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A Review of Studies on the Active Ingredients of Herba *Polygoni Pubescentis* and Their Applications

Yitong Wang[1], Mengjia Chu[1], Yutong Zhu[1], Weixiang Qian[1]

[1]School of life and environmental sciences, Shaoxing University, Shaoxing, China

*Corresponding author: 582705156@qq.com

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Abstract

Herba *Polygoni Pubescentis* (HPP) is a traditional Chinese herb known for its various health benefits. It has been widely applied for conditions such as rheumatism, arthritis and skin disorders thanks to its antibacterial, anti-inflammatory, anti-tumour, antioxidant, antiviral and anti-fodder properties. There is widespread growing interest to further understand HPP, the natural-based herbal remedy. Therefore, this study starts with a general introduction of HPP including its taxonomical classification, distribution and botanical characteristics etc. Through literature review, both domestic and abroad, on the past and ongoing research on the active compounds and extraction methods, this study aims to provide comprehensive information on HPP' phytochemistry, therapeutic efficacy and pharmacological uses, as well as its applications in feed, wine making, ecological restoration and pharmaceutical applications. Thus, this study will serve as a source of theoretical basis for the various applications of HPP *and* shed the light on its direction of further research and development opportunities.

Keywords: HPP Active ingredients Physiological effects Production applications

1. Introduction

HPP belongs to *Polygonaceae* and *Polygonum*, which has a unique spicy flavour and pharmacological effects. It is an extremely common fodder and weed in rural areas and is widely distributed around different regions of the world. With in-depth research, it has been found that HPP contains many active substances that are beneficial to human health including flavonoids, terpenoids, volatile oils with pharmacological activities such as antioxidant, antibacterial, anti-inflammatory and antiviral. This provides HPP with a broad prospect for the medicine development and medical application. In the field of food, it is known as "natural wine", a raw material for wine making. As HPP can adapt to harsh environments, it can also be broadly applied for environmental restoration. In this study, we reviewed the botanical characteristics, active ingredients, physiological effects and production applications of HPP.

2. Polygonaceae

Most genera of *Polygonoideae* originated in Asia and evolved, and a few genera experienced multiple long-distance dispersal events from Eurasia to North America after the Miocene, with a few dispersal events to the Southern Hemisphere also being detected (Zhang et al., 2022a). The family *Polygonaceae* has a complex taxonomic history and now comprises about 50 genera and 1150 species. In the past, the classification of *Polygonaceae* was mainly based on the uniqueness of morphological characters. With the development of molecular biology, the relationship within the family had been explored in depth using ITS, chloroplast gene fragments, and nuclear DNA fragments. Many species under the subfamily of *Polygonoideae* have high economical values (Zhang et al., 2023). At the same time, *Polygonaceae* contained a variety of active substances such as flavonoids and terpenoids which have antioxidant and antibacterial effect (Ayaz et al., 2020; Nasir et al., 2021). In ethnomedicine, the family *Polygonaceae* was famous for its efficacy against cancer (Farooq et al., 2019). In addition, with its resilience against harsh environment, *Polygonum* has also been used for wetland restoration, soil preservation and water conservation, thanks to its widespread habitats such as valleys, field margins, river gullies and roadsides.

2.1 Common *Polygonum* Plants

2.1.1 Persicaria Hydropiper L.

Polygonum hydropiper L. (previously known as *Polygonum hydropiper L.*) has gained tremendous attention due to its diverse phytochemistry and medical applications (Ayaz et al., 2020). It was known as a "natural wine yeast" and plays a significant role in improving the quality of wine. In some Asian countries, *Polygonum* was used as a food flavouring because of its strong spicy taste. One study also reported the use of steam obtained from boiling *Polygonum hydropiper L.* ‘s leaves in the treatment of hemorrhoids (Ningthoujam et al., 2013). HPP is the general name for *Persicaria hydropiper L.*, which belongs to *Polygonaceae* and *Polygonum* group. It is an annual herb with erect and glabrous stem that branches out widely. Its leaves are lanceolate or elliptic-lanceolate with pendulous spikes. *Persicaria hydropiper L.* is one of the traditional Chinese herbs that reduce swelling and detoxifies, acting as a diuretic for dysentery while having anti-microbial, anti-oxidation, anti-tumour effects. *Persicaria hydropiper L.* is widely distributed along riverbanks, gullies, valleys and wetlands in China. With abundant plant presence as a raw material, there is great potential for further development into medicine, food, plant-derived pesticides and other aspects.

2.1.2 Amphibious Polygonum L.

Amphibious polygonum L. an amphibious perennial herb, distinct aquatic and terrestrial forms that are often considered as two kinds of plant. The former has underwater stems and glabrous leaves while the latter has erect or decumbent stems and pubescent leaves. Aquatic *Polygonum* is predominantly racemose in nature. Widely distributed with rapid vegetative spread, it is native in aquatic habitats and adventive in disturbed habitats; it is particularly adapted to fluctuated water-levels (Partridge, 2001). The whole plant is medicinally useful for clearing heat and dampness to treat dysentery and oedema.

2.1.3 Persicaria Orientalis L.

Persicaria orientalis L. is an annual herb belonging to *Polygonaceae* and *Polygonum*. It features a stout erect stem that branches out at the top with villous multi-branched upper parts. Its leaves are broadly ovate or elliptic with spicate raceme. Its fruit, commonly called “water saffron seed”, is a traditional Chinese herbal medicine that has a wide range of pharmacological effects including treatment for rheumatoid arthritis, coronary heart disease, hernia, carbuncle sore, enhanced immunity, antimicrobial, osteogenic and dilated bronchiectasis (Gou et al., 2020).

2.1.4 Persicaria Tinctoria A.

Persicaria tinctoria A. features an erect stem that usually branches bearing ovate or broadly elliptic leaves with racemes. *Persicaria tinctoria*, which has been cultivated since ancient times, is used as raw material to produce indigo dye. This is because its leave contains cells that produce specialized metabolite indican (indoxyl-β-D-glucoside), a precursor of indigo (Inoue et al., 2020). Its medicinal potential includes clearing heat and removing toxins from body; while active compounds found from indigo plants includes tryptanthrin known for its anti-cancer and anti-inflammatory properties; 3.5,4′-trihydroxy-6,7-methylenedioxyflavone and *O*-β-D-glucopyranoside which act effectively against blood coagulation (Kimura et al., 2021).

2.1.5 Polygonum Chinense L.

Polygonum chinense L. commonly known as *Polygonum multiflorum*, is a perennial herb with an erect, hairless and multi-branched stem. Its leaves are ovate or long ovate, with head-like inflorescence. *Polygonum chinense L.* is effective in clearing heat and dampness, cooling blood and removing toxins, activating the blood and relaxing the tendons, as well as brightening the eyes to relief cataracts. It has multiple functions such as treating dysentery and diarrhoea, sore throat, diphtheria, lung-heat cough, whooping cough, hepatitis, eczema, otitis media, vertigo, tinnitus, bruises, and breast hyperplasia. Zheng et al. (2018) had isolated and extracted five new compounds with anti-complementary activity from *Polygonum chinense L.*

2.1.6 Polygonum Aviculare L.

Polygonum aviculare L. also known as bamboo slice leaf, is a terrestrial annual herb. Its stem is procumbent, slanting up or erect, with branches at base. The leaves are elliptic or lanceolate, with blue-green color and smooth leaf margin. The flowers are solitary or clustered at the auxiliary bud. It is a Chinese herb with cold nature, bitter taste and diuretic property.

2.1.7 Persicaria Viscosa B.

Persicaria viscosa B. commonly known as Vietnamese coriander, is a native species in Southeast Asia. Young leaves were used as a pungent additive to dishes of south-eastern Asian cuisine (Vietnamese, Cambodian, Singaporean, Malaysian, Laotian and in some regions of Thailand) (Pawłowska et al., 2020). The aromatic annual herb features an erect or ascending stem with much branched, ovate-lanceolate or elliptic-lanceolate leaves and spiky racemes that are either terminal or axillary. The whole herb can be used as medicine for upper respiratory tract infections, bronchitis, sore throat, dysentery, enteritis, eczema and other conditions.

2.1.8 Persicaria Capitata B.

Persicaria capitata B., also known as grass stone pepper, is a perennial herb with creeping, multi-branched and tufted stems. Its leaves are ovate or elliptic with capitate inflorescence. *Persicaria capitata B.* is used as traditional Chinese medicine to treat various urologic disorders by the Miao people in China because of its antibacterial and anti-inflammatory properties (Han et al., 2018). Its colourful flowers and widespread coverage make it an excellent ornamental plant.

2.1.9 Persicaria Officinalis B.

Bistorta officinalis B. is a perennial herb with papery leaves, spikelike racemes, erect and glabrous stem and unbranched. The rhizome of *Bistorta officinalis B.* has fertile roots which contributes significantly for its medicinal use. Its main pharmacological effects include analgesic, anti-tumour, and protection of the cardiovascular system (Liu et al., 2017).

2.2 Classification of the Genus *Polygonum*

In addition to the above-mentioned *Polygonum*, there are also *Persicaria lapathifoloa L.* and *Persicaria longiseta B*. Plants of the same genus sharing various macromorphological characteristics. Most of them are annual or perennial herbs, with a few being semi shrubs or small shrubs. They have erected, prostrate or ascending stems that can be glabrous, hairy, or with anatropous glochids, and are usually inflated at the nodes. They have alternate leaves that are linear, lanceolate, ovate, elliptic, arrow-shaped or hastate; they have membranous or herbaceous stipular sheaths are tubular and truncate or oblique at the tip. Their inflorescences are spikelike, racemose, capitate or paniculate. The flowers are mostly terminal or axillary, and a few are in clusters and growing in the auxiliary bud. Their flowers are bisexual or rarely unisexual, clustered or rarely solitary; bracts and bracteoles membranous; pedicels jointed; perianth are mostly 5-parted or rarely 4-parted. Disks are mostly glandular or annular, but sometimes absent; There are 8 stamens, rarely 4-7; ovary ovate;

styles 2-3, free or united in middle and lower parts; stigma capitate. Achenes ovate, 3-angled or biconvex lenticular, enclosed in persistent perianth or protruding beyond perianth (Editorial Committee of Flora of China, Chinese Academy of Sciences, 1998). However, there was significant variability in the macroscopic and microscopic morphological structure of *Polygonum* (Zheng et al., 2014).

2.2.1 Differences in Macro-Morphological Structure

As shown in Table 1, the stem morphology varied greatly and was mainly divided into three types: erect, semi-erect or prostrate, and floating, with erect stems dominating. The life type was mainly divided into annual and perennial herbs, of which annual herbs accounted for a larger proportion. *Polygonum* had a wide range of flower colours, which were easy to distinguish. Plant life environments terrestrial or aquatic, life type annual or perennial, were macro-classification basis.

Table 1. Biological characteristics of *Polygonum spp*

Number	Scientific Name	Morphological Type of Stem	Life Type	Ecotype	Flower color
1	*Polygonum aviculare L.*	prostrate/erect	herbs annual	terrestrial	perianth green, margin white or pinkish
2	*Polygonum plebeium R.*	prostrate/erect	herbs annual	terrestrial	perianth green, margin white or pinkish
3	*Persicaria posumbu B.*	erect	herbs annual	terrestrial	perianth pinkish
4	*Persicaria amphibia L.*	floating(aquatic)	herbs perennial	aquatic	perianth white or pinkish
5	*Persicaria assamica M*	erect	herbs annual	hygromorphism	perianth red
6	*Persicaria barbata L.*	erect	herbs perennial	hygromorphism	perianth white or light green
7	*Persicaria foliosa H.*	erect	herbs annual	hygromorphism	perianth pinkish
8	*Persicaria glabra W.*	erect	herbs annual	hygromorphism	perianth white or pinkish
9	*Persicaria huananensis A.*	erect	herbs perennial	hygromorphism	perianth white
10	*Persicaria hydropiper L.*	erect	herbs annual	hygromorphism	perianth green, upper white or light red
11	*Persicaria japonica M.*	erect	herbs perennial	hygromorphism	perianth white or pinkish
12	*Persicaria lapathifolia L.*	erect	herbs annual	hygromorphism	perianth white or pinkish
13	*Persicaria limicola S.*	prostrate	herbs annual	hygromorphism	perianth white or pinkish
14	*Persicaria longiseta B.*	prostrate/erect	herbs annual	terrestrial	perianth light red or purplish red
15	*Persicaria orientalis L.*	erect	herbs	terrestrial	perianth white

Number	Scientific Name	Morphological Type of Stem	Life Type	Ecotype	Flower color
			annual		or pinkish
16	*Persicaria paralimicola A.*	erect	herbs annual	terrestrial	perianth light red, yellowish brown glandular dots
17	*Persicaria maculosa L.*	erect	herbs annual	hygromorphism	perianth purplish red
18	*Persicaria pubescens B.*	erect	herbs annual	hygromorphism	perianth green, upper red
19	*Persicaria pulchra B.*	erect	herbs perennial	hygromorphism	perianth white
20	*Persicaria taquetii H.*	prostrate	herbs annual	hygromorphism	perianth pinkish
21	*Persicaria tinctoria A.*	erect	herbs annual	terrestrial	perianth pinkish
22	*Persicaria viscofera M.*	erect	herbs annual	hygromorphism	perianth light green
23	*Persicaria capitata B.*	prostrate	herbs perennial	hygromorphism	perianth pinkish
24	*Bistorta officinalis B.*	erect	herbs perennial	terrestrial	perianth white or pinkish
25	*Persicaria viscosa B.*	erect	herbs annual	hygromorphism	perianth pinkish

2.2.2 Micromorphological Structural Differences

With the deepening of molecular phylogenetic studies, the basis of classification had been continuously improved. Galasso et al. combined molecular phylogeny with the results of previous morphological studies to resolve the phylogeny of some controversial genera and species, obtaining consistent support from molecular and morphological aspects (Galasso et al., 2013). KS Choi et al. analysed gene sequences and found that the largest regions of sequence divergence were the rps16-trnQ, trnQ- psbK, trnW-trnP, ndhF-rpl32, and rpl32-trnL regions (Choi et al., 2022).

3. Active Ingredients and Physiological Effects of HPP

There are many phytochemicals compounds in HPP. Analysis of extracts in methanol, ethanol, chloroform, petroleum ether, and n-hexane showed that flavonoids, volatile oils, terpenoids, organic acids, and steroids were the main compounds. Due to the presence of bioactive molecules in chemical compounds of HPP, the plant exhibits pharmacological effects as shown in Table 2 (Bairagi et al., 2022).

Table 2. Main active ingredients of HPP and their physiological effects

Main active ingredients	Corresponding species	Physiological and pharmacological effects	Active ingredients
Flavonoids	*Polygonum aviculare L.* *Persicaria hydropiper L.*	Antioxidant activity	Quercetin, Flavone Glycoside, Hyperoside, Rutin
	Polygonum capitatum B.	Anti-inflammatory,	Quercetin, Luteolin, Rutin,

Main active ingredients	Corresponding species	Physiological and pharmacological effects	Active ingredients
	Persicaria orientalis L. *Persicaria tinctorium A.*	Analgesic activity	Kaempferol
	Persicaria hydropiper L. *Persicaria amphibiumL.*	Anti-disease and anti-virus activity	Procyanidins, Quercetin, Flavonoid glycoside
	Persicaria. hydropiper L. *Polygonum viscosum M.*	Anti-cancer activity	Liquiritigenin, Naringenin, Hesperetin, Aglycone-luteolin, Quercetin,Emodin
	Polygonum chinense L. *Persicaria orientalis L.*	Antibacterial activity	Sesquiterpene dialdehydes, Caryophyllene, Triterpenoid saponin
Terpenoid	*Persicaria hydropiper L.*	Antifeedant and insecticidal activity	Saponin, Drimane-type sesquiterpenes
	Polygonum aviculare L.	Hepatoprotective activity	β-Caryophyllene, Caryophyllene oxide
Volatile oil	*Polygonum viscosum M.*	Protects nervous system activity	Thymol,neral, 1-methyl-4-cyclohex-1-ene
Steroid	*Polygonum bistorta B.*	Anti-cancer, Anti-tumour, Anti-hypercholesterolemic	Stigmasterol, β-sitosterol
Polysaccharid e	*Persicaria hydropiper L.*	Immunomodulator	Polymerised Sugar Polymer Carbohydrates
Polyphenol	*Polygonum bistorta B.*	Diuretic, Antihypertensive, Antibacterial activity	Phenolic acids (chlorogenic acid, coumaric acid, caffeic acid), Flavonoid
	Persicaria hydropiper L.	Immunomodulator	Anthraquinone glycoside
	Persicaria amphibium L.	Antiviral activity	Gallic acid

3.1 Flavonoids

Flavonoids are plant metabolites that compose of two benzene rings and a heterocyclic bared ring. They are phenolic compounds that can be classified into different groups based on their chemical substituents (Dias et al., 2021; Jakimiuk et al., 2022). The flavonoids present in *Persicaria orientalis* can be extracted by solvent extraction, supercritical fluid extraction (SFE), ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE). The total content can be determined by high-performance liquid chromatography, high-resolution tandem mass spectrometry (HPLC-MSIMS), and ultraviolet-visible absorbance spectroscopy (UV-VIS) (Chávez-González et al., 2020; Shin et al., 2018). Sulfated flavonoids could be isolated from *Persicaria hydropiper*. Ayaz et al. (2020) isolated five compounds of sulfated flavonoids from the leaves: thymosin, quercetin 3-sulfate, isorhamnetin 3,7-disulfate, etc. The flavonoid fraction could also be modified by glycosylation, hydroxylation, hydrogenation which can affect its biological and pharmacological activity. The presence of hydroxyl groups will determine the extent to which it can be utilised by humans (Dias et al., 2021; Jakimiuk et al., 2022). Flavonoids have various health benefits including antioxidant, anti-inflammatory, analgesic, anti-disease and anti-cancer activities.

3.1.1 Antioxidant Activity

The antioxidant property of flavonoid has received significant attention, particularly in relation to their ability to scavenge superoxide anion radicals produced by Xanthine oxidase (XOD). Yagi et al. used the ferric thiocyanate method to investigate the antioxidant properties of flavonoids in *Persicaria hydropiper* and found it effective to scavenge superoxide anion free radicals (Kong et al., 2023; Zheng et al., 2014). This suggests that flavonoids can inhibit both xanthine oxidase and xanthine, leading to their hypothesized antioxidant activity. In another study, the antioxidant activity of *Polygonum aviculare L.* was detected using the DPPH method to measure free radical scavenging capacity (Salama & Marraiki, 2010). Results showed that methanol extract had a higher scavenging capacity for the DPPH free radicals than positive drugs in vitro experiments, and methanol extracts also demonstrated stronger antioxidant activity (Salama & Marraiki, 2010). However, its antioxidant ability was also related to the type of functional groups presented in the nuclear structure, in which the number and position of hydroxyl groups played an important role (Dias et al., 2021).

3.1.2 Anti-Inflammatory and Analgesic Activity

Due to the anti-inflammatory and analgesic properties of flavonoids, HPP has been found to have anti-inflammatory and analgesic effects. Studies using animal models have shown that flavonoids found in *Persicaria capitata* (e.g. quercetin, luteolin, rutin, etc.) could alleviate inflammation and inhibit it. Quercetin has been found to balance the proliferation and apoptosis of gastric cells, which could be used to prevent and treat *H. pylori-associated inflammation* (e.g., inflammation of the gastric mucosa) and to repair gastric damage (Gou et al., 2017; Lin et al., 2022). In addition, flavonoids found in methanol and butanol extracts could lower lipopolysaccharide-induced inflammation by inhibiting MAPKS and IRAK/AP-1/CREB (Tao et al., 2015). Kaempferol found in *Persicaria tinctoria* has anti-inflammatory activity and plays an important role in the treatment of intestinal damage and metabolic inflammation caused by obesity (Kawaguchi et al., 2023). The methanolic extract of *Persicaria orientalis* has a significant inhibitory effect on peripheral and supra-neural nociception in animals. Flavonoids have been found to have analgesic effects on peripheral pain in mice, as evidenced by the dose-dependent inhibitory effect (Ansari et al., 2017; Gou et al., 2017) observed in models like acetic acid-induced writhing in mice.

3.1.3 Anti-Disease and Anti-Virus Activity

The potential antidiabetic effect of *Persicaria hydropiper's* ethanolic extract was studied, and it was found that flavonoids may be responsible for its hypoglycaemic and anti-disease properties via the animal models and in vitro experiments (Ayaz et al., 2022). Two flavonoid glycosidic acids were extracted from *Persicaria amphibia,* and they were found to induce an intense apoptotic reaction in leukaemia cells (Smolarz et al., 2008). Proantho cyanidins (PC) were also isolated from ethanolic extracts, and they were found to activate HIV transcription. This suggests that proanthocyanidins could be used in conjunction with high-potency antiretroviral therapy to eliminate inactive latent HIV (Ke et al., 2023). In vitro experiments have shown that flavonoids could block viral binding, interfere with viral replication or translation, and inhibit viral development. Quercetin and other flavonoids have been found to have antiviral activity against several strains of influenza virus (Dias et al., 2021). In addition, certain substances found in flavonoids could inhibit viral soluble proteins and transcribed genes, preventing viruses from entering the living organism (Ke et al., 2023).

3.1.4 Anticancer Activity

Flavonoids found in *Persicaria hydropiper* had shown anti-cancer properties. Both in vivo and in vitro experiment have demonstrated that flavonoids could inhibit the activity of cancer cells by blocking the transformation of different growth factors and proteins, proteases, thus preventing growth (Ke et al., 2023). Among them, liquiritigenin, naringenin and hesperetin are found to be beneficial in treating breast cancer. Liquiritigenin is found to attenuate the attack of breast cancer cells, naringenin could prevent breast cancer cells from dividing and multiplying, and hesperetin could limit the expression of aromatase, which inhibits the secretion of estrogen (Hao et al., 2021). Lin et al. (2022) explored that emodin was effective in controlling the generation of HCC cell lines in a dose-dependent manner and could also reverse adriamycin resistance in cancer cells (Smolarz et al., 2008). Besides, the aglycon-luteolin also inhibited the expression of pro-oncogenic proteins, and methylation would affect the anticancer activity of flavonoids (Hao et al., 2021; Jakimiuk et al., 2022). Finally, quercetin and its derivatives from *Persicaria viscofera* were useful in the treatment of cervical and ovarian cancers in women (Datta et al., 2004).

3.2 Terpenoids

Terpenes are a class of compounds consisting of multiple isoprene units. The most common types are monoterpenoids (C10), sesquiterpenes (C15) and triterpenoids (C30). Terpenes exist in various forms, including terpene olefins and different oxygenated derivatives such as alcohols, aldehydes, carboxylic acids, ketones and esters (Yang et al., 2019). Terpenoids represent one of the largest classes of naturally occurring organic compounds, with a wide range of structural diversity. To date, nearly 50,000 terpenoids had been found in nature, with the majority of them being isolated from plants. Sesquiterpenes of the drimane type were found in the extracts such as 11-ethoxycinnamic acid and polyacetals (Bairagi et al., 2022). Terpenes presents in diverse structures to isolate the desired terpenes and determine the content of terpenoids in Herba *Polygoni Pubescentis,* it is necessary to employ appropriate solvents for extraction and to utilize techniques such as gas chromatography [GC], thin-layer chromatography [TLC] or liquid chromatography [LC] (Jiang et al., 2016). Terpenoids play important roles such as antimicrobial activity, antifeedant and insecticidal activity, as well as hepatoprotective function.

3.2.1 Antibacterial Activity

The compounds extracted from HPP showed strong antimicrobial activity. After analysing the compounds, it was found that apart from flavonoids, terpenoids also had strong antimicrobial activity. One specific terpenoid, Sesquiterpene dialdehyde, exhibited anti-fungal properties when its extracts were separated using HPLC (Bairagi et al., 2022). The extracts obtained using ethanol and acetone from *Polygonum chinense* exhibited anti-fungal activity and the terpenoids inhibited the growth of Staphylococcus aureus, Salmonella paratyphi, Bacillus subtilis etc (Zeng et al., 2022). Through preliminary anti-fungal and antibacterial experiments, caryophyllene and triterpenoid saponins (triterpenoids and sugars combined) demonstrated inhibitory effects on pathogenic bacteria and fungi with antibacterial activity (Ayaz et al., 2016). Another plant, *Persicaria orientalis* was found to exhibit effective antimicrobial activity against *Pectobacterium carotovorum subsp. carotovorum* (Pcc) by antimicrobial activity assay, which might be related to compounds like Phytol, 1-octen-3-ol (Cai et al., 2022).

3.2.2 Antifeedant and Insecticidal Activity

Persicaria hydropiper has properties that repel insects and prevent them from feeding, which are likely related to terpenoids. The most effective repellency was observed in the extracts obtained through ether, methanol and petroleum ether, and ovicidal and acaricidal activity was demonstrated in the extracts derived from petroleum ether and acetone. Analysis of the extracts revealed insecticidal properties against different vector mosquitoes (e.g. dengue vector mosquitoes, Aedes albopictus), and the drainage-type sesquiterpenes were found to have potential antifeedant activity (Bairagi et al., 2022). By testing the insecticidal potential of plant extracts, it was found that saponins (possibly steroid or triterpenoid secondary metabolites) exhibits a high level of insecticidal activity. Moreover, HPP demonstrated an antimalarial effect (Ayaz et al., 2016). High concentrations of volatile terpenoids could be toxic to insects, e.g. eucalyptus alcohol is a volatile monoterpene used as an insecticide; terpenoids could also act as elicitors, indirectly leading to the disruption of reproduction and development of pests, which enhances a plant's defenses against pests (Boncan et al., 2020).

3.2.3 Hepatoprotective Activity

A class of bicyclic sesquiterpenoids known as β-Caryophyllene has been found to have a protective effect on the liver. Through experiments conducted on NAFLD (excess triglycerides in hepatocytes stresses the liver) and NASH (excess lipid accumulation may be serious enough to cause cirrhosis and hepatocellular carcinoma) it was revealed that caryophyllene administration can help with inflammation due to liver injury (Scandiffio et al., 2020). Caryophyllen extracted from *Polygonum aviculare* was found to be hepatoprotective, inhibiting oxidative stress and inflammation, and having a denfensive effect against liver failure (Demirpolat, 2022). In addition, caryophyllene oxides were found to inhibit the proliferation and growth of cancer cells, increase apoptosis, enhance ferritin phagocytosis and induce iron death in cancer cells (Xiu et al., 2022). The hypolipidemic effect of β-caryophyllene and its effect on hepatic antioxidant enzymes were evaluated by establishing a rat hyperlipidaemia model. Results showed that β-caryophyllene has a hypolipidemic effect (Ayaz et al., 2015), which could prevent liver diseases, maintain the metabolic capacity of the liver, and aid in the treatment of fatty liver.

3.3 Volatile Oils Protect Nervous System Activity

The volatile oils present in HPP have a complex composition, containing terpenes, enol tautomerism and sterols (Kong et al., 2023). These volatile oils could be extracted and analysed using various methods such as a Clevenger instrument, supercritical and GC-MS coupling techniques, steam distillation, or solid phase extraction (Das & Ganapaty, 2015; Kong et al., 2023). One of the terpenes, β-caryophyllene, isolated from HPP could reduce free radical loading in brain tissue, as shown in a transgenic animal model. Acetylcholinesterase (AchE) is a key enzyme in nerve conduction that degrades acetylcholine and terminates neural excitation. Acetylcholinesterase inhibitors are effective tool in treating neurological disorders. *Persicaria viscofera* extract has an inhibitory effect on acetylcholinesterase activity and CNS depressant activity, which is useful in treating Alzheimer's disease (Lizarraga-Valderrama, 2021). In addition, exposure to volatile oils through olfaction has shown to enhance cognitive performance and attention in both healthy and temporal lobe epilepsy (TLE) patients, demonstrating neuropharmacological effects (Lin et al., 2015).

3.4 Pharmacological Effects of Other Substances

Polysaccharides and Polyphenol in extracts of *Persicaria hydropiper* acted as immunomodulators. The role of polysaccharides was explored by establishing a model of cyclophosphamide-induced anaemia in mice and by using different doses administered orally to mice, which revealed that polysaccharides were potential immunomodulators, and similar outcomes were found for anthraquinone glycosides (Svirčev et al., 2012). Polyphenolic compounds were also found to have diuretic, antihypertensive and antibacterial effects. The most abundant phenolic acid in the extract of *Persicaria amphibia* is gallic acid, which has antiviral properties (Mezerji et al., 2023; Smolarz et al., 2008). Animal models have shown that phenolic-rich extracts of *Bistorta officinalis* were antimicrobial and diuretic (Pillai Manoharan et al., 2007). *Polygonum bistorta B. also* contained a range of steroids, phytosterins and other steroids including β-sitosterol, γ-sitosterol and stigmasterol. These compounds could be isolated from chloroform and ethyl acetate, and their anticancer effects were detected by cytotoxicity detection of sarcoma carcinoma cells in mice (Bakrim et al., 2022). Bae et al. found that stigmasterol could play a role to prevent ovarian and breast cancer by enhancing the expression of endoplasmic reticulum-mitochondrial axis proteins and stressed transducer proteins in cancer cells, inhibiting the growth and migration of cancer cells (Antwi et al., 2017). Additionally, stigmasterol also exhibited anti-inflammatory and anti-hypercholesterolemic activity. The effect of stigmasterol on asthma (chronic airway inflammation) was investigated by establishing a model of ovalbumin-induced asthma. Stigmasterol attenuates ovalbumin-induced oxidative stress, inhibited allergy-triggered asthma, and exerted anti-inflammatory activity against it (Baldissera et al., 2017).

4. Current Status of Domestic and International Application of HPP

HPP is a vigorous and adaptable plant that is found in many regions across the world, especially in the temperate regions of Asia and North America. HPP has been used for centuries in China to brew samshu and yellow rice wine. In the ancient brewing process, it was added to enhance the brewing effect. In addition, it has been used to treat various diseases such as high blood pressure, arthritis, rheumatism, lung cancer, liver cancer etc. It is also a natural bio-pesticide, which plays an important role in the restoration of water and soil. With time, it is also used in feed additives. Overall, it has a wide range of production and application potential both in China and abroad, as shown in Table 3.

Table 3. Current status of domestic and international production and application of HPP

Production field	**Corresponding species**	**Specific applications**
Feed	*Persicaria hydropiper L.*	Development of feed additives and optimisation of the process
	Polygonum aviculare L.	Development of feed additives combining *P.hydropiper L.* and other Chinese herbs and Application of high-quality protozoan feeds
Wine making	*Persicaria hydropiper L.*	Applying the production of small wine and yellow wine tunes
	Polygonum lapathifolium L.	Application of new chemical water wine liquor medicine production
Ecological restoration	*Persicaria lapathifolia L.*	Removal of heavy metals manganese, nickel and zinc from soil
	Persicaria hydropiper L.	Increasing species density for adaptation to drought stress
	Polygonum chinense L.	Biological herbicide
Medicine	*Persicaria hydropiper L.*	Application of hypertension, liver protection, coronary heart disease, arthritis disease
	Persicaria tinctoria A.	Anti-inflammatory drugs
	Persicaria orientalis L.	Anti-cancer, complex cardiovascular diseases
	Persicaria capitata B.	Potential treatment for *Helicobacter pylori gastritis*

4.1 HPP in Feed Applications

HPP is a plant rich in nutrients such as proteins, minerals and vitamins with a special aroma and flavour. It provides a natural and sustainable feed resource for the livestock industry, promoting the growth and development of livestock, improving the digestibility and absorption rate of the feed, increasing muscle mass and eating quality. Therefore, many farmers in rural areas use HPP to feed poultry and pigs to reduce feed costs. The nutrient composition of these highly mentioned wild fodder plants was studied through ethnobotanical surveys. Laboratory analysis showed that crude protein content of HPP was as high as 21.88%, making it of high nutritional value and thus capable to improve livestock and poultry productivity and managing wild forage resources (Geng et al., 2020).

Persicaria hydropiper L. has a variety of biological activities such as anti-microbial, anti-inflammatory, analgesic and antioxidant (Yang et al., 2012). Song & Zhu, (2017) conducted experiment on feed additives made from *polygonum hydropiper L.* and cassava pulp with flavonoid-leaching, in order to explore the modernization of traditional Chinese medicines. Kupczyński et al. (2019) conducted experiment on a rabbit model of infection with *Escherichia coli* and found that *Polygonum aviculare* had a significant effect on reducing the colonization of intestinal parts. They also discovered that adding mixed herbs to the feed reduced the number of *Escherichia coli* in the cecum more than adding herbs to the water. After microbial mixed fermentation treatment and mutual combination with other herbal ingredients, the content of active ingredients, feed palatability and nutritional value of *Polygonum aviculare* were enhanced in different ways. Kamalak et al. (2010) conducted studies on the quality of the pasture and found that *Polygonum aviculare* could be used as a good quality forage for protozoa. The results also showed that *Polygonum aviculare* could be used as an acceptable and high-quality fodder for ruminants during the grazing period, and its quality of the pasture was very high before the flowering period. As an annual herbaceous plant, HPP has a short growth cycle, while it can be grown and widely distributed in the wild. Thus, it could reduce the cost of feed and increase the economic benefits of animal husbandry. Meanwhile, it could reduce the dependence on traditional feed resources and lower the environmental pressure, thus realizing green and sustainable development. However, even so, in the actual industrial production of HPP as a feed additive accounted for less, the application of feed on the need to strengthen the research and promotion.

4.2 Application of HPP in Wine-Making

HPP has functions of dispelling wind and dampness, dispersing blood stasis, relieving pain, killing worms and inhibiting bacteria. Being used in wine-making, it can effectively improve the quality and stability of wine. HPP is also rich in nutrients needed for the growth of yeasts and root mould, which promotes the growth and reproduction of fungi and mould, making the wine richer in flavour and more mellow in taste. Additionally, HPP had a unique aroma and flavour which added a special taste to the wine.

According to study of Lu & Li, (2006) *Persicaria hydropiper L.* is commonly used as the only herbal ingredient in many liquor medicines, especially in the production of small quarts of wines and yellow wines. The study investigated the effects of adding different amounts of *Persicaria hydropiper L.* to small quarts of wines on microbial species and number, liquefaction force, saccharification force and fermentation rate (Lu & Li, 2006). The results suggested that adding a certain proportion of *Persicaria hydropiper L.* to the production of liquor medicine could promote the growth and reproduction of beneficial microorganisms in liquor medicine and effectively inhibited the growth of stray bacteria. Another study by Chen H et al. showed that adding a certain proportion of *Persicaria hydropiperr L.* to the production process of liquor medicine of Xinhua watery wine has a promotional effect on the saccharification force and the fermentation force of the medicine (Chen et al., 2019). This could improve the quality of watery wine and the rate of liquor production to a certain extent. *Persicaria hydropiper L.* was added to the production of liquor medicine in Fang County, and it was one of the important sources of terpenoids in liquor medicine. This made the brewing obtained with anti-tumour, anti-bacterial, anti-viral and anti-inflammatory activities (Zhang et al., 2022b). It is clear that *Persicaria hydropiper L.* played a crucial role in wine-making. However, attention should be paid to the amount of HPP being added during the actual wine-making process. Concerns have been raised about the level of heavy metals, particularly manganese, which were associated to a number of health problems. HPP enriched manganese in the soil with leaves containing up to 3.7 g/kg (Qu, 2023). However, HPP was mostly harvested from swampy areas, where soil samples contained high levels of heavy metals that might come from drainage. The heavy metal content of HPP varies depending on the irrigation system and environment, which requires manufacturers to strictly control the growing environment and irrigation techniques (Ayaz et al., 2020). Based on population data, there was one case of skin irritation after taking 50 g of saffron seed, which is the fruit of *Persicaria orientalis*. Another case of nausea and vomiting is after taking 30 g of *Persicaria hydropiper L.* If the maximum daily alcohol consumption of adults was 2 kg, the exposure to *Persicaria hydropiper L.* should not exceed 1 g/kg (Qu, 2023). However, due to the limited toxicological data of HPP, there was no detailed report on the upper limit of HPP added in the production of alcohol. Therefore, more in-depth research should be conducted to reduce the adverse effects and potential risks caused by the addition of excessive amounts of HPP.

4.3 Application of HPP in Ecological Restoration

Polygonum are well-known for their ability to hyper-accumulate manganese. Among them, *Polygonum lapathifolium L.* is a particularly promising phytoremediation material (Li et al., 2020; K. Liu et al., 2016). Because of its ability to remove heavy metal from the soil through biosorption, thus reducing its biotoxicity. In the meantime, *Polygonum lapathifolium* also has an enrichment effect on other heavy metals such as nickel and zinc, and transfers most of the heavy metals to the above-ground parts. This makes it useful to remediate heavy metal-contaminated soils with a positive impact on ecological remediation.
HPP has a well-developed root system, which could improve the water and fertiliser retention capacity of the soil and resist drought stress. Study of Feng Li et al. showed that increasing the density of *Persicaria hydropiper L.* helped with plant's adaptation to drought stress. In addition, *Persicaria hydropiper L.* is a phosphorus-rich herb used for plant phosphorus extraction, which played an important role in mobilizing soil mineral phosphorus and promoting phosphorus uptake (Li et al., 2014).

Polygonum had various pharmacological properties such as antibacterial, anti-fungal, cytotoxic, antioxidant and antimicrobial properties (A.R. et al., 2012). Lun T L et al. studied the effects of extracts from the quince of *Polygonum chinense L.* and confirmed that it could be used as a chemosensory substance for bioherbicide (Lun et al., 2023). *Polygonum chinense L.* could be used as a natural source of bioherbicides, which contributes to the structural stability of ecosystems.

HPP is important in ecological restoration with many potential applications. Further studies on the applications of HPP can be carried out such as the use of HPP to improve soil fertility, the development of new HPP *bioremediation* technology, etc.

4.4 Pharmaceutical applications of HPP

HPP contained several significant pharmacologically active compounds. For example, polydialdehyde isolated from HPP is a stimulating ingredient with food-repelling, antibacterial, anti-inflammatory and anticancer properties (De La Chapa et al., 2020). HPP, as a promising multipurpose herb, has shown strong capabilities in drug preparation such as antibacterial, anti-fungal, anthelmintic, food refusal, anticancer, anti-inflammatory, antiprogestogen, estrogen, anti-fertility, anti-allergenic, anti-allergenic, antilipemic, and neuroprotective properties (Huq et al., 2014). Devarajan et al. (2018) found that HPP leaves had an inhibitory effect in the treatment of salt-sensitive hypertension. Although a wide range of drugs are already available in the market for the treatment of salt-sensitive hypertension, they were relatively expensive. The shorter growth cycle and wider distribution of HPP could better compensate for this pain point. Chiu et al. (2018) showed that the ethanolic extract of the fruit of HPP exerted hepatoprotective potential by enhancing hepatic antioxidant enzyme activity, inhibiting lipid peroxidation and decreasing the activity of pro-inflammatory mediators.

HPP is a well-known Chinese herb widely used in the treatment of coronary heart disease and many bone diseases including rheumatism, fractures, falls, muscle injuries and various inflammatory conditions such as joint pain and arthritis. Ma et al. (2020) demonstrated that HPP had a positive potential for preventing ovariectomy-induced weight gain, regulating bone metabolism, improving bone mineral density and bone mechanics, and attenuating loss of bone trabecular. Gou et al. (2018) showed that HPP would be used for rheumatoid arthritis and rheumatoid arthritis in the long term in terms of clinical application in Traditional Chinese Medicine. The leaves of *Persicaria tinctorium* contained high levels of flavonol O-glycosides, with TMF as the glycosidic element. The results of Kimura et al. (2021) demonstrated the efficient digestion of TMF-O-glycosides and subsequent absorption of free TMF in the mouse intestine. Therefore, *Persicaria tinctorium* possessing TMF-O-glycosides was considered to be a useful source of medicinal and culinary with in vivo anti-inflammatory effects. Zhang et al. (2015) used *Helicobacter pylori* to establish a mouse model of gastritis, and the results of their study revealed that this *Polygonum capitatum* had therapeutic effects on gastritis and protects against gastric injury, and that flavonoid glycosides therein were potential medicines for the treatment of *Helicobacter pylori* gastritis.

The ethyl acetate and n-butanol extracts of HPP had anticancer effects on malignant tumour such as lung cancer and liver cancer. Meanwhile, the interaction of *Persicaria orientalis* with other herbs would have therapeutic effects on cancer (Gou et al., 2020). Nonetheless, human body functions following complex mechanisms with interactions among various factors. A single Chinese herb, HPP, was not able to provide a comprehensive treatment for all complex diseases. S Wan et al. showed that in the face of complex cardiovascular diseases, a single-drug-for-a-single-target therapeutic strategy failed to produce favourable pharmacological effects (Gou et al., 2018; Wan et al., 2021). Through the synergistic effect of the three active ingredients, namely, *Persicaria orientalis*, Quercetin, and Ouija-vinyl acetate, a potential therapeutic approach is developed for cardiovascular OQV-e, a component-based TCM for cardiovascular diseases, deserved further mechanistic and clinical studied. Therefore, in the face of complex diseases, HPP and other herbs need to work in synergy to achieve better therapeutic effects.

5. Perspectives for Future Development

The multiple bioactive compounds of HPP make it a natural herbal resource with vast potential applications. However, there are still knowledge gaps among its research that require further exploration and investigation. Firstly, the extraction and separation methods for various active ingredients in HPP need to be further optimized in order to improve the separation purity and extraction efficiency. Secondly, the biological activities and corresponding pharmacological effects of the various chemical active compounds in HPP need to be further investigated, so as to pave the way to identify new drugs in the future. Thirdly, expanding the breadth and depth of the application of HPP is crutial, especially in the food industry and the medical fields, by developing novel food and drugs incorporating the herb. Additionally, there is a need for in-depth research on the mechanism of action of the active compounds in HPP, and the requirement and dosage for its long-term use to ensure its effectiveness, safety and stability in practical applications. Reviewing the research on HPP and their applications provides the understanding on current research gaps while contemplating future development directions towards better applications for the health of human beings and sustainable development.

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Declaration of Conflicting Interests

All authors declare that they have no conflicts of interest.

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