



A Phytopharmacological Overview on *Perilla frutescens*

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ABSTRACT

Since the dawn of civilization, human being is dependent on higher plant species for their foods, clothing, shelter and health care needs. The plant species were the main parts of folk medicine practiced by the ancient peoples in different parts of the world. *Perilla frutescens* (L.) is an annual short-day plant belonging to the family Labiatae which is used by ancient people in different parts of world. The *P. frutescens* have been used as an important traditional herbal medicine for treating various disease including depression, anxiety, tumor, cough, antioxidant, allergy, intoxication, and some intestinal disorders. *Perilla* seeds contain considerably high levels (approx. 60%) of α -linolenic acid, which can be expected to possess various biological activities. The leaves are said to be helpful for asthma, colds and flu's. The current review is about collection of all the available data on identified chemical constituents as well as the reported pharmacological activities of *Perilla frutescens*.

Keywords: *Perilla frutescens*, phytochemical, antioxidant activity.

INTRODUCTION

Lamiaceae, also called Labiatae, the mint family of flowering plants, with 236 genera and more than 7,000 species, the largest family of the order Lamiales. It is important to humans for herb plants useful for flavour, fragrance, or medicinal properties. Most members of the family have square stems; paired, opposite, simple leaves; and two-lipped, open-mouthed, tubular corollas (united petals), with five-lobed, bell-like calyxes (united sepals).

The 40 to 50 species of the genus *Lamium* are known as dead nettles; they are low weedy plants that are sometimes cultivated. There are about 350 species in the genus *Thymus*, all Eurasian. Wild thyme (*T. serpyllum*), with scented leaves, is a creeping plant that is native in Europe but naturalized in eastern North America. Its foliage and flower heads resemble those of garden thyme (*T. vulgaris*), the source of the kitchen herb¹.

Perilla is cultivated as one commercial oilseed crop in other countries like Japan, Korea and northern India²⁻⁴. Now, it has also been introduced to Europe, Russia and USA as an oilseed crop⁵.

Botanical Description

Perilla frutescens, commonly called beefsteak plant, is an upright, bushy annual that is native from the Himalayas to Southeast Asia. It is related to coleus and basil. It has become a very popular foliage annual and salad herb plant. It grows to 1-3' (less frequently to 4') tall, wrinkled, serrate, broad ovate, medium green leaves (to 4" long) are sometimes tinged with purple leaves⁶. Several analyses have reported that this characteristic odor is due to the various essential oil components which affect their nutritional and medical function and toxicity⁷⁻⁹.

Perilla plants have distinctive square stems and four stamens as with most species in the family Lamiaceae. However, the best diagnostic features of *Perilla* are the net-patterned testa of the nutlets as well as the typical minty odor of the crushed foliage¹⁰⁻¹¹.

Perilla frutescens synonym is *Ocimum frutescens* L. It is known by different name in different country. In Chinese: *zisu*, English: *Perilla*, Wild *Coleus*, Folk: *Bhanjeer*, *Bantulasi*, *Banjiraa*, *Bhasindi*, French: *Shiso*, Korea: *deulkkae* or *tŭlkkae*, Japanese: *shiso*, Polish: *Pachnotka zwyczajna*, Thai: *ขมิ้น*, Vietnamese: *Tía tó*¹².

Traditional uses

Perilla frutescens (L.) have been used as an important traditional herbal medicine for treating various disease including depression, anxiety, tumor, cough, antioxidant, allergy, intoxication, and some intestinal disorders. In northern India the stem of the plant is traditionally used as an analgesic and anti-abortive agent. The leaves are said to be helpful for asthma, colds and flu's, and regulate stomach function¹³. *Perilla* is listed in the Chinese Pharmacopoeia and has been used for centuries as a medicinal plant for asthma, influenza, cough, chronic bronchitis and vomiting¹⁴⁻¹⁵.

Edible young leaves of *perilla* are cooked as vegetable. Older leaves are used as a garnish or flavouring, the leaves can also be dried for later use. The juice of the leaves is applied to cuts and wounds. Seed oil is used as edible oil for centuries by local people of northern India and also used by local women of the region for massaging newborn infants. The seeds are used as spice and also roasted to prepare a very delicious sauce (chutney), one of the famous traditional dishes of Uttarakhand, India⁴.



This plant is commonly known as “Dlggae” in Korea and the leaves are widely used in sushi and herb salad and as a spice, garnish, and food colorant. Perilla seeds are a traditional source of oils produced in Korea¹⁶. A *perilla* line from Bangladesh is a potential commercial source of rosfuran, a compound of interest in flavoring and perfumery¹⁷, Asian herbalists prescribe *perilla* for cough and lung afflictions, influenza prevention, restless fetus, seafood poisoning, incorrect energy balance, etc. *Perilla* alcohol prepared from perilla aldehyde, is used in fragrances, and has legal food status in the United States and Europe¹⁸.

The leaves of *Perilla frutescens* Britton are one of the most popular garnishes in Japan, used as an antidote for fish and crab meat allergy or as a food colorant¹⁹. Leaves of the plants are used in traditional, Japanese herbal medicine (Kampo medicine). The quality of Perilla plants used for Kampo medicine is determined by the concentrations of essential oil components in leaves and the appearance such as redness of leaves attributed to anthocyanin²⁰. Recently, Kampo medicine has become popular worldwide as an alternative therapy²¹⁻²³.

Phytochemical

In one study the glycosidic constituents of two varieties of *Perilla frutescens* have been compared. A new phenylpropanoid glucoside named perilloside E has been isolated from the fresh leaves of the purple type plant²⁴. Besides 7-(2-*O*- β -D-glucuronyl- β -D-glucuronyloxy)-5,3',4'-trihydroxyflavone, scutellarin, rosmarinic acid and caffeic acid, two cyanogenic glycosides have been isolated from the dried leaves of *Perilla frutescens* var. *acuta*. One of them is prunasin and the other is (*R*)-2-(2-*O*- β -D-glucopyranosyl- β -D-glucopyranosyloxy)-phenylacetone nitrile, a new isomer of amygdalin²⁵.

Perilla seeds are a good source of linolenic acid, linoleic acid, oleic acid, stearic acid, and palmitic acid²⁶⁻²⁷. Major fatty acids of the oil are unsaturated fatty acids (USFAs) like γ -linolenic acid (54-64%), oleic acid (14-23%), linoleic acid (11-16%) and the saturated fatty acids (SFAs) (6.7-7.6%). The Perilla seeds are small and weight about 4 gms/1000 seeds²⁸. A new monoterpene glucoside named perilloside A has been isolated from the fresh leaves of *Perilla frutescens*. Its structure has been characterized on the basis of spectral and chemical evidence²⁹. Three new monoterpene glucosides have been isolated from the fresh leaves of *Perilla frutescens*. The structures were determined on the basis of spectral and chemical evidence³⁰. In a study Perilla seed collected from five provinces in China were analyzed to determine their fatty acid composition. Result shows that oil from seeds obtained in regions with lower average growth temperature has relatively higher percentage of unsaturated fatty acids³¹.

Active Components of Perilla seed extract

Perilla seed extract is rich in polyphenols such as luteolin, chrysoeriol and apigenin as aglycons. Luteolin and so on are main polyphenols and main active ingredients in Perilla seed extract to shown anti-dental caries and antiperiodontal disease effect³².

Another study in the year 2009 Gu, *et al*³³ Fig. 2 four antioxidant compounds from fruit of *Perilla frutescens* were isolated. These compounds were identified as rosmarinic acid (1), luteolin (2), apigenin (3), and chrysoeriol (4) (Figure 1 by means of UV, NMR, and ESI MS).

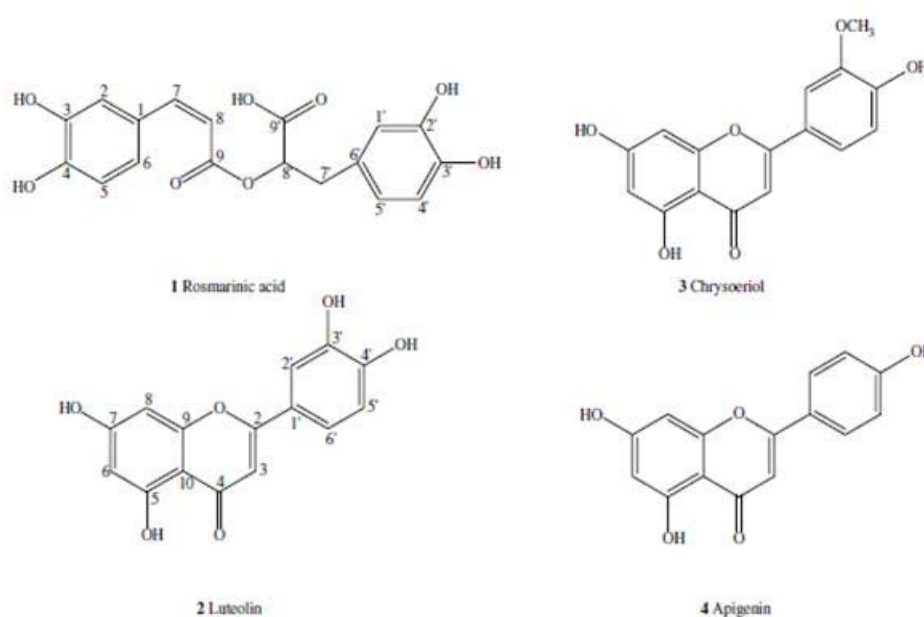


Figure 1: Chemical structures of compounds (1–4) isolated from fruit of *Perilla frutescens* var. *acuta*; Source: Gu *et al*³³

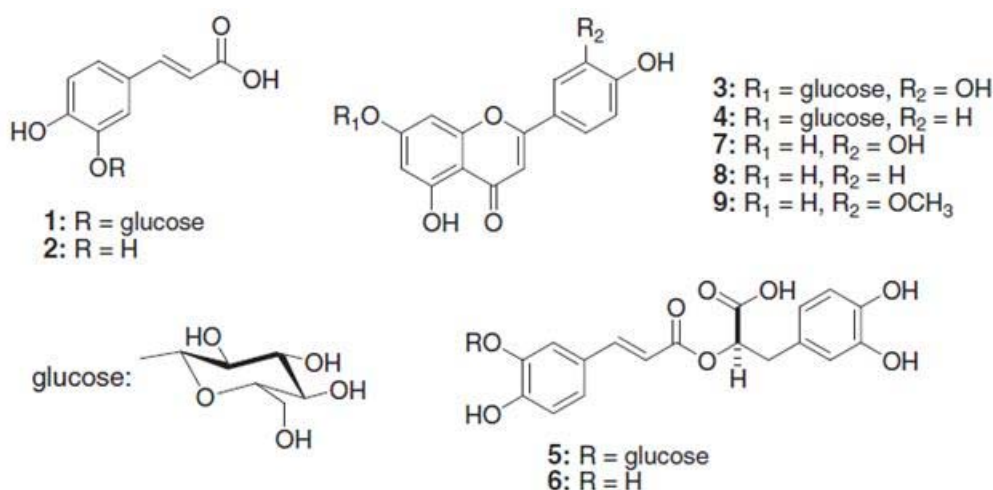


Figure 2: Chemical structures of the phenolic compounds isolated from the seeds of perilla; Source: Lee *et al*³⁴

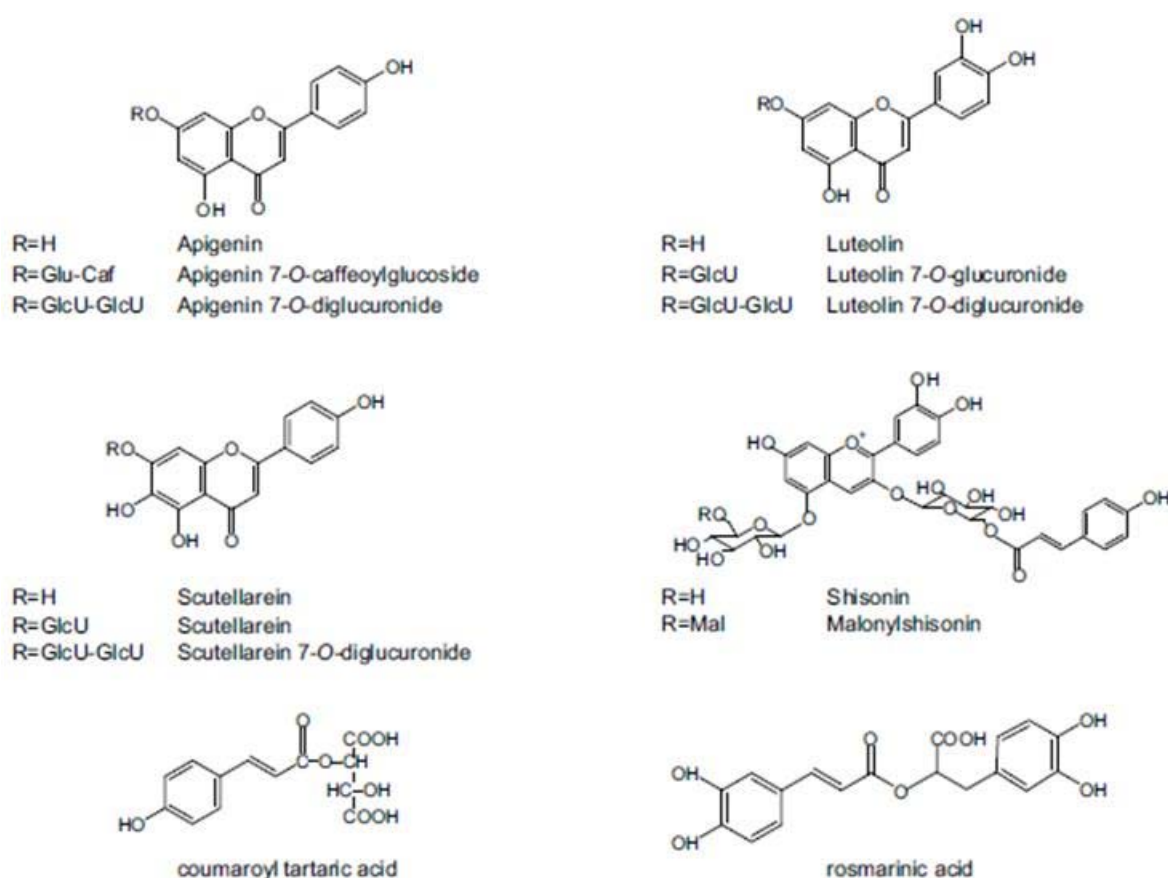


Figure 3: Chemical structures of major polyphenolic compounds in *P. frutescens* leaves; Source: Meng *et al*³⁵

Lee *et al*³⁴ in year 2013 investigate phenolic compound in the seeds of various perilla (*Perilla frutescens*) cultivars. Phenolic compounds were characterized by nuclear magnetic resonance (NMR) spectroscopy, and ultra performance liquid chromatography with photodiode array detector and electrospray ionisation/mass (UPLC-PDA-ESI/MS) analysis. Nine compounds were elucidated as caffeic acid-3-O-glucoside (1), caffeic acid (2), luteolin-7-O-glucoside (3), apigenin-7-O-glucoside (4), rosmarinic acid-3-O-glucoside (5), rosmarinic acid (6), luteolin (7), apigenin (8), and chrysoeriol (9) Fig. 2. The individual and total phenolic contents were remarkably different.

Six flavonoids (apigenin 7-O-caffeoylglucoside, scutellarein 7-O-diglucuronide, luteolin 7-O-diglucuronide, apigenin 7-O-diglucuronide, luteolin 7-O-glucuronide, and scutellarein 7-O-glucuronide) were isolated from leaves of *Perilla frutescens*³⁵ as shown in figure 3.

A study characterises the metabolites of *Perilla frutescens* var. *crispa* leaf and flower for by NMR. Results showed higher metabolite content in leaves compared to flowers, showing the presence of amino acids, organic acids, saccharides and large amounts of aromatic compounds, mainly in the form of rosmarinic acid. Cultivated *Perilla*

has been also confirmed to be a good bee plant for both nectar and pollen³⁶.

Antioxidant activity of fruit

Gu *et al.*³³ for the first time isolated four antioxidant compounds from fruit of *P. frutescens* var. *acuta*. They determined the antioxidant activity of fruit of *Perilla frutescens* using 1,1-diphenyl-2-picryl-hydrazyl radical (DPPH). These compounds were identified as rosmarinic acid, luteolin, apigenin, and chrysoeriol. Rosmarinic acid and luteolin showed significant DPPH scavenging capacities, with IC₅₀ values of 8.61 and 7.50 mM, respectively.

Lee *et al.*³⁴ investigate phenolic compound profiles and antioxidant properties in the seeds of various perilla (*Perilla frutescens*) cultivars. The 80% methanol extract (50 µg/ml) of this species showed potent antioxidant activities against 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) radicals. Another study demonstrated that 2',3'-dihydroxy-4',6'-dimethoxychalcone (DDC) contained in green perilla enhanced cellular resistance to oxidative damage through activation of the Nrf2-antioxidant response element (ARE) pathway³⁷. One study was conducted to investigate the profiles of phenolic phytochemicals in the leaves of Korean purple perilla using reversed-phase C18 column chromatography and HPLC with DAD-ESI/MS analysis. Changes in their contents were also the first reported through eight different harvest times during two months³⁸. In another study the of *Perilla frutescens* shows antioxidant activities against LDL oxidation *in vitro* and *in vivo*³⁹⁻⁴⁰.

In one study, investigation on the hepatoprotective effects of *P. frutescens* leaves grown in different concentrations of sucrose was done. Result shows that sucrose-treated perilla leaves, which had better antioxidant activities than untreated leaves, can be used as a potential dietary source⁴¹.

Antidepressant-like Effect of l-perillaldehyde

l-Perillaldehyde (PAH) is a major component in the essential oil containing in Perilla leaf and its antidepressant activity was studied in 2011 on mice. Results suggest that the inhalation of l-Perillaldehyde shows antidepressant-like activity through the olfactory nervous function⁴².

Anti-allergic and Anti-inflammatory Activity

Ueda *et al.*⁴⁴ in year 2002 isolated luteolin, rosmarinic acid and caffeic acid as active components from the perilla leaf extract. Among the isolated compounds, only luteolin showed *in vivo* activity. Oral administration of the perilla leaf extract (PLE) to mice inhibits inflammation, allergic response, and tumor necrosis factor-α production. Another study was conducted to evaluate its anti-allergic effect of perilla aqueous extract on mice which shows that perilla and rosmarinic acid are potentially promising agents for the treatment of allergic diseases⁴³. Another

study observed the effects of perilla seed extracts in volunteers with allergic symptoms such as sneezing, nasal obstruction, and itchy skin and eyes. 20 participants were given perilla seed extracts for 2-4 weeks, and their change in symptoms was evaluated. Symptoms were improved in all 20 patients, with significant improvements in sneezing (almost 40%), stuffed nose (over 60%) and itchy eyes (50%)⁴⁴. One study shows that isogomaketone isolated from *perilla frutescens* shows the anti-inflammatory activity⁴⁵.

Anti-HIV-1 activity

In one study the aqueous extract of *Perilla frutescens* showed potent anti-HIV-1 activity. The active components in the extract samples were found to be water-soluble polar substances. The aqueous extract of *Perilla frutescens* inhibited giant cell formation in co-culture of Molt-4 cells with and without HIV-1 infection and showed inhibitory activity against HIV-1 reverse transcriptase⁴⁶.

Antitumor activity

Lin *et al.*⁴⁷, 2007 evaluated the effects of *Perilla frutescens* leaf extract (PLE) on proliferation and apoptosis inducing in human hepatoma HepG2 cells using a cell proliferation assay, flow cytometry, and cDNA microarrays. Result shows that growth inhibitory and apoptosis inducing effect of *Perilla frutescens* extract on human hepatoma HepG2 cells. There are many reports which support the anti-cancer activity of *Perilla frutescens*⁴⁸⁻⁵⁰. Rosmarinic acid, frequently found as a secondary metabolite in herbs and medicinal plants, has exhibited antioxidative and anti-inflammatory activities. Rosmarinic acid inhibited Jurkat cell proliferation by altering the expression of cyclins and cyclin-dependent kinase inhibitors and induced apoptosis most likely acting through the mitochondrial pathway and possessed no anti-oxidant properties⁵¹.

Antibacterial activity

In one study Perilla seed extract was examined for its antibacterial activity against oral cariogenic streptococci and periodontopathic *porphyromonas gingivallis*. The ethanolic extract of defatted perilla seed weakly inhibited the growth of the oral pathogenic bacterial strain. The ethyl acetate extract exhibits strong antibacterial activity against

oral streptococci and various strain *porphyromonas gingivallis*. Luteolin and quercetin showed marked antibacterial activity against oral bacterial tested⁵². This study is also supported by another study in which polyphenol from Perilla seed extract shows anti-dental caries and antiperiodontal disease effect³².

Miscellaneous use

Perilla oil has its many other benefits. In animal experiments, perilla oil proved superior to either soybean or safflower oil in inhibiting mammary, colon and kidney cancers⁵³⁻⁵⁵. In one study, the preparation and



trophic characterization of perilla chewable tablet were investigated. Results from nutrient analysis showed that perilla chewable tablet was rich in essential vitamins and mineral substances, which are good for human health⁵⁶. In another study has been conducted to study the effects of increasing levels of *perilla frutescens* L. seed (PFS) in the diet on the performance, meat quality traits, lipid oxidation and fatty acid profile of rabbit fat and meat. These results shown that the use of a diet supplemented with PFS is effective in reducing the saturation, atherogenic and thrombogenic indexes in the rabbit tissues²⁷. In another study rosmarinic acid, a major polyphenolic component of *Perilla frutescens*, reduces lipopolysaccharide (lps)-induced liver Injury in d-galactosamine (d-galn)-sensitized mice⁵⁷.

Toxicity

Perilla is ordinarily avoided by cattle but has been implicated in cattle poisoning. Plants are most toxic if cut and dried for hay late in the summer, during seed production. Perilla ketone causes pulmonary edema (fluid in the lung cavity) in many animal species, although not in pigs or dogs. In Japan 20 to 50% of long-term workers in the perilla industry develop dermatitis on their hands due to contact with perillaldehyde⁵⁸ (<http://www.hort.purdue.edu>). Perilla toxicity is reviewed by Brenner³ in the year 1993. One report available on determination of toxic perilla ketone from five *Perilla frutescens*⁵⁹.

CONCLUSION

The use of medicinal plants for the treatment of various diseases has being dated from ancient times in various parts of world. Recent trends have shown a drastic rise among people in developed nations in the use of herbal medicines for the cure of several disorders as they provide better therapeutic efficacy with lesser side effects. *Perrilla frutescens* is a widely traditionally used and potent medicinal plant amongst all the thousands of medicinal plants. The pharmacological activities reported in the present review confirm that the therapeutic value of *Perrilla frutescens* is much more. The presence of phytochemical constituents and pharmacological activities proved that the plant has a leading capacity for the development of new good efficacy drugs in future.

REFERENCES

- <http://www.britannica.com/EBchecked/topic/328710/Lamiaceae>.
- Choi IS, Son SY, Kwon OH. Effect of seedling age and planting density on the yield and its component of *Perilla* (*Ocymcides* Var. *Typica* Makino) intercropped with tobacco or after cropped, Korean Soc. Hort. Sci., 25, 1980, 68-75.
- Brenner DM . *Perilla*: Botany, uses and genetic resources new crops, (edited by J.Janick and J.E. Simon). New York: Wiley, 1993, 322-328.
- Negi VS, Rawat LS, Phondani PC, Chandra A. *Perilla frutescens* in Transition: a medicinal and oil yielding plant need instant conservation, a case study from Central Himalaya, India. *Environ. We Int. J. Sci. Tech.*, 6, 2011, 193-200.
- Nitta M, Lee JK, Ohnishi O. Asian *Perilla* crops and their weedy forms: their cultivation, utilization and genetic relationships. *Econ. Bot.*, 57, 2003, 245-253.
- <http://www.missouribotanicalgarden.org/gardens-gardening/your-garden/plantfinder/plant-details/kc/b761/perilla-frutescens.aspx>.
- Ito M, Toyoda M, Honda G. Chemical composition of essential oil of *Perilla frutescens*. *Nat. Med.*, 53, 1999a, 32-36.
- Ito M, Toyoda M, Honda G (1999b). Essential oil composition of hybrids and amphidiploids of Japanese wild *Perilla*. *Nat. Med.* 53, 1999b, 118-122.
- Ito M, Kiuchi F, Yang LL, Honda G. A new type of essential oil from *Perilla frutescens* from Thailand. *J. Essent. Oil Res.*, 14, 2002, 416- 419.
- Miller W. *Perilla*. In: *The Standard Cyclopedia of Horticulture*, (edited by L.H. Bailey), London, Macmillan, 1992, 2553.
- Tanaka T. *Tanaka's cyclopedia of edible plants of the world*. Keigaku Publishing Company: Tokyo, 1976.
- <http://medplants.blogspot.com/2012/08/perilla-frutescens-shiso-pachnotka.html>
- Saklani S, Chandra S, Gautam AK. Phytochemical investigation and contribution of *Perilla frutescens* as spices in traditional health care system. *International Journal of Pharmacy Technology*, 3(4), 2011, 3543-3554.
- Ueda H, Yamazaki C, Yamazaki M. Luteolin as an Anti-inflammatory and Anti-allergic Constituent of *PerillaFrutescens*. *Biol. Pharm. Bull.*, 25(9), 2002, 1197–1202.
- Takano H, Osakabe N, Sanbongi C, Yanagisawa R, Inoue K, Yasuda A, Natsume M, Baba S, Ichiishi E, Yoshikawa T (2004). Extract of *Perilla frutescens* enriched for rosmarinic acid inhibits seasonal allergic rhinoconjunctivitis in humans. *Exp. Biol. Med.*, 229, 2004, 247-254.
- Ha TJ, Lee JH, Lee MH, Lee BW, Park HSKCH, Shim KB, Kim HT, Baek IY, Jang DS. Isolation and identification of phenolic compounds from the seeds of *Perilla frutescens* (L.) and their inhibitory activities against α -glucosidase and aldose reductase. *Food Chemistry*, 135, 2012, 1397–1403.
- Misra, L.N. and Husain, A. The essential oils of *Perilla ocimoides*: a rich source of rosefuran. *Planta Med*, 53, 1987, 379-390.
- Opdyke, D.L.J. Monographs on fragrance raw materials. *Food Cosmet. Toxicol* 19, 1981, 237-254.
- Makino T, Furuta Y, Wakushima H, Fujii H, Saito K, Kano Y. Anti-allergic Effect of *Perilla frutescens* and Its Active Constituents. *Phytother. Res.*, 17, 2003, 240–243.
- Nagao, Y., Komiya, T., Fujioka, S., Matsuoka, T. Studies on the quality of the Chinese drug "Soyo" and the cultivation of the original plant. *J. Takeda Res. Lab.*, 33, 1974, 111–118.



21. Matsumoto, M., Inoue, K., Kajii, E. Integrating traditional medicine in Japan: the case of Kampo medicines. *Comp. Ther. Med.*, 7, 1999, 254–255.
22. Kanda, T., Yamakawa, J., Moriya, J., Saegusa, S., Kawaura, K., Yu, F., Kusaka, K., Takahashi, T., Itoh, T. Globalization of Kampo medicine. *J. Kanazawa Med. Univ.*, 30, 2005, 297–301.
23. Oka, T. The role of Kampo (Japanese traditional herbal) medicine in psychosomatic medicine practice in Japan. *Intern. Congr. Ser.* 1287, 2006, 304–308.
24. Fujita T, Funayoshi A, Nakayama M. A phenylpropanoid glucoside from *Perilla frutescens*. *Phytochemistry* 37(2), 1994, 543-546.
25. Aritomi M, Kumori T, Kawasaki T. Cyanogenic glycosides in leaves of *Perilla frutescens* var. *acuta*. *Phytochemistry*, 24(10), 1985, 2438-2439.
26. Chang, H. H., Chen, C. S., & Lin, J. Y. Dietary perilla oil lowers serum lipids and ovalbumin-specific IgG1, but increase total IgE levels ovalbumin challenged mice. *Food and Chemical Toxicology*, 47, 2009, 848–854.
27. Peiretti PG, Gasco L, Brugiapaglia A, Gai F. Effects of perilla (*Perilla frutescens* L.) seeds supplementation on performance, carcass characteristics, meat quality and fatty acid composition of rabbits. *Livestock Science*, 38, 2011, 118–124.
28. Asif M. Chemical and Nutritional Characterization of *Perilla frutescens* seed Oil. *The Libyan J Pharm & Clin Pharmacol*, 1, 2012, 623012.
29. Fujita T, Nakayama M. Perilloside a, a monoterpene glucoside from *Perilla frutescens*. *Phytochemistry*, 31(9), 1992, 3265-3267.
30. Fujita T, Nakayama M. Monoterpene glucosides and other constituents from *Perilla frutescens*. *Phytochemistry*, 34(6), 1993, 1545-1548.
31. Ding Y, Neo M, Yan HU, Lingling SHI, Chao MA, LIU YJ. Characterization of fatty acid composition from five perilla seed oils in China and its relationship to annual growth temperature. *Journal of Medicinal Plants Research*, 6(9), 2012, 1645-1651.
32. www.oryza.co.jp/html/english/pdf/oral2.pdf
33. Gu L, Wua T, Wang Z. TLC bioautography-guided isolation of antioxidants from fruit of *Perilla frutescens* var. *acuta*. *Food Science and Technology*, 42, 2009, 131–136.
34. Lee JH, Park KH, Lee MH, Kim HT, Seo WD, Kim JY, Baek I, Jang DS, Ha TJ. Identification, characterisation, and quantification of phenolic compounds in the antioxidant activity-containing fraction from the seeds of Korean perilla (*Perilla frutescens*) cultivars. *Food Chemistry*, 136, 2013, 843–852.
35. Meng L, Lozano Y, Bombarda I, Gaydou EM, Li B. Polyphenol extraction from eight *Perilla frutescens* cultivars. *C. R. Chimie* 12, 2009, 602-611.
36. Consonni R, Cagliani LR, Docimo T, Romane A, Paola Ferrazzi P. *Perilla frutescens* (L.) Britton: honeybee forage and preliminary results on the metabolic profiling by NMR spectroscopy. *Natural Product Research: Formerly Natural Product Letters*, 2012, DOI:10.1080/14786419.2012.751598.
37. Izumi Y., Matumura A., Wakita S., Akagi K., Fukuda H., Kume T., Irie K., Takatori Y., Sugimoto H., Hashimoto T., Akaike A. Isolation, identification, and biological evaluation of Nrf2-ARE activator from the leaves of green perilla (*Perilla frutescens* var. *crispa* f. *viridis*). *Free radical Biology and medicine*, 53(4), 2012, 669–679.
38. Kang NS, Jin Hwan Lee JS. Characterisation of phenolic phytochemicals and quality changes related to the harvest times from the leaves of Korean purple perilla (*Perilla frutescens*) *Food Chemistry*, 124, 2011, 556–562.
39. Saita E, Kishimoto Y, Iizuka M, Suzuki K, Toyozaki M, Nagai M, Murakami MK, Sugihara N, Takenaka K, Tani M, Kondo K. The antioxidant activities of *perilla frutescens* against LDL oxidation *in vitro* and *in vivo*. *Atherosclerosis*, 10(2), 2009.
40. Saita, E., Kishimoto, Y., Tani, M., Iizuka, M., Toyozaki, M., Sugihara, N., & Kondo, K. Antioxidant activities of *Perilla frutescens* against low-density lipoprotein oxidation *in vitro* and in human subjects. *Journal of Oleo Science*, 61, 2012, 113–120.
41. Yang SY, Hong C, Lee H, Park S, Park B, Lee KW. Protective effect of extracts of *Perilla frutescens* treated with sucrose on tert-butyl hydroperoxide-induced oxidative hepatotoxicity *in vitro* and *in vivo*. *Food Chemistry*, 133, 2012, 337–343.
42. Ito N, Nagai T, Oikawa T, Yamada H, Hanawa T. Antidepressant-like Effect of l-perillaldehyde in Stress-induced Depression-like Model Mice through Regulation of the Olfactory Nervous System. *Evidence-Based Complementary and Alternative Medicine Article ID 512697*, 2011. Doi:10.1093/ecam/nen045
43. Makino T, Furuta Y, Wakushima H, Fujii H, Saito K, Kano Y. Anti-allergic Effect of *Perilla frutescens* and Its Active Constituents. *Phytother. Res.*, 17, 2003, 240–243.
44. <http://www.aor.ca/assets/Research/pdf/Perilla%20An%20Allergy%20Fighting%20Herb.pdf>
45. Park YD, Jin CH, Dae Seong Choi DS, Myung-Woo Byun MW, Jeong Y. Biological Evaluation of Isoeugenol Isolated from *Perilla frutescens* and its Synthetic derivatives as anti-inflammatory agents *Arch Pharma Res*, 349(8), 2011, 1277-1282.
46. Yamasaki K, Nakano M, Kawahata T, Mori H, Otake T, Ueba N, Oishi I, Inami R, Yamane M, Nakamura M, Murata H, Nakanishi T. Anti-HIV-1 activity of herbs in Labiatae. *Biol Pharm Bull.* 21(8), 1998, 829-33.
47. Lin CS, Kuo CL, Wang JP, Cheng JS, Huang ZW, Chen CF. Growth inhibitory and apoptosis inducing effect of *Perilla frutescens* extract on human hepatoma HepG2 cells. *Journal of Ethnopharmacology*, 112(3), 2007, 557–567.
48. Asif, M. Health effects of omega-3,6,9 fatty acids: *Perilla frutescens* is a good example of plant oils. *Oriental Pharmacy and Experimental Medicine*, 11, 2011, 51–59.
49. Osakabe, N., Yasuda, A., Natsume, M., & Yoshikawa, T. Rosmarinic acid inhibits epidermal inflammatory responses: Anticarcinogenic effect of *Perilla frutescens* extract in the murine two-stage skin model. *Carcinogenesis*, 25, 2004, 549–55.



50. Ueda, H., Yamazaki, C, Yamazaki, M. Inhibitory effect of Perilla leaf extract and luteolin on mouse skin tumor promotion. *Biological & Pharmaceutical Bulletin*, 26, 2003, 560–563.
51. Kolettas E, Thomas C, Leneti E, Ioannis Skoufos I, Mbatsi C, Sisoula C. Rosmarinic acid failed to suppress hydrogen peroxide-mediated apoptosis but induced apoptosis of Jurkat cells which was suppressed by Bcl-2. *Molecular and Cellular Biochemistry*, 285(1-2), 2006, 111-120.
52. Yamamoto H, Ogawa T. Antimicrobial activity of perilla seed polyphenols against oral pathogenic bacteria. *Biosci Biotechnol Biochem*, 66, 2002, 921-924,
53. Okuyama, H. Minimum requirements of n-3 and n-6 essential fatty acids for the function of central nervous system and for the prevention of chronic disease (uses refer in cancer and other uses), *Proceedings of the Society for Experimental Biology and Medicine*, 200, 1992, 174–176.
54. Onogi N, Okuno M, Komaki C, Moriwaki H, Kawamori T, Tanaka T. Suppressing effect of perilla oil on azoxymethane-induced foci of colonic aberrant crypts in rats, *Carcinogenesis* 17, 1996, 1291–1296.
55. Tripathi, K. D. *Drugs for constipation and diarrhoea, essentials of medical pharmacology*, 5th edition, New Delhi: Jaypee Brothers Medical Publishers (P) Ltd, 2008, 610–623.
56. Wu J, Yang C, Rong Y, Wang Z. Preparation and Nutritional Characterization of Perilla Chewable Tablet. *Procedia Engineering*, 37, 2012, 202 – 207.
57. Osakabe N, Yasuda A, Natsume M, Sanbongi C, Kato Y, Osawa T, Yoshikawa T. Rosmarinic acid, a major polyphenolic component of *Perilla frutescens*, reduces lipopolysaccharide (lps)-induced liver injury in d-galactosamine (d-galn)-sensitized mice. *Free Radical Biology & Medicine*, 3(6), 2002,798–806.
58. <http://www.hort.purdue.edu/newcrop/cropfactsheets/perilla.pdf>
59. Waldeck FM, Sitzmann J, Schnitzler WH, Grasmann J. Determination of toxic perilla ketone, secondary plant metabolites and antioxidative capacity in five *Perilla frutescens* L. varieties *Food and Chemical Toxicology*, 48, 2010, 264–270.

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