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Review Article

BIOLOGICAL IMPORTANCE AND HEALTH EFFECT OF *Perilla frutescence* PLANT

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ABSTRACT

The study was designed to study the Biological importance and nutritional benefits of *Perilla frutescence* plant. This plant has very high biological activities. It contains various phyto-constituents such as different phenolic compounds (like rosemarinic acids, luteolin chrysoeriol, quercetin, catcehin, apigenin, etc), vitamins, minerals etc. Perilla seeds contained 30-40% fixed oil, contained both saturated (palmitic acid 5-7%, stearic acid 1-3%), unsaturated (UFAs) or polyunsaturated (PUFAs) (oleic acid 12-22%, linoleic acid 13-20%, γ-linolenic acid 0-1%, α-linolenic acid 52-64%, icosanoic acid 0-1%) fatty acids. Perilla oil is highly unsaturated oil among the all current discovered natural vegetable oils. Whole perilla plant has many important functions on improving and accelerating human health and is effective in prevention of various diseases.

Key words: *Perilla frutescence,* biological activities, phyto-constituents, polyphenols, polyunsatured fatty acids.

INTRODUCTION

The *Perilla frutescens* (Lamiaceae) is commonly known as perilla or sisho. Perilla is native to E. Asia and it is a traditional crop of China, Japan, Korea and Thailand. In India it is found in North hill regions. It is an annual, herbaceous, approximate three feet tall, aromatic plant, stems are square, reddish-purple leaves and flowers are small and tubular. Perilla is widely cultivated as a source of medicine, spices and edible oil. Perilla seeds are small, weight about 4g/1000 seeds. Other species of perilla are also found such as *P.calophylla, P.abrotanoides, P.americana, P.alliacea* and *P.crispum* (Longvah *et al*., 2000; Diggs *et al.,* 1999; Borchers *et al.,* 1997; Bown 1995; Brenner, 1993).

Chemical constituents

The perilla plant contained different phytoconstituents like flavonoid aglycons, luteolin, apigenin, chrysoeriol, rosemarinic acid, caffeic acid, monoterpenes, alkaloids, xanthine oxidase, ascorbic acid, β-carotene, citral, dillapiol, elemicin, limonene, myristicin, protocatechuic acid, etc (Figure 1). The seeds of perilla having different saturated and unsaturated fatty acids such as palmitic acid, oleic acid, linolenic acid, γ-linolenic acid and α-Linolenic acid (Figure 2). Perilla also contained volatile oil with several chemotype such as perilla aldehyde (PA), perilla ketone (PK), isoegoma ketone (IK) and perillene (PL), elsholzia ketone (EK), anginas ketone (AK), citral (C), isoegoma ketone (IK), phenyl propanoids (PP): myricitin, dillapiol, elemicin, and safrole. Other constituents are limonene, linalool, β-caryophyllene, menthol, α-penene, and elemicin. It is also contained rose furane (Siriamornpun *et al*., 2006; Peng *et al.,* 2005; Gulcin *et al*., 2005; Osakabe *et al*., 2002).

Seeds oil

The seeds of perilla produced approximate 30-40% oil. It is a light yellow clear transparent liquid, without any flavor. It contain different saturated (palmitic and stearic) and unsaturated fatty acids includes (linolenic, linoleic, and oleic acid) etc (Table I). It is a very rich source of α-linolenic acid or ω-3FA, which is PUFAs. The linoleic and linolenic acids are "essential oil" because they cannot be synthesized by the body and must be supplied in the diet. However, Arachidonic acid (AA) can be synthesized by the body from linoleic acid so AA is considered an essential fatty acid (EFA) because it is an essential component of membranes and a precursor of a group of

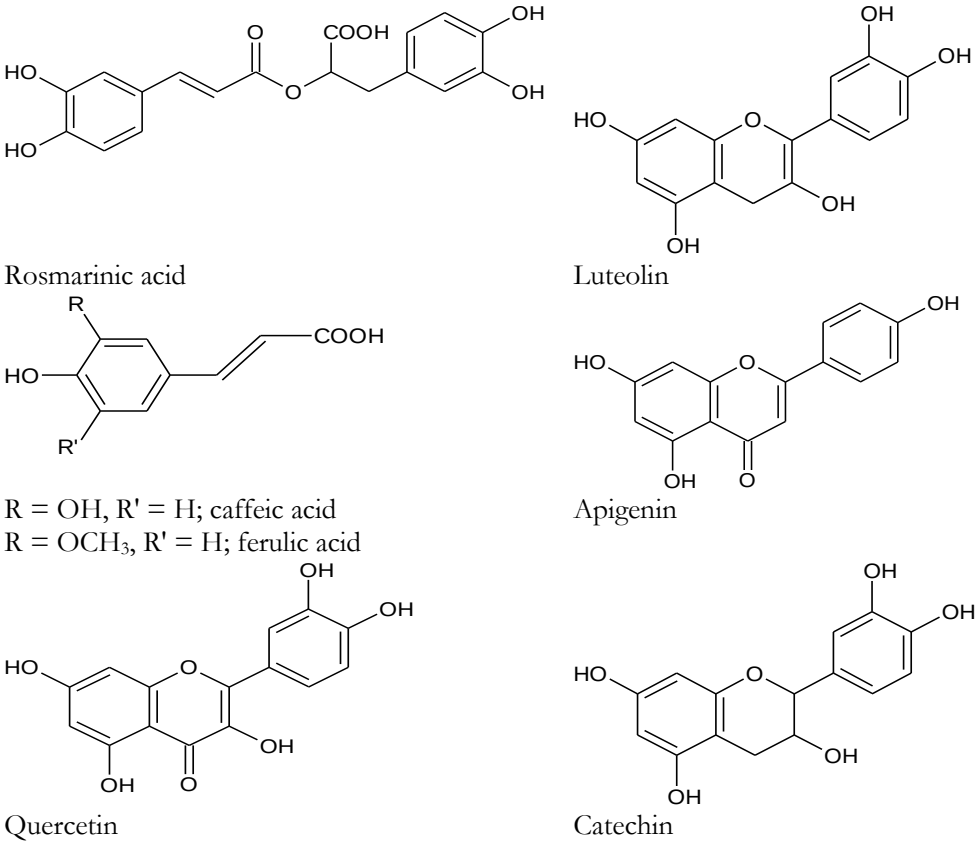

Figure 1. Structure of some polyphenolic compounds in perilla oil

Table I. Major saturated and saturated fatty acids

Saturated fatty acids	**Molecular formula**
Palmitic acid	$CH_3(CH_2)_{14}COOH$
Stearic acid	$CH_3(CH_2)_{16}COOH$
Unsaturated fatty acids	**Molecular formula**
Oleic acid	$CH_3(CH_2)_7CH=CH\ (CH_2)_7COOH$
Linoleic acid	$CH_3(CH_2)_4CH=CHCH_2CH=CH\text{-}(CH_2)_7COOH$
Linolenic acid	$CH_3CH_2CH=CHCH_2CH=CHCH_2CH=CH(CH_2)_7COOH$

hormone-like compounds like eicosanoids including prostaglandins, thromboxanes, and prostacy-clins, which are important in the regulation of diverse physiological processes (Siriamornpun *et al*., 2006; Asif, 2011).

The seeds oil of perilla having different fatty acids with different percentage such as palmitic acid 5-7%, oleic acid 12-22%, linoleic acid 13-20%, γ-linolenic acid 0-1% and α-Linolenic acid 52-64%, hexadecanoic acid 4.18% and stearic acid 1.15% (Figure 2 and Table II). Perilla oil analysis showed different value such as specific gravity, 0.925~0.931 g/cm^3, peroxide value, % ≤5, acid value ≤1.0, iodine number 180-205, saponification value 185-200 and unsaponi-fiable matter ≤1.5% (Talbott and Hughes, 2006; Siriamornpun *et al*., 2006; Jackson and Shelton, *2*002).

Volatile oil

Perilla contained volatile oil in fresh leaves, stem and flowers at 0.17%, 0.01% and 0.16% w/w respectively. The volatile oil mainly consists of perillaldehyde (PA), caryophyllene oxide, limonene and caryophyllene. Perillaldehyde is a main constituent (32-34%) and used to treat phlegm and asthma. Volatile oil (mainly Perilla aldehyde and perilla alcohol) is used in aromatherapy and flavoring agent in perfume or fragrances. (Peng *et al.,* 2005; Osakabe *et al*., 2002).

Properties and uses

The entire plant of perilla is very nutritious, due to presence of various phytochemicals, vitamins and minerals. Perilla has vegetable, spice, medicinal and industrial value, edible seed oil, perfumery volatile oil. The leaves have a very pleasant sweet taste and are used as a spice, as well as giving color and flavor to many dishes. Perilla seeds oil are used as cooking oil, preservative and industrial uses like varnish, paints, ink, water proof coating on cloth etc. Perilla are beneficial on different organ of body particularly heart, liver, kidney and brain.

There are many scientifically proven medicinal uses of perilla such as antiasthmatic, antibacterial, antiseptic, antispasmodic, antitussive, carminative, diaphoretic, emollient, expectorant, antioxidant, analgesic, rheumatoid arthritis, antiinflammatory, antiallergic, cardio protective, antiproleferative, hypertension, tonic, insecticidal, anti influenza, anti constipative and to restore health (Asif and Atul, 2010; Gardner *et al*., 1995). The stems of perilla are used in traditional Chinese remedy for morning sickness and restless fetus in pregnancy. One of the aldehyde isomers found in perilla is 2,000 times as sweet as sugar and 4-8 times as sweet as sachharin, it is used as a tobacco sweetener. Perilla alcohal prepared from perilla aldehyde, is used in fragrances (Longvah *et al*., 2000; Borchers *et al*., 1997; Bown, 1995).

Anti-inflammatory and anti-arthritic

The α-linoleic acid (ALA) is a type of ω-3fatty acid, a key nutrient to the human body. The ALA is changed into eicosapentaenoic Acid (EPA) and Docosahexaenoic acid (DHA) inside the body, is a precursor of the series–3 prostaglandins, the series–5 leukotrienes and the series–3 thromboxanes. These eicosanoids have anti-inflammatory and anti-therogenic properties (Sanbongi *et al.,* 2004; Osakabe *et al*., 2004; Simopoulos. 2002; Ueda *et al*., 2002; Valirek *et al.,* 2001; James *et al.,* 2000). EPA is structurally identical to AA and can be converted to resemble eicosanoids. In addition to antiinflammatory effect, perilla oils have been shown to reduce the production of the inflammatory cytokines IL-1β and TNF-α. These cytokines are important molecules in inflammatory responses and TNF-α blocking agents are used to treat rheumatoid disease. Addition, it also contains a little of such medicinal ingredients as rosmarinic acid-perillaldehyde and l-perillaalcohol, among which the rosmarinic acid is remarkably effective on inflammation (Leslie *et al*., 2005; Osakabe *et al*., 2004; Simopoulos, 2002; Takano *et al*., 1997).

Cardiotonic

The effect of the perilla extract on the myocardial contractility may have dose-dependent positive inotropic and lusitropic effect on the rabbit myocardium. It is also hematoblastic aggregation control and thrombi reduction action. Serum cholesterol and triglyceride levels decreased in rats fed perilla oil. Research showed ALA can reduce blood pressure, cholesterol and glyceride contents in the blood (Kim and Choi, 2005; Schacky *et al*., 2001). For instance, it may reduce inflammation of the blood vessels, which is known as a leading cause of cardiovascular disease. The effect of consuming PUSFs causes decrease in both LDL and HDL cholesterol. It also may inhibit blood clots, acting as a blood thinner and anti-coagulant (Calder, 2004; Osakabe *et al.* 2002; Ezaki *et al*., 1999).

Anti-allergic effect

Oral treatment of *P. frutescens* and its constituents are effective in treatment of allergies such as bronchial asthma. The anti-allergic effect of orally administered perilla decoction that contains 5.3% of luteolin β–glucuronosyl/β-glucuronide, 1.6% of apigenin β-glucuronosyl/β-glucuronide, 0.49% of scutellarin, and 2.5% of rosmarinic acid

respectively. Perilla contains two ingredients luteolin and rosmarinic acid that have a powerful impact on decreasing allergy symptoms, depends primarily on rosmarinic acid (Baolin *et al.,* 2005; Hu *et al.,* 2002; Ziment and Tashkin. 2000; Okamoto *et al.,* 2000a; Pullerits *et al.,* 1999). Perilla oil suppresses the generation of leukotrienes (LTC4) in asthamatic patient and associated with respiratory function and lipo metabolism. Rosmarinic acid, suppresses allergic immunoglobulin responses and inflammation caused by polymorph nuclear leukocytes (PMNL) in mice. Oral supplementation with rosmarinic acid is an effective intervention for patients with seasonal allergic rhino conjunctivitis (SAR). In Japan Perilla leaves are added to seafood as a garnish and inhibit shellfish allergies (Yoko *et al.,* 2004; Sanbongi *et al*., 2004; Ueda *et al*., 2002; Makino *et al*., 2001; Okamoto *et al.,* 2000b; Shin *et al*., 2000; Yamamoto, 1997).

Antioxidant activity

Phenolic and steroid compounds of the leaves of Perilla like β-sitosterol, shisonin, kaempferol 3-O-rutinoside, rosmarinic acid, rosmarinicacid methyl ester, 4-glucopyranosylcinnamic acid, and caffeic acid methyl ester revealed remarkable super oxide scavenging activity (Gulcin *et al*., 2005; Nagatsu *et al*., 1995). Rosaminic acid has antioxidative and anti-inflammatory activity (Gediminas *et al*., 2008; Povilaitytė and Venskutonis, 2000).

Anticancer and anti AIDS

The seeds of perilla have show the suppressing effect on azoxymethane induced foci of colonic aberrant crypts in rats even in small amounts, and a possible preventive agent in the early stage of colon cancer (Onogi *et al*., 1996). α-linolenic acid has inhibitory action on the growth and metabolism of breast cancer. Inhibitory effects of Perilla and its phenolic constituents on cytokine-induced proliferation of murine cultured mesangial cells were investigated. Perilla extract inhibited DNA synthesis of mesangial cells stimulated by platelet derived growth factor or tumor necrosis factor (TNF). Perilla leaf extract on proliferation and apoptosis inducing in human hepatoma HepG2 cells using a cell proliferation assay, flow cytometry, and cDNA micro arrays. In the PLE-treated HepG2 cells, antiproliferative activity was observed. The extract of Perilla showed marked reduction on tumorigenesis in a murine, two-stage skin carcinogenesis model. Topical application of a perilla-derived fraction caused significant inhibition of tumorigenesis (Osakabe *et al*., 2004; Yang *et al*., 1998; Thompson *at al*., 1997).

Perilla oil proved superior to either soyabean or safflower oil in inhibiting mammary, colon and kidney cancers. Similarly, ω-3 fatty acids suppress cancer formation. Oleic acid and SFAs have not been found to have any specific effects on carcinogenesis. Conjugated linoleic acids (CLA), appears to be unique among fatty acids because low levels in the diet produce significant cancer protection. Accumulating evidence suggests that diets rich in antioxidant may help reduce the risk of some cancers. Vitamin E is an antioxidant vitamin found principally in vegetable oil products. A group of isomers of the essential fatty acid linoleic acid, CLA, appear to have both anticarcinogenic and antiatherogenic properties. The CLA reduces the incidence of tumors induced by carcinogens (Grimble *et al*., 2002; Caughey *et al*., 1996; Ip *et al*., 1996).

Immunoinhance, antimicrobial and wound healing

Polyphenols of the perilla extract (PE) showed antimicrobial activity against oral pathogenic bacteria (carcinogenic streptococci and periodontopathic porphyromonas gingivalis). Polyphenols luteolin, showed the strongest antimicrobial effects among the phenolic compounds (rosemarinic acid, luteolin, chrysoeriol, quercetin, catcehin and apegenin.) and prevent dental caries and periodontal diseases. Immunoenhancing effects have been described for a crude polysaccharide extract of perilla and also showed marked antimicrobial activity against oral bacteria commonly associated with dental caries (Yamamoto *et al.,* 2002; Hiroyo and Tomohiko. 2002). In mice, fed a diet enriched with perilla oil exhibited better learning performance and less hyperactive behavior. Perilla extracts significantly suppressed proteinuria and glomerular IgA disposition. The decreased serum IgA concentration showed a significant correction with glomerular IgA disposition.

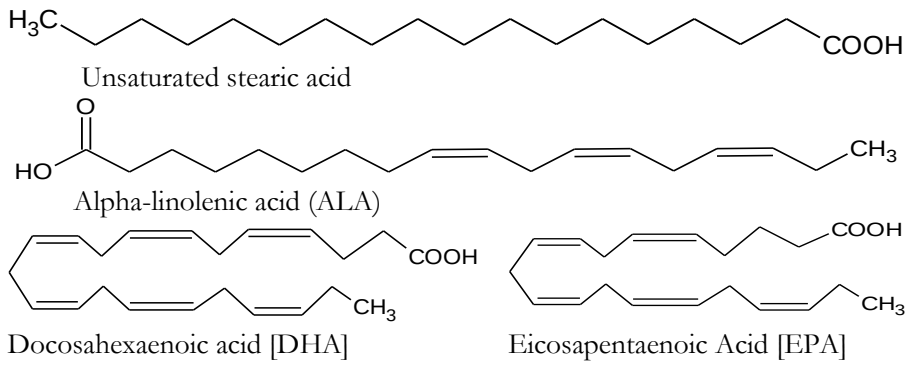

Figure 2 Structure of some fatty acids present in perilla oil and its metabolites

Table II. Different fatty acids present in perilla seeds oil

S No.	Fatty acid	No. of C atoms	No. of unsaturation	%
1	Palmitic acid	C16	00.00	5-7%
2	Stearic acid	C18	00.00	1-3%
3	Oliec acid	C18	1.00	12-22%
4	linoleic acid	C18	2.00	13-20%
5	γ-linolenic acid	C18	3.00	0-1%
6	α-linolenic acid	C18	3.00	52-64%

Perilla reduced glomerular IgA deposition via suppression, of IgA production in the serum. Suggesting that perilla might either directly prevented mesangial cell proliferation or prevent proliferation (Ragažinskienė *et al*., 2004; Simopoulos, 2002; Borchers *et al*., 1997). Extract of many plants of the Lamiaceae or mint family has anti-HIV activity. Perilla component apigenin and 2,4,5-trimethoxy-cinnamic acids, have antidepressant like effects central noradrenergic, dopaminergic and serotonergic activities in mice (Asif, 2011).

Culinary and ornamental

Perilla foliage and seeds oil are used in Korean, Japani, Chinese cooking. Perilla is an important vegetable in ancient time. The foliage of perilla serves as a garnish and also provides a red food coloring; specialized red-leaved perilla varieties are used. Perilla seeds are eaten in and oil used in cooking. Entrox is a dietary supplement derived from the perilla seeds. It is a rich source of omega-3 fatty acids (ALA). Perilla plant are used as an ornamental flower garden plant. *P. frutescens* is easy to grow in sun or light shade (Jackson and Shelton, 2002; Longvah *et al*., 2000).

Toxicology

Perilla is ordinarily avoided by cattle but has been implicate in cattle poisoning. Plants are most toxic if cut and dried for hay late in the summer during seed production. Perilla toxin, perilla ketone causes pulmonary edema in many animals. Perilla developed dermatitis due to contact with perillaldehyde (PA). Perilla ketone has a potent of pulmonary edemagenic agent for experimental animals. Perilla ketone is toxic and effective as a laxative without causing diarrhea in animals. The phenyl propanoind chemo type contains myricitin, which reported to have hallucinogenic properties. Perillaldehyde can cause skin allergies. The use of perilla in oriental foods and medicinal preparations suggests possible hazards to human health (Longvah *et al*., 2000).

The whole perilla plant is very nutritious, due to presence of different phytoconstituents, vitamins and minerals. It is used as vegetable, spice, medicine in various diseases and disorders and also has different industrial value, such as lubrication, paint, perfumery volatile oil, varnish, paints, ink, water proof coating on cloth etc. Perilla is a beneficial on different organ of body and different diseases. The medicinal uses of perilla in different ailment as antiasthmatic, antibacterial, antispasmodic, anti-tussive, expectorant, carminative, diaphoretic, emollient, antioxidant, analgesic, arthritis, antiinflammatory, cardiotonic, anticancer, hypertension, insecticidal, anticonstipative etc (Asif and Atul, 2010; Gardner *et al*., 1995). Perilla alcohal prepared from perilla aldehyde, is used in fragrances. It is a commercial source of rose furan, a compound interest in flavoring and perfumery. Perilla seed oil improved learning ability when feed a in diet. The seed cake can be used as an animal feed (Longvah *et al*., 2000; Borchers *et al*., 1997; Bown, 1995).

CONCLUSION

P. frutescens has been reported to possess wide variety of activities. Various phyto-constituents of perilla confirm its uses in alternative medicines. This plant is useful in curing many diseases and disorders. Dietary intake of perilla and its oil, to help reduce the risk of constipation, allergies, colitis, carcinogenesis and coronary heart disease (due to the inhibition of cholesterol absorption during the digestive process). Perilla oil is potentially effective in reducing allergic hypersensitivity in humans, and may be useful for in treatment of asthma and improving lung function. Herbalists also prescribe PUFAs of perilla seeds oil are effective in prevention of cardiac, cancer, inflammation, colitis, asthma, cancer allergy, and support lungs protecting them from colds, and flu. Its general benefits include protecting the heart, anticoagulant, blood thinner, analgesic, anti-inflammatory, immune-modulator, intestinal dryness and constipation. It is naturally highly unsaturated oil, containing ALA 52-64%. Perilla is an indispensible plant to the human body and has many important functions on improving and accelerating human health.

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