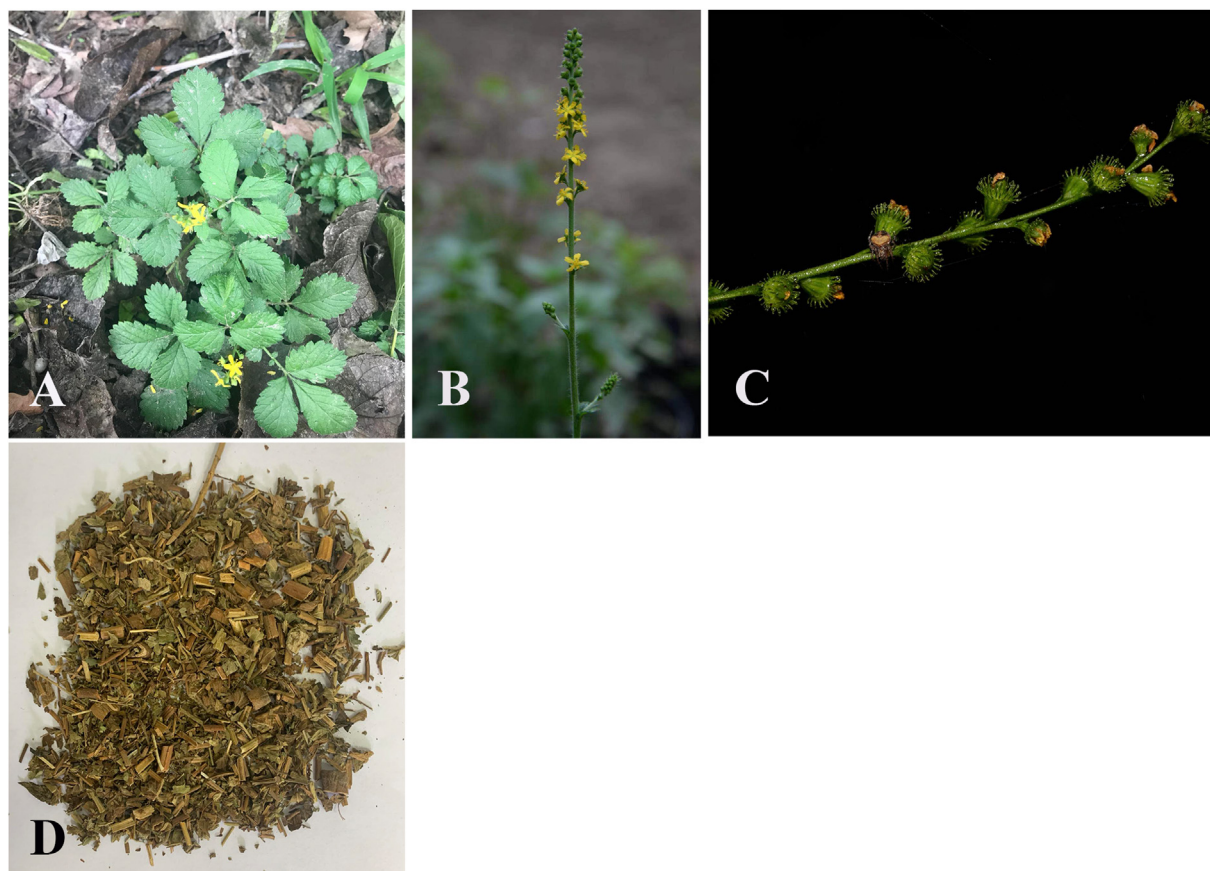
Table 1 (continued)

Preparation name	Main compositions	Preparation method	Part used	Traditional and clinical uses	References
	Dioscoreae Rhizoma, Dexamethasone Acetate, Polygonati Rhizoma, Codonopsisradix, gypenosides, Polygalae Radix, Euryales Semen, Spironolactone				
Fuyanling Shuan	Benzalkonium Bromide, Cnidii Fructus, Alumen, Sophorae Flavescentis Radix, Borneolum Syntheticum, Agrimoniae Herba, Stemonae Radix, Camphor, Callicarpae Formosanae Folium, Boric Acid	Water decocting	Whole grass	Clearing heat and drying dampness, killing worms and relieving itching	[95]
Yiqi Hewei Jiaonang	Glycyrrhizae Radix Et Rhizoma, Agrimoniae Herba, Atractylodis Macrocephalae Rhizoma, Paeoniae Radix Alba, Aurantii Fructus, Scutellariae Radix, Codonopsisradix, Salviae Miltiorrhizae Radix Et Rhizoma, Astragali Radix, Santali Albi Lignum	Water decocting	Whole grass	Strengthening the spleen, harmonizing the stomach, clearing ligaments and relieving pain	[95]
Yiqi Xiaoke 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	Powerdered Buffalo Horn Extract, Atractylodis Macrocephalae Rhizoma, Asini Corii Colla, Cibotii Rhizoma, Moutan Cortex, Ligustri Lucidi Fructus, Placenta Hominis, Cervi Cornu Pantotrichum, Acanthopanax Senticosi Radix Et Rhizoma Seu Caulis, Astragali Radix, Polygoni Multiflori Radix Praeparata, Psoraleae Fructus, Paeoniae Radix Rubra, Forsythiae Fructus, Rumex patientia L., Polygoni Cuspidati Rhizoma Et Radix, Chuanxiong Rhizoma, Agrimoniae Herba, Lycii Fructus, Cinnamomi Ramulus, Aconiti Lateralis Radix Praeparata, Spatholobi 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 g, Caealpinia cucullata 12.2 g, Chimonanthi Radix 12.2 g, Bletillae Rhizoma 12.2 g, Verbenae Herba 12.2 g, Aconiti Kusnezoffii 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, Paeoniae 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, Paeoniae Radix Alba, Sojae Semen Nigrum, Aucklandiae Radix, Lablab Semen Album, Dioscoreae Rhizoma, Agrimoniae Herba, Mahonia, Poria, Schisandrae Chinensis Fructus, Acori Tatarinowii Rhizoma, Triticum aestivum L, Glycyrrhizae Radix Et Rhizoma, Ostreae Concha, Citri Reticulatae Pericarpium, Polygalae Radix, Jujubae Fructus	Water decocting	Whole grass	Benefiting Qi and strengthening the spleen, tonifying the brain and strengthening the body	[86]
Zaizao Shengxue Pian	Ginseng Radix Et Rhizoma Rubra 25.5 g, Spatholobi Caulis 59.5 g, Asini Corii Colla 25.5 g, Angelicae Sinensis Radix 42.5 g, Ligustri Lucidi Fructus 25.5 g, Astragali Radix 42.5 g, Leonur Herba 25.5 g, Rehmanniae Radix Praeparata 42.5 g, Paeoniae Radix Alba 25.5 g, Polygoni Multiflori Radix Praeparata 42.5 g, Epimedii Folium 25.5 g, Polygonati Rhizoma 34 g, Cervi Cornu Pantotrichum 2.55 g, Codonopsisradix 34 g, Ophiopogonis Radix 25.5 g, Agrimoniae Herba 34 g, Atractylodis Macrocephalae Rhizoma 25.5 g, Psoraleae 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]
Longqing Pian	Alismatis Rhizoma 174 g, Plantaginis Semen 35 g, Patrinia villosa 348 g, Lonicerae Japonicae Flos 174 g, Moutan Cortex 174 g, Hedyotis diffusa 348 g, Paeoniae Radix Rubra 174 g, Agrimoniae Herba 174 g, Coptidis Rhizoma 174 g, Phellodendri Chinensis Cortex 174 g	Water decocting	Whole grass	Clearing heat and removing toxins, cooling the blood and promoting draining	[85]
Longqing Jiaonang	Alismatis Rhizoma 261 g, Plantaginis Semen 52.5 g, Patrinia villosa 522 g, Lonicerae Japonicae Flos 261 g, Moutan Cortex 261 g, Hedyotis diffusa 522 g, Paeoniae	Water decocting	Whole grass	Clearing heat and removing toxins, cooling the blood and promoting draining	[85]

(continued on next page)

Table 1 (continued)

Preparation name	Main compositions	Preparation method	Part used	Traditional and clinical uses	References
	Radix Rubra 261 g, Agrimoniae Herba 261 g, Coptidis Rhizoma 261 g, Phellodendri Chinensis Cortex 261 g				

Figure 2. Photograph of *Agrimonia pilosa ledeb.*

(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), Longofolene (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, 8-dihydroxy-3,4-dihydro-2H-naphthalen-1-one (146), 3-xanthoxylin (147), 1,2-benzenedicarboxylic acid bis(2-methylpropyl) ester (148), Palmitic acid (149), Ethyl palmitate (150), 9-butyl-9H-fluoren-9-yl-3,8-dimethyldecane (151), (Z, Z, Z)-9, 12, 15-octadecatrienoic acid (152), Ethyllinoleate (153), (Z,Z,Z)-9,12,15-octadecatrienoic acid, ethyl ester (154), Ethyl stearate (155), bis(2-ethylhexyl) adipate (156), 3-pentadecyl-phenol (157), 3,8-dimethyldecane (158), Geranylinalool (159), (E,E,E,E)-squalene (160), Hentriacontane (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), Pseudoaspidin (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), Pseudoaspidin (195) [15, 30, 31, 32].

Table 2. Chemical compounds isolated from *Agrimonia pilosa* Ledeb.

Classification	No.	Chemical component	Reference
Flavonoids	1	Rutin	[8]
	2	Luteolin-7-O-glucoside	[8]
	3	Luteolin-7-O-glucuronide	[8]
	4	Quercitrin	[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	Agriflavone	[10]
	12	Kaempferol-3-O-[(S)-3-hydroxy-3-methylglutaryl (1→6)]-β-D-Glucoside	[10]
	13	Trlriroside	[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	Isoquercitrin	[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-O-butylglucuronate	[18]
	30	Luteolin-7-O-sophoroside	[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	PilosanolA	[16]
	37	PilosanolB	[16]
	38	PilosanolC	[16]
	39	(2R, 3R)-(+)-Taxifolin	[15]
	40	(2R, 3R)-(+)-Taxifolin-3-O-β-D-glucopyranoside	[16]
	41	(2S, 3S) - (-) -Taxifolin	[20]
	42	Dehydrodicatchin 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-diacetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-Dibenzofurandione9bh-dibenzofurandione	[23]

Table 2 (continued)

Classification	No.	Chemical component	Reference
	52	2,6-Di-tert-butylphenol	[23]
	53	2,5-Dimethyl-3-butylpyrazine	[23]
	54	Lauric acid	[23]
	55	Nerolidol	[23]
	56	1-Dodecatriene methyl ether	[23]
	57	1,1-dimethoxyhexadecane	[23]
	58	Decahydro-1, 1, 7-trimethyl-1-hydro-cyclopropyl-4-methylene-7-ol	[23]
	59	4-Methyl-2-tert-octylphenol	[23]
	60	1, 2, 3, 5, 6, 8α-hexahydroxynaphthalene	[23]
	61	Hornitol	[23]
	62	α-Myrrholol	[23]
	63	Pentatriacontane	[23]
	64	3,7,11-Trimethyl-2,6,10-dodecatrien-1-ol	[23]
	65	7-Tetradecene	[23]
	66	Thi-(2-aminoethyl) thiosulfate	[23]
	67	Heptacosane	[23]
	68	Tetatriacontane	[23]
	69	1-Vinyloxyhexadecane	[23]
	70	6,10,14-trimethyl- 2-pentadecanone	[23]
	71	α-Pinene	[24]
	72	Camphene	[24]
	73	β-Pinene	[24]
	74	3-Octanol	[24]
	75	Cymene	[24]
	76	D-limonene	[24]
	77	Eucalyptol	[24]
	78	α-Trans- ocimene	[24]
	79	α-Campholenal	[24]
	80	Camphor	[24]
	81	Borneol	[24]
	82	4-terpineol	[24]
	83	α-Terpineol	[24]
	84	Pulegone	[24]
	85	1-(2-Furyl)-1-hexanone	[24]
	86	Bergamot Oil	[24]
	87	2-Methyl- 4-hydroxyacetophenone	[24]
	88	Thymol	[24]
	89	Carvacrol	[24]
	90	Neryl acetate	[24]
	91	Eugenol methyl ether	[24]
	92	Caryophyllene	[24]
	93	Geraniol acetate	[24]
	94	β-Cedrene	[24]
	95	α-Cedrene	[24]
	96	Geranyl acetone	[24]
	97	Aromadendrene	[24]
	98	Curcumene	[24]
	99	β-Selinene	[24]
	100	α-Selinene	[24]
	101	δ-Guaiene	[24]
	102	α-bisabolene	[24]
	103	Cuparene	[24]
	104	Myristicin	[24]
	105	e-Cadinene	[24]
	106	Trans-nerolidol	[24]
	107	Caryophyllene oxide	[24]
	108	Cedrol	[24]
	109	epi-cedrol	[24]
	110	Muurolol	[24]

(continued on next page)

Table 2 (continued)

Classification	No.	Chemical component	Reference
	111	α -cadinol	[24]
	112	Patchoulol	[24]
	113	Cedryl acetate	[24]
	114	Farnesyl acetate	[24]
	115	Hexahydrofarnesyl acetone	[24]
	116	Hexanal	[25]
	117	Anethole	[25]
	118	Limonene	[25]
	119	Bomyl acetate	[25]
	120	2,5-dibutyl- Furan	[25]
	121	Linalool	[25]
	122	Decanoic acid	[25]
	123	L-camphor	[25]
	124	α -longipinene	[25]
	125	Caryophyllene	[25]
	126	Copaene	[25]
	127	Longofolene	[25]
	128	3, 4-dimethylbenzaldehyde	[25]
	129	2,4- dimethylbenzaldehyde	[25]
	130	Fenchol	[25]
	131	Aromadendrene	[25]
	132	Nonanoic acid	[25]
	133	α -himachalene	[25]
	134	Acoradiene	[25]
	135	α -guaiene	[25]
	136	Dibutyl phthalate	[25]
	137	Phytol	[25]
	138	Linoleic acid	[25]
	139	Epiglobulol	[25]
	140	Elemicin	[25]
	141	Torreyol	[25]
	142	Farnesyl acetate	[25]
	143	α -eudesmol	[25]
	144	Dimethyl phthalate	[26]
	145	5, 6, 7, 7a-tetrahydro-4, 4, 7a-trimethyl-2 (4H) -benzofuranone	[26]
	146	3, 8-dihydroxy-3, 4-dihydro-2H-naphthalen-1-one	[26]
	147	3-xanthoxylin	[26]
	148	1, 2-benzenedicarboxylicacidbis (2-methylpropyl) ester	[26]
	149	Palmiticacid	[26]
	150	Ethyl palmitate	[26]
	151	9-butyl-9H-fluoren-9-ol3, 8-dimethyl decane	[26]
	152	(Z, Z, Z)-9, 12, 15-octadecatrienoic acid	[26]
	153	Ethyllinoleate	[26]
	154	(Z, Z, Z)-9, 12, 15-octadecatrienoicacid, ethyl ester	[26]
	155	Octadecanoicacid, ethylester	[26]
	156	bis (2-ethylhexyl) adipate	[26]
	157	3-pentadecyl-phenol	[26]
	158	3, 8-dimethyl- decane	[26]
	159	geranylinalool	[26]
	160	(E, E, E, E)-squalene	[26]
	161	Hentriacontane	[26]
	162	VitaminE	[26]
	163	γ -sitosterol	[26]
	164	Cineole	[27]
	165	1-(2-furyl)-1-hexanone	[27]
	166	Bergamot oil	[27]

Table 2 (continued)

Classification	No.	Chemical component	Reference
	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]
Phenolic	177	Pilosanol N	[28]
	178	Agrimophol	[16]
	179	B3 Proanthocyanidins	[30]
	180	Ellagic acid	[29]
	181	Ellagic acid 4-O-D-xylopyranoside	[29]
Phloroglucinol derivatives	182	Aripinol A	[31]
	183	Aripinol B	[31]
	184	Aripinol C	[31]
	185	Pseudo-aspidin	[31]
	186	α -kosin	[31]
	187	Agrimol A	[32]
	188	Agrimol B	[32]
	189	Agrimol C	[32]
	190	Agrimol D	[32]
	191	Agrimol E	[32]
	192	Agrimol F	[16]
	193	Agrimol G	[16]
	194	Agrimophol	[33]
	195	Pseudoaspidin	[33]
Tannins	196	Agritannin	[10]
	197	Potentillin	[16]
	198	Pedunculagin	[16]
	199	Casuarinin	[16]
	200	Agrimoniin	[16]
	201	Alagrimonic A	[16]
	202	Alagrimonic B	[16]
Isocoumarins	203	Arimonolide	[34]
	204	Dmethylagrimonolide	[34]
	205	(3S)-Agrimonolide-6-O- β -D-glucopyrano-side	[34]
	206	(3S)-Desmethylagrimonolide-6-O- β -D-glucopyrano-side	[34]
	207	(3S)-Desmethylagrimonolide-4'-O- β -D-glucopyrano-side	[34]
	208	(3S)-Agrimonolide-6-O- α -L-Arabinofuranose-(1 \rightarrow 6)- β -D-side	[34]
	209	(3S,4R)-4-Hydroxyagrimonolide-6-O- β -D-glucopyrano-side	[34]
	210	Penylethylisocou-marin glycoside	[35]
	211	Agrimonolide-6-O- β -D-glucosid	[35]
	212	(3S)-esmethyagrimonolide-4'-O- β -D-glucopyranoside	[37]
Pentacyclic triterpenoids	213	1S,3R,17R,18R,19R,20R,22R)-1,3,19,22-tetrahydroxy-28-norurs-12-en-2-one	[38]
	214	Corosolic acid	[38]
	215	Pomolic acid	[38]
	216	Tormentic acid	[38]
	217	epi-tormentic acid	[38]
	218	1 β ,2 β ,3 β ,19 α -tetrahydroxyurs-12-en-28-oic acid	[38]
	219	Ursolic acid	[39]

(continued on next page)

Table 2 (continued)

Classification	No.	Chemical component	Reference
	220	Euscaphic acid	[16]
	221	Pomolic acid	[16]
	222	Rosamultin	[16]
	223	Tormentic acid	[16]
	224	1 β ,2 α ,3 β ,19 α -tetrahydroxyurs-12-en-28-oic acid	[16]
	225	27-hydroxy- α -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	Neochlorogenic acid	[30]
	233	Cryptochlorogenic acid	[30]
	234	p-Coumaric acid	[42]
lignans	235	Pilosaneolignan ester	[43]
	236	Pilosaneolignanside A	[43]
	237	Picraquassioside C	[43]
	238	Longifloroside B	[43]
	239	(7R,8S)-4,7,9,9'-tetrahydroxy-3,3'-dimethoxy-8,4'-oxyneolignan-7-O- β -D-glucoside	[43]
	240	(7S,8S)-3-methoxy-8,4'-oxyneoligna-3',4',7,9,9'-pentol	[43]
	241	Rourinoside	[43]
	242	(7S,8R)-1-[4-O-(β -D-glucopyranosyl)-3-methoxyphenyl]-2-[4-(3-hydroxy-propyl)-2,6-imethoxyphenoxy]-1,3-propanediol	[43]
	243	Densispicoside	[43]
	244	Icariol A2	[43]
Others	245	Nnautthracene	[44]
	246	β -sitosterol	[44]
	247	Dihydrodehydrodiconifeyl alcohol 9'-O- β -D-glucose	[44]
	248	5,7-Dihydroxy-2-propylchromone 7-O-beta-D-glucopyranoside	[44]
	249	Takanechromone C	[44]
	250	(24R)-24-ethyl-5 α -cholestane-3 β ,5,6 β -triol	[44]
	251	Protocachaic aldehyde	[44]
	252	β -daucosterol	[44]

5.5. Tannins

Seven tannin compounds have been isolated and identified from APL, including Agritannin (196), Potentillin (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 Arimonolide (203), Dmethylagrimonolide (204), (3S)-Agrimonolide-6-O- β -D-glucopyrano-side (205), (3S)-Desmethylagrimonolide-6-O- β -D-glucopyrano-side (206), (3S)-Desmethylagrimonolide-4'-O- β -D-glucopyrano-side (207), (3S)-Agrimonolide-6-O- α -L-Arabinofuranose-(1 \rightarrow 6)- β -D-side (208), (3S,4R)-4-Hydroxyagrimonolide-6-O- β -D-glucopyrano-side (209), Penylethylisocoumarin glycoside (210), Agrimonolide-6-O- β -D-glucosid (211), (3S)-esmethytagrimonolide-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 β ,2 β ,3 β ,19 α -tetrahydroxyurs-12-en-28-oic acid (218), Ursolic acid (219), Euscaphic acid (220), Pomolic acid (221), Rosamultin (222), Tormentic acid (223), 1 β ,2 α ,3 β ,19 α -tetrahydroxyurs-12-en-28-oic acid (224), 27-hydroxy- α -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), (7R,8S)-4,7,9,9'-tetrahydroxy-3,3'-dimethoxy-8,4'-oxyneolignan-7-O- β -D-glucoside (239), (7S,8S)-3-methoxy-8,4'-oxyneoligna-3',4',7,9,9'-pentol (240), Rourinoside (241), (7S,8R)-1-[4-O-(β -D-glucopyranosyl)-3-methoxyphenyl]-2-[4-(3-hydroxy-propyl)-2,6-imethoxyphenoxy]-1,3-propanediol (242), Densispicoside (243), Icariol A2 (244) [43].

5.10. Others

Other compounds have also been found in APL, including Nnautthracene (245), β -sitosterol (246), Dihydrodehydrodiconifeyl alcohol 9'-O- β -D-glucose (247), 5,7-Dihydroxy-2-propylchromone 7-O-beta-D-glucopyranoside (248), Takanechromone C (249), (24R)-24-ethyl-5 α -cholestane-3 β ,5,6 β -triol (250), Protocachaic 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

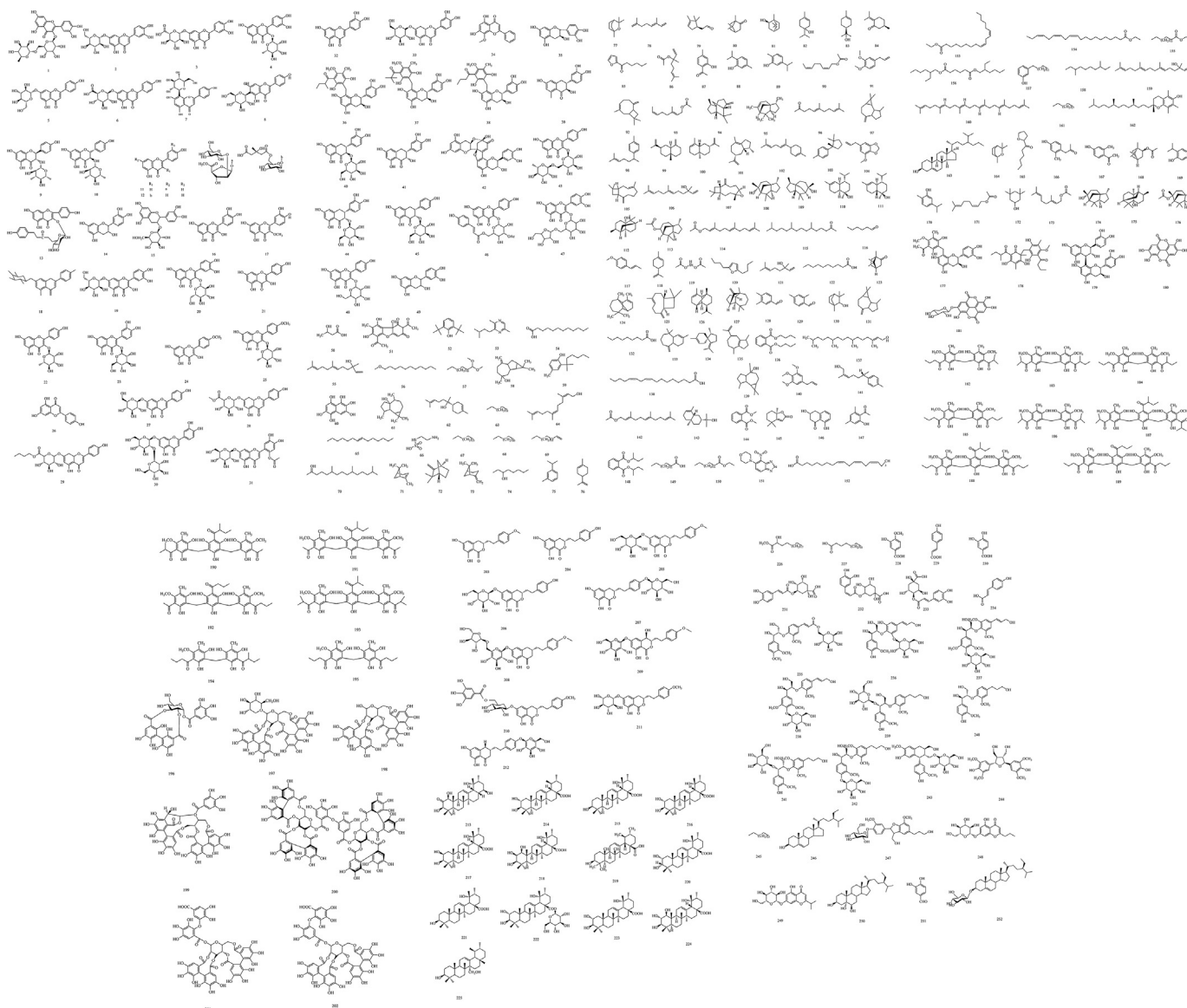


Figure 3. The structural formula of the compound isolated from *Agrimonia pilosa* Ledeb.

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 a catechin, Pilosanol N, 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-1 β (IL-1 β), 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,

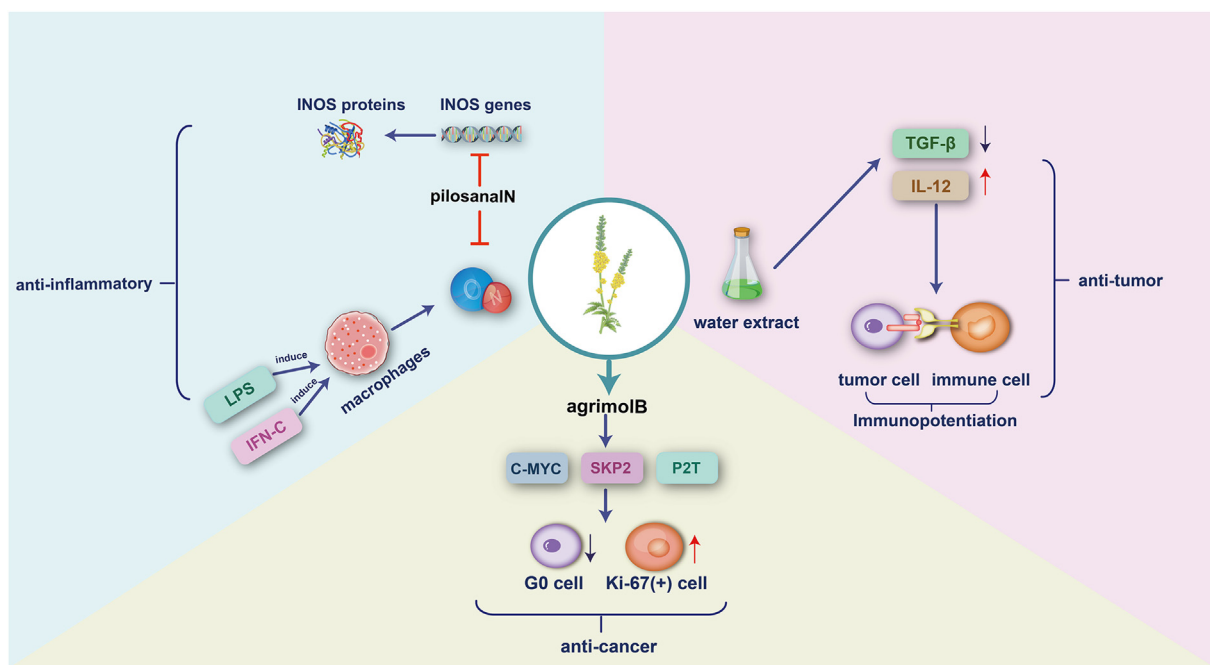


Figure 4. Pharmacological action diagram.

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 BXP-3 and PANC-1 by SRB assay. The effect of APL aqueous extract on the cycle distribution of BXP-3 pancreatic cancer cells was detected by flow cytometry. The

results showed that the aqueous extract of APL significantly inhibited the proliferation of BXP-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 BXP-3 cells. The aqueous extract of APL inhibited the proliferation of pancreatic cancer cells by inducing apoptosis of BXP-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 °C	1.67	15	3	9.92	[49]
polyphenol	ultrasonic extraction	60% methanol	35 °C	0.417	20	/	1.46	[50]
polyphenol	ultrasonic extraction	71% ethanol	60 °C	0.333	24	/	3.56	[51]
flavonoid	ultrasonic extraction	72% ethanol	60 °C	0.333	25	/	9.02	[52]
flavonoid	Ethanol reflux method	70% ethanol	80 °C	1	10	3	10.52	[53]
polysaccharide	leaching	/	80 °C	12	15	/	2.15	[54]
polysaccharide	ultrasonic extraction	/	/	0.333	80	/	8.04	[55]
flavonoid	leaching	40% ethanol	70 °C	0.5	10	3	/	[56]

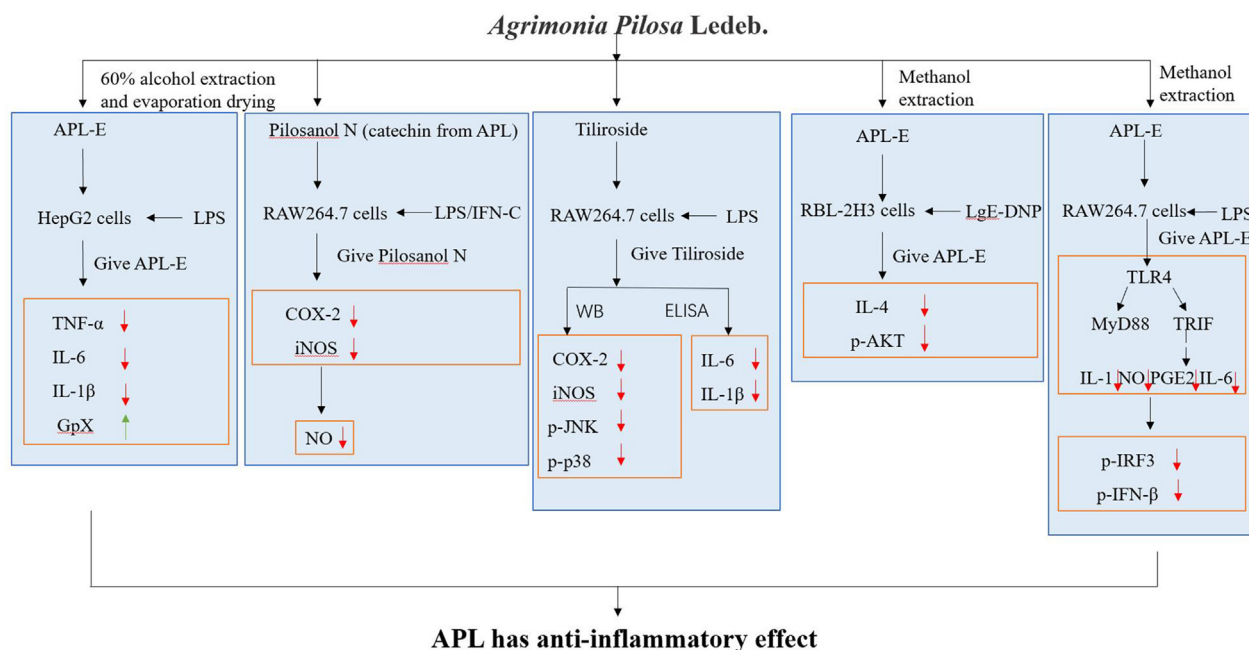


Figure 5. Anti-inflammatory effect of *Agrimonia Pilosa* Ledeb.

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

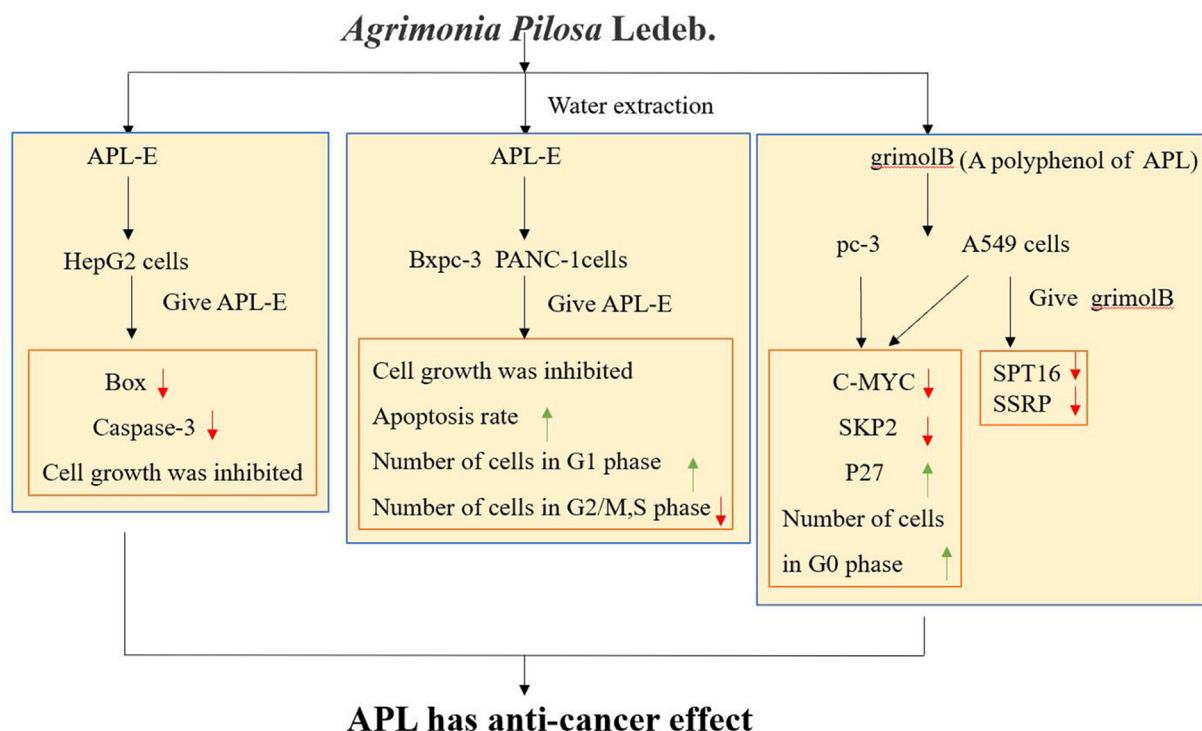


Figure 6. Anti-cancer effect of *Agrimonia pilosa* Ledeb.

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 herbal 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- κ B 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-, meth-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-sulphonic 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 1 β , 2 β , 3 β , 19 α -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 α 2-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.

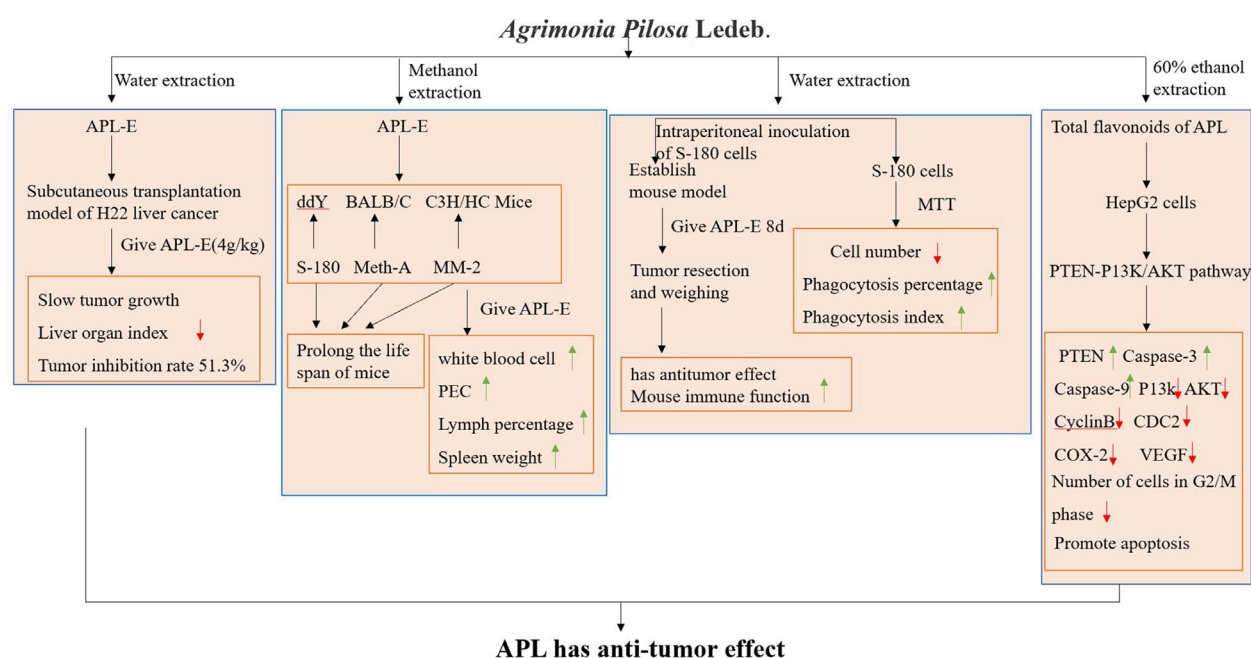


Figure 7. Anti-tumor effect of *Agrimonia pilosa* Ledeb.

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 DPPH and hydroxyl radical scavenging activity.	APL water extract effectively inhibited free radical generation, in DPPH and hydroxy radical scavenging activity, <i>Agrimonia pilosa</i> 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, PGE ₂ 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和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 vivo	[102]
	Anti-inflammatory activity of agrimonolide isolated from APL was evaluated using LPS stimulated RAW 264.7 cell models.	The pre-treatment with agrimonolide significantly reduced the levels of pro-inflammatory cytokines (IL-1 β , 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 root extracts suppressed nitrite concentrations, pro-inflammatory cytokines such as IL-1 β , 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]
	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 (1 μ g/ml) or without for indicated times. Cell 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-1 β , 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- κ B in nuclear and cytosol was detected by Western blot.	APL was extracted by 30% ethanol extract significantly decreased lipopolysaccharide-induced NO production in RAW264.7 cells and inhibited the mRNA expression of iNOS, COX-2, TNF- α , IL-1 β , and IL-6 in LPS-stimulated cells with a dose-dependent manner, indicating anti-inflammatory activity in macrophages-mediated inflammation.	in vitro	[107]
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]
Anti-tumor effects	The effect of agrimoniin, a tannin contained in APL, on ascites type and solid type rodent tumors was investigated.	Agrimoniin 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. Agrimoniin was isolated from the antitumor active fractions. Agrimoniin itself showed antitumor activity when given	in vitro	[111]

Table 4 (continued)

Pharmacological action	Details	Result	in vitro/ in vivo	Ref.
		as a pre- or posttreatment; a single dose of 10–30 mg/kg of agrimoniin resulted in almost complete rejection of the tumor by the test mice.		
	LLC had been inoculated to induce tumor Mice were divided into normal, control, APL100 (100 mg/kg), APL150 (150 mg/kg) four groups were 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 was decreased 62%, 75% in CYP3A11 and MRP1a respectively.	in vivo	[112]
	Inhibitory effect of <i>Agrimonia pilosa</i> 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 <i>Agrimonia pilosa</i> has inhibitory effect on S180 tumor cells.	in vitro	[113]
	SMMC-7721 cells were cultured with the medium containing different concentrations of APL water extracts, and at different time points, cell viabilities were measured by the MTT assay and inhibitory rates were calculated; cell morphologic changes were observed under a light microscope; apoptotic ratios were measured by flow cytometry; and the expressions of Bcl-2 and P53 proteins were examined by immunocytochemistry.	The water extracts of APL are able to inhibit proliferation and induce apoptosis of SMMC-7721 cells dose-time depend-ently in vitro	in vitro	[114]
	The effects of the ethanol extract from the plant on several transplantable rodent tumors were investigated in vitro by 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxy phenyl)-2-(4-sulphophenyl)-2H-tetrazolium, inner salt assay.	compared to normal cells, APL led selectively to the extinction of cells only in human gastric cancer. the traditional herbal medicine APL induced caspase-dependent apoptosis in AGS cells. Next, APL inhibited the growth of LLC-bearing mouse tumor.	in vitro	[115]
	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 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.	in vitro	[72]
	used the CCK-8 colorimetric assay to detect cell proliferation	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.	in vitro	[73]
	a mouse H22 tumor model to observe the effect of APL on tumor growth.	tumor inhibition rate of APL was 51.3%, which met the screening criteria for anti-tumor herbal activity and confirmed its exact anti-tumor effect.	in vivo	[75]
Analgesic effects	APL extract administered orally (200 mg/kg) showed an antinociceptive 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 (i.t.) injection of substance P (0.7 μg) was diminished by APL extract. APL extract shows an antinociceptive property in various pain models.	in vivo	[116]
	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 n-butanol components of APL achieved analgesic effects by inhibiting acute inflammation.	in vivo	[79]
Other pharmacological effects	KM mice in the experiment were regularly trained in batches for 2 weeks. We randomly divided exercise-induced fatigue mice that met the molding criteria. Each drug group was observed by intragastric administration of APL extract 2.4 g/kg	The n-butanol and ethyl acetate extracts of <i>Agrimonia</i> may be the main effective parts of its anti-fatigue.	in vivo	[83]
	Preventive and therapeutic effects of APL on gastric mucosal injury induced by indomethacin and absolute ethanol in rats	APL (16g/kg, 8g/kg) can prevent and treat gastric mucosal injury induced by absolute ethanol in rats, indicating that it has a protective effect on gastrointestinal tract	in vivo	[80]
	A mouse model of hyperglycemia was established by intraperitoneal injection of streptozotocin in male Kunming mice.given intragastric administration every day for 30 days. The changes of weight, volume diet, urine output, mental and motor status, blood glucose of mice were observed.	Compared with the initial blood glucose value, the blood glucose concentration of model control group was increased by about 10 mmol/L, the blood glucose concentration of high dose group was decreased by about 3 mmol/L, and the blood glucose concentration of drug control group was decreased by about 12.5 mmol/L. Compared with the model control group, the blood glucose levels could be reduced in the high dose group and the drug control group.	in vivo	[82]

7.6. Other pharmacological potential

Studies have shown that APL has gastroprotective effects. Zeng Xiping [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 Agrimoniin 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 Agrimoniin 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 toxicology 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.

Declarations

Author contribution statement

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Data availability statement

No data was used for the research described in the article.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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