Progress in Chemical Constituents and Bioactivities of *Perilla frutescens* (L.) Britt

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**Abstract**  *Perilla frutescens* (L.) Britt is an annual herb of the genus *Perilla* in the labiaceae. Its leaves, stalks and fruits can be used as folk medicine. The chemical components in *Perilla frutescens* (L.) Britt can be divided into volatile oil, terpenoids, triterpenoids, steroids, glycosides, phenylpropanoids and phenolic acids, flavonoids and pigments, which have anti-allergy, antibacterial, hypolipidemia, antioxidation, antitumor, antitussive and antipyretic activities. In this paper, we reviewed research progress of chemical constituents and pharmacological effects of *Perilla frutescens* to provide new ideas for subsequent development of *Perilla frutescens* (L.) Britt.

**Keywords**  *Perilla frutescens*, chemical constituent, bioactivities, progress

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**Introduction**

*Perilla frutescens* (L.) Britt is an annual erect herb of the genus *Perilla* in the labiaceae, with one species and three varieties. It is native to the Himalayas and central and southern China, and has been commercially cultivated on a large scale in the United States, Canada, Bhutan, India and other regions. *P. frutescens* is an important traditional Chinese medicine in China. Its leaves, stems and fruits can be used in folk medicine. The leaves of *Perilla frutescens* have the effect of relieving the surface and dispersing cold, regulating qi and stomach. *Perilla terreri* has the effect of regulating qi, relieving pain and calming fetus. *Perilla* seed has the effect of reducing qi and eliminating phlegm, relieving asthma and moistening intestines. Therefore, *perilla* has been added to more than ten kinds of Chinese herbal formulae such as Huoxiang Zhengqi Oral Liquid, Tongxuanlif Pills, Shensu Pills and Children Qingfei Pills. In this study, "chemical constituents of *Perilla frutescens*" and "activity of *Perilla frutescens*" were used as keywords, and relevant literatures and books were searched on SciFinder, web of Science, China Knowledge Infrastructure academic database and websites. We summarized the chemical constituents and activity of *Perilla frutescens* to provide a new idea for the development of *Perilla frutescens* in the future.

**Chemical Constituents**

Many researchers have carried out a lot of detailed studies on its chemical composition. Up to now, 74 compounds have been isolated and mainly classified into volatile oils, terpenoids, triterpenoids, steroids, glycosides, phenylpropanoids and phenolic acids, flavonoids, pigments, and so on (Figure 1).

**Volatile oils**

Volatile oils are the main component of leaves in *Perilla frutescens*. Thirteen compounds from volatile oils were identified by GC-MS, named perillahydate (1), limonene (2), elsholtziaketone (3), naginataketone (4), shisofuran (5), perilaketone (6), isoeogmaketone (7), perilene (8), citral (9), myristicin (10), dillapiole (11), elemicin (12), piperteneone (13). Compounds 1 and 2 were the most important volatile constituents.

**Terpenoids**

Five compounds have been isolated from *P. frutescens*, which were identified as perilloside A (14), perilloside B (15), perilloside C (16), perilloside D (17) and phytole (18).

**Triterpenoids**

Nine triterpenoids were isolated from the leaves of *P. frutescens*, named oleanolic acid (19), ursolic acid (20), tormentic acid (21), corosolic acid (22), 3-spicoricosolic acid (23), pomolic acid (24), hyptallic acid (25), augustic acid (26), 3-epimasilic acid (27). Among them, compound 26 constituted the most predominant triterpene acid.

**Steroids**

Four compounds were isolated from *P. frutescens*, which were identified as daucosterol (28), β-sitosterol (29), stigmastanol (30) and campesterol (31).

**Glycosides**

Eight glycosides have been isolated from *P. frutescens*, and named as benzyl-β-D-glucopyranoside (32), prunasin (33), sambunigrin (34), amygdalin position isomer (35), 5-β-D-glucopyranosyloxyjasmonic acid (36), 3-β-D-glucopyranosyloxyjasmonic acid (37), 3-β-D-glucopyranosyl-5-phenylvaleric acid (38) and methyl-α-D-galactoside (39). Compound 35 was the first report of cyanogenic glycosides in the Labiatae. The aglycone of compound 38 was found firstly in the nature.
Phenylpropanoids and phenolic acids

Eighteen phenylpropanoid and phenolic acids were isolated from *P. frutescens*, which were identified as perilloside E (40), eugenyl-β-D-glucopyranoside (41), rosmarinic acid (42), methyl rosmarinate (43), ethyl rosmarinate (44), 3,3’-O-diethoxy rosmarinic acid (45), methyl ferulate (46), protocatechuic aldehyde (47), caffeic acid (48), (Z,E)-2-(3,4-dihydroxyphenyl)-ethenylcaffeate (49), (Z,E)-2-(3,5-dihydroxyphenyl)-ethenylcaffeate (50), methyl caffeate (51), vinyl caffeate (52), trans-shisoyl caffeate (53), methyl-3,4-dihydroxybenzotate (54), 6,7-dihydroxy-coumarin (55), magnosalin (56), andamanicin (57).

Flavonoids

Nine flavonoids isolated from *P. frutescens* have been
reported, which were identified as apigenin (58), apigenin-7-glucuronic acid (59), apigenin-7-diglucuronic acid (60), luteolin (61), luteolin-7-glucoside (62), luteolin-7-O-diglucuronic acid (63), scutellarein (64), scutellarein-7-O-diglucuronic acid (65) and chrysoeriol (66). The main flavonoids in perilla leaf were compounds 58 and 60, and the content of flavonoids in the leaves of P. frutescens was the highest.\[14\]

**Pigments**

Eight pigments were identified from P. frutescens, namely as cyanidin (67), cyanin (68), β-carotene (69), lutein (70), neoxanthin (71), antheraxanthin (72), violaxanthin (73) crocetin (74).\[15,16\]

**Bioactivities**

**Antiallergic activity**

Liu et al.\[17\] reported that the volatile oil extracted from leaves of P. frutescens had anti-inflammatory effects, inhibiting the expression of endothelial cell adhesion molecule (ICAM-1) induced by TNF-α, preventing the adhesion of vascular endothelial cells to white blood cells, and inhibiting the migration of white blood cells to blood vessels.

Toshiaki et al.\[18\] found that rosmarinic acid (42) extracted from P. frutescens has a significant antiallergic effect, which is 8 times of the antiallergic effect of tranilast.

**Antibacterial activity**

Guo et al.\[19\] isolated and purified four antibacterial active ingredients 3,3′-O-diethoxy rosmarinic acid (45), luteolin (61), caffeic acid (48) and rosmarinic acid (42) from P. frutescens, which had inhibitory activity against the growth of Staphylococcus aureus and Escherichia coli, among which 3,3′-O-diethoxy rosmarinic acid (45) and rosmarinic acid (42) had stronger antibacterial activity.

Liu et al.\[19\] found that the extraction of P. frutescens var. acuta (Thunb.) Kudo with different solvents had a certain inhibitory effect on deep fungi, but it had a better antibacterial activity on dermatomycosis. The antibacterial activity was not different from that of Perilla frutescens var. typica (Makino) makino, and the acute toxicity of both showed no significant difference, indicating that P. frutescens var. typica (Makino) makino could be used as an alternative drug to P. frutescens var. acuta (Thunb.) Kudo.

**Hypolipidemia**

Xu et al.\[20\] found that the contents of triglyceride and low-density lipoprotein in the oil extracted from P. frutescens group rich in α-linolenic acid were significantly lower than those in the lard group by grouping mice fed with oil extracted from P. frutescens, lard and basic feed for 78 days, suggesting that the oil extracted from P. frutescens has a good effect of preventing and reducing blood lipids.

**Antioxidation activity**

Zang et al.\[21\] extracted rosmarinic acid (45) by the method of ultrasound-assisted extraction and purified it, then studied its antioxidation activity. The result revealed that antioxidative capacity of rosmarinic acid to DPPH, hydroxyl radical and superoxide anion was stronger than VC.

**Antitumor activity**

He et al.\[22\] obtained perilla protein by the method of ultrasound-assisted extraction. HepG2 cells were used as target cells to investigate the apoptosis effect of PSP3c on tumor cells. After the treatment with seven perilla peptides PSP3c, HepG2 cells will appear the phenomenon of nuclear condensation, fracture and marginalization. This phenomenon will increase with the increased concentration of PSP3c, especially in high concentration sample group can see chromosome fragments of apoptotic body formation. It showed PSP3c had a certain inhibitory effect on HepG2.

Wang et al.\[23\] reported that oleanolic acid (19), ursolic acid (20), rosmarinic acid (45), and luteolin (61) had a certain inhibitory effect on tumor cells, which could resist breast cancer, cervical cancer, endometrial cancer, prostate cancer, nasopharyngeal cancer, lung cancer, etc.

**Antitussive activity**

The asthmatic mice model was established by intraperitoneal injection of ovalbumin and atomization attack. Perilla seed oil was injected on the 11th day for intervention. Then EOS cells in peripheral blood and lung tissue were counted and compared. It was found that EOS cells in Perilla seed oil were significantly reduced compared with asthma group.\[24\]

**Antipyretic activity**

The mice were subcutaneously injected with 0.6% 2,4-dinitrophenol suspension on the back to raise their body temperature, and then treated with analgin and high-dose perilla leaf volatile oil by gavage, and their body temperature was measured every 30 min. The results showed that the high-dose group of perilla leaf volatile oil began to cool down 30 min after administration, and there was no significant difference compared with analgin.\[25\]

**Conclusions and Perspectives**

In a word, perilla is a kind of health resource with great development value. The chemical constituents of Perilla frutescens can be divided into volatile oil, terpenoids, triterpenoids, steroids, glycosides, phenylpropanoid and phenolic acids, flavonoids, pigments, and so on. Because of its various components, it has a wide range of pharmacological effects, such as antiallergy, antibacterial, hypolipidemic, antioxidant, anti-tumor, antiasthma activities, and so on. However, the research on its pharmacological mechanism is not deep enough, which is unfavorable to the application of Perilla in the treatment of specific diseases. It is worthy for us to focus on research of pharmacological mechanism.

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**Conflict of Interest**

The authors declare no conflict of interest.
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