

**NUTRITIONAL IMPORTANCE OF MONOUNSATURATED AND
POLYUNSATURATED FATTY ACIDS OF *PERILLA* OIL**

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Abstract

The perilla oil has wide range of therapeutic and culinary applications. *Perilla frutescens* seeds contain saturated (SFAs), unsaturated (USFAs) like monounsaturated (MUFAs) and polyunsaturated fatty acids (PUFAs). The Perilla seeds are small and weight about 4g/1000 seeds. These seeds contained approximately 35-45% oil. It also contains the ω -3 fatty acid (54-64%) i.e. α -linolenic acid (ALA), ω -6 (\approx 14%) i.e. Linoleic acid (LA) and ω -9 (small amount) i.e. Oleic acid (OA). It also contains SFAs at 6.7-7.6%. In comparing to other plant oils, Perilla oil contains one of the highest proportions of ω -3 fatty acids. Perilla oil has most beneficial to human health and in prevention and control of various diseases such as cancer, inflammation, rheumatoid arthritis, coronary heart disease (CHD), specifically for its ability to reduce blood pressure and low-density lipoprotein (LDL) cholesterol and other health benefits.

Keywords: *Andrographis Paniculata*; andrographolide; Quantitative HPLC

1. Introduction:

Perilla frutescens (Labiatae) is commonly called Perilla is an annual crop. It is native to East Asia and major producing countries of Perilla are China, Japan, Korea, Thailand, India other East Asian countries. The herb is about 1 m high with small flowers and gray brown fruits.^[1-3] The applicable parts of Perilla are leaves and seeds. Perilla seed oil is a light yellow clear and transparent liquid, with aromatic odor and slight soluble in ethanol. Major fatty acids of the oil are unsaturated fatty acids like α -linolenic acid 54-64%, Oleic acid 14-23%, linoleic acid 11-16% and also contains saturated fatty acids (SFAs) 6.7-7.6% (Figure 1). The perilla seeds contain 30%–35% of oil. Perilla oil is used as cooking oil. It is also used in paint, varnish and ink manufacturing. The seed cakes are used as animals and birds feed.^[3-5] Perilla oil revealed linked to a reduced incidence of degenerative diseases, particularly coronary heart disease (CHD), cancers, inflammation, arthritis, asthma etc. However, perilla oil in the as the diet is associated with a low incidence of cancer and CHD, despite the high fat intake, it has been suggested the type of fat is more important than the total amount consumed. Although the composition of perilla oil is complex, the major groups of compounds thought to contribute to its observed health benefits include MUFAs and PUFAs.

1.2 Cooking with Perilla Oil: In the diet, perilla oil is consumed cold as a dressing for salads and pasta and frying. Therefore, it is important to determine the stability of the identified active components when subjected to heat. The major process contributing to the instability of perilla oil when stored or heated is fat oxidation.^[6] Sufficient exposure and degradation can lead to significant changes in the composition of perilla oil, and these changes affect its biological properties. Cooking with perilla oil produces a number of degradation products, with lipid peroxidation occurring to a limited extent. The heating method also affects degradation. In cooking, olive oil is boiled or heated conventionally. Lipid peroxidation products have been linked to cancer and cardiovascular disease. Compared with other oils used for cooking, perilla oil has MUFAs and PUFAs. This means fewer targets for reactive oxygen species (ROS), making perilla oil more stable and less likely to undergo peroxidation. In addition, perilla oil contains many antioxidants that reduce lipid peroxidation. Although antioxidants protect perilla oil from thermal degradation, frying reduces the oil's antioxidative capacity, a particularly important fact when the same oil is used repeatedly. Deep fat frying has both advantages and disadvantages related to olive oil degradation. The low oxygen exposure of the oil and a short cooking time reduce the potential for lipid peroxidation. However,

because the oil is more likely to be re-used, accumulation of polymeric compounds occurs as the antioxidant capacity is being reduced. Compared to other oils, olive oil has a relatively long deep-fat frying “shelf-life” and is comparatively more stable than other oils for repeated frying.^[7] Because exchange between lipids in the food and the oil occurs during cooking, the type of food fried also plays a role. For example, frying fish increases the oil’s instability because the oil becomes enriched with PUFAs, which are more susceptible to oxidative degradation than MUFAs. Although frying foods with a high protein content such as meat, fish, and eggs can potentially produce carcinogenic heterocyclic amines (HCAs), the antioxidants present in olive oil limit the formation of HCAs.^[8]

2. Chemistry of Perilla seed oil

Perilla is a source of fatty acids that contains both SFAs and USFAs (MUFAs & PUFAs) fatty acids (Table 1). Fatty acids, those having saturated carbon chain called saturated fatty acid (SFAs), those having single double bond called monounsaturated fatty acids (MUFAs) and those having more than one double bond are termed as polyunsaturated fatty acids (PUFAs). Perilla oil contains saturated fatty acids mainly Palmitic acid (PA) 5-7%, Stearic acid (SA) 1-3%, MUFAs is Oleic acid (OA) 12-22%, and PUFAs are Linoleic acid (LA) 13-20%, γ -linolenic acid (GLA) 0-1%, α -linolenic acid (ALA) 52-64%, icosanoic acid (IA) 0-1% (Table 2). Unsaturated fatty acids are lower melting point than saturated fatty acids^[9-12]. Thus, Oleic acid, which has its double bond 9 carbons from the methyl end, is considered a ω -9 (or an n-9) fatty acid. Similarly, linoleic acid, is a ω -6 (n-6) fatty acid because its second double bond is 6 carbons from the methyl end of the molecule (i.e., between C-12 and C-13 from the carboxyl end).^[3,9]

2. Importance of unsaturated fatty acid

2.1 Polyunsaturated fatty acids: The ω -3 and ω -6 fatty acids are essential fatty acids (EFAs), because these fatty acids cannot synthesize by body itself. ω -9 fatty acids are “conditionally essential”, which means that if we have the other fatty acids in our diet, then our body can manufacture ω -9 fatty acids. Otherwise, omega 9 fatty acids must be consumed or supplemented as well^[12-14]. Among plant oils, the balance between ω -3, ω -6 and ω -9 fatty acids must dictate which oil is chosen. Oils which predominate in ω -3 component would be most likely to promote health. Most would actually contribute to the imbalance of ω -6 fatty acids because they contain more ω -6 than ω -3. Any amount of ω -9 is beneficial, but in balancing these fatty acids, the ω -3 component is the most important^[15-18]. Perilla oil is a rich source of ω -3 PUFAs, specifically α -linolenic acid (ALA). It also contains ω -6 and ω -9 PUFAs. These PUFAs are essential for human health, so these PUFAs must be obtained through diet or by supplementation. Perilla oil suppresses the production of chemical mediator in the allergy and inflammatory responses. These essential fatty acids (EFAs) have been associated with benefits in a wide range of heart diseases, colitis/Crohn’s disease, asthma, antimicrobial, anticancer, various skin conditions, etc. Anti-inflammatory doses of perilla oil have been shown to reduce the hypertensive and nephrotoxic effects of cyclosporin. It prevent the formation of LTB4 have been used in treating asthma, rheumatoid arthritis, colitis, lupus, multiple sclerosis, and psoriasis etc.^[17-20].

2.1.1 Cardio-vascular Benefits: *In-vivo* metabolism of ω -3 PUFAs, it mainly exists in the form of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) at a rate of roughly 7-10% that can help to prevent heart diseases. These two specific ω -3 fatty acids metabolites are inserted in cell membranes throughout the body, where cellular machinery converts them into substances which prevent abnormal clotting, and relax blood vessels and improved ventilatory parameters. The ω -3 rich fatty acids, which may lead to prevention of coronary heart disease and decrease blood clotting^[21,22]. In platelets, the cell products in the blood which aid in clotting, ω -6 fatty acids are converted to thromboxane-A2 (TXA2). This makes the platelets more likely to burst or degranulate, releasing their clotting substances and cell messengers. These cell messengers constrict blood vessels and cause other platelets to burst-causing a clotting cascade. On the other hand, when ω -3 fatty acids are used in the same machinery in platelets, thromboxane-A3 (TXA3) is made, which is inactive. In cut or injury, the bleeding is stop with the help of platelets. However, in normal uncut or uninjured, clotting is abnormal and may block flow to areas which need it causing a heart attack or stroke. The ω -6 fatty acids make more inflammatory substances. These substances include leukotriene-B4, (LTB4), which is a cell messenger responsible for inflammation throughout the body. LTB4 actually causes these WBC’s to absorb oxidized LDL cholesterol (cholesterol plaque is formed). In contrast, when ω -3 fatty

acids are used in the same cellular machinery, leukotriene B5 (LTB5) is made. LTB5 is anti-inflammatory. Health demands normal functioning of both systems^[20-22].

2.1.2 Anti-inflammatory and rheumatoid arthritis benefits: Perilla oil is rich in the ω -3 fatty acids, on metabolism gives EPA and DHA, which can displace arachidonic acid (AA) from cell membranes. These ω -3 fatty acids are also released with AA by phospholipases and act as substrate inhibitors of conversion of AA by cyclooxygenases (COX) and the terminal synthases to the pro-inflammatory oxygenated inflammatory mediators known as eicosanoids. EPA is structurally identical to AA with the exception of its additional n-3 double bond and can be converted to eicosanoids that resemble eicosanoids. In addition to these effects on inflammatory eicosanoid synthesis, perilla oils have been shown to reduce the production of the inflammatory cytokines IL-1 β and TNF- α by monocytes stimulated in vitro. These cytokines are important effector molecules in inflammatory responses and TNF- α blocking agents are now used widely to treat rheumatoid disease that has proven refractory to less expensive therapies. In vitro studies have also shown inhibition of release of the metalloproteinases that are implicated in the tissue damage that is the hallmark of rheumatoid arthritis and other inflammatory diseases^[23,24]. Perilla oil reduces recourse to NSAIDs for analgesia in rheumatoid arthritis and thereby reduces risk for upper GI hemorrhage contrasts with the highly selective COX-2 inhibitor Rofecoxib, which has been associated with increased serious cardiovascular risks. The result is fewer AA derived eicosanoids with production of homologous metabolites products such as PGE1 (one less double bond than AA derived PGE2). ALA rich oils appear to reduce symptoms in rheumatoid arthritis but available evidence is far less than that for perilla oil in rheumatoid arthritis^[23,24].

2.1.3 Cancer benefits: The ω -3 fatty acids may suppress cancer formation, but there is no direct evidence for protective effects in humans. The essential fatty acid linoleic acid (LA) has both anti carcinogenic and antiatherogenic properties^[17, 19]. Animal studies have indicated that LA reduces the incidence of tumors induced by carcinogens. The LA, appears to be unique among fatty acids because low levels in the diet produce significant cancer protection^[20,22, 25].

2.1.4 Antiallergic benefits: Perilla seed oil suppressed a wide range of allergic mediators in experimental animals. These findings raise the potential for perilla oil to be effective in reducing allergic hypersensitivity in humans. The Perilla oil also showed benefits in terms of lung function, breathing parameters and may be useful for the treatment of asthma. The reduction in asthma symptoms due to the ALA effects on leukotrienes^[12,21, 24].

2.2 Monounsaturated fatty acids: Perilla oil is unique with respect to the high saturated fatty acids because the majority of seed oils are composed primarily of polyunsaturated fatty acids (PUFAs) and Monounsaturated fatty acids (MUFAs), including the essential, linoleic acid (PUFAs) and oleic acid (MUFAs). Compared to PUFAs, oleic acid (MUFAs), meaning it has one double bond, making it much less susceptible to oxidation and contributing to the antioxidant action, high stability, and long shelf life of oil.^[26] The health benefits of oleic acid are conflicting. It has been reported that oleic acid plays a role in cancer prevention. Whether this is a secondary effect of the fatty acid on oil stability or a direct anticancer effect remains debatable.^[26] Other examples are beef and poultry contain 30-45 percent oleic acid, while oils such as palm, peanut, soybean, and sunflower contain 25-49 percent oleic acid.^[27]

Several studies have examined the effect of oleic acid on cancer. The effect of perilla oil or oleic acid on colorectal neoplasia, MUFAs induces apoptosis and cell differentiation and down-regulates the expression of cyclooxygenase-2 (COX-2) and Bcl-2. COX-2 is believed to play an important role in colorectal cancer development, while Bcl-2 is an intracellular protein that inhibits apoptosis. Oleic acid alone exhibited cell-line specific apoptotic induction, since HT-29 cells were affected but not Caco-2 cells. Oleic acid had no effect on the down-regulation of COX-2 and Bcl-2. The researchers concluded oleic acid plays a minor role, if any, in colorectal chemo-protection and that other components of perilla oil are involved in this protective process. The effect of oleic acid on breast cancer cell lines^[28,29]. The oleic acid down-regulates the over-expression of Her-2/neu, an oncogene over-expressed in breast carcinomas. The gene, also know as erb-B2, encodes for the p185Her-2/neu oncoprotein, a transmembrane tyrosine kinase orphan receptor that, under normal cellular conditions, is highly regulated because it controls many cell functions, such as differentiation, proliferation, and apoptosis. Deregulation of p185Her-2/neu greatly increases the risk of cancer development. Oleic acid acts synergistically to enhance its action when used against cell cultures that over-express the Her-2/neu oncogene^[28]. Oleic acid up-regulates PEA3. Low levels of PEA3 are found in cells over-

expressing Her-2/neu; whereas, high levels of PEA3 are associated with low p185Her-2/ neu expression.^[30]

2.2.1 Coronary Heart Disease: Epidemiological studies demonstrate the olive oil might help prevent atherosclerosis, atherosclerotic plaque formation is in order. Oxidation of LDL cholesterol has been identified as one of the first steps in the development of atherosclerotic lesions by promoting injury to the arterial wall through several mechanisms, including growth factor and chemotactic protein expression, inflammation, and increased local macrophages. Macrophages bind to and engulf oxidized LDL– an innate immune response to tissue damage. This engulfment produces a fatty foam cell, which, when combined with other cells, produces a fatty streak in the blood vessel. Oxidized LDL can also be taken up directly by endothelial and smooth muscles cells, leading to formation of fatty streaks, which is the first sign of atherosclerosis. The lesions forming atherosclerotic plaques are made up of lipids, endothelial and smooth muscle cells, and extracellular matrix. The plaque environment is proinflammatory^[6]. Inflammation occurring prior to the formation of fatty streaks and atherosclerotic lesions causes alterations to the endothelial cell wall, which increases the adhesion of leukocytes, LDL cholesterol, and platelets. This contributes to the development of atherosclerosis and cardiovascular disease^[31].

2.2.2 Hypertension: As with other aspects of cardiovascular diseases, there is a reduced incidence of hypertension in populations that consume the UFAs diet, and adherence to the UFAs diet is inversely related to systolic and diastolic blood pressure.^[32,33] Several studies have demonstrated the antihypertensive properties of perilla oil.^[34] UFAs reduced systolic, diastolic, and mean arterial blood pressures in normotensive animals. Epidemiological studies suggested a protective effect for MUFAs. Compare a diet rich in PUFAs with a diet high in MUFAs in patients taking antihypertensive medications and found individuals who consumed an olive oil-rich diet were able to reduce the dosage of antihypertensive medication. The precise mechanism of action for blood pressure reduction is unknown, although several theories have been proposed. like calcium channel antagonist, closely mimicking the effects of the calcium channel blocker drug verapamil. Another suggested mechanism is via improved endothelial function.^[35] Oleic acid may contribute to improved endothelial function by reducing ROS. Other potential mechanisms have been suggested, including decreasing vascular tone and changes to the fatty acid and phospholipid composition of the aorta.^[34]

2.2.3 Cancer: Because strong epidemiological evidence suggests people who consume the PUFAs diet have a lower incidence of certain cancers, including breast, skin, and colon,^[6] Oxidation of proteins, DNA, and lipids has been shown to contribute to cancer development, and consumption of antioxidants is believed to reduce the risk of mutagenesis and carcinogenesis.^[7,8] The exact contribution olive oil makes to the apparent dietary chemoprotection. Saturated animal fats and plant PUFAs in the diet have been implicated in colon, breast, prostate, and ovarian cancers. The substitution of perilla oil may explain its apparent cancer-protective effect and accentuate the importance of the type, rather than the amount, of fat consumed.

Perilla oil has a protective effect against colon cancer. The effect of perilla oil phenols on colorectal carcinogenesis. Using specific cell lines, they investigated processes involved in cancer initiation, promotion, and metastasis– perilla oil phenols exert beneficial effects in all three stages. The oil extract was shown to reduce DNA damage (initiation), increase barrier function (promotion), and reduce cell invasion of surrounding tissue (metastasis). In addition, oleic acid is incorporated into the phospholipid membrane of breast tissue cells, resulting in a reduction in lipid peroxidation. Epidemiological data show women in the PUFAs fatty diet have a lower incidence of breast cancer than women in higher PUFAs diets.^[36]

2.2.4 Rheumatoid Arthritis: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic joint inflammation and damage. The initial autoimmune stimulus is unknown; however, joint and tissue damage occurs by a variety of mechanisms, many of which involve reactive oxygen species. ROS can cause destruction of hyaluronic acid and disruption to collagen, proteoglycans, protease inhibitors, and membrane function, the latter via oxidation of membrane fatty acids. The initiation of RA is believed to result in an increase in the concentration of macrophages and neutrophils in the synovial fluid and free-radical-producing enzymes. This leads to high levels of ROS in the joints, which increases and prolongs inflammation and damage. The antioxidant effect of UFAs oil has been found to reduce inflammation. In addition, dietary MUFAs, such as oleic acid, have been found to replace PUFAs in several aspects of cell metabolism. Reducing the competition between omega-6 and omega-3-PUFAs can lead to an increased use and incorporation of omega-3-PUFAs. A

number of studies that examined the benefits of fish oils (PUFAs) in RA used an olive oil (MUFAs) placebo for the control groups.^[367,38] Although results highlighted the benefits of fish oils, unexpected significant improvements were also seen in the control groups. Benefits including pain reduction, reduced morning stiffness, and improved patient evaluation of global disease were reported by patients receiving olive oil only. No explanation of the improvements shown by the olive oil groups were proposed, although changes in immune function may be responsible. Olive (MUFAs) oil improved RA symptoms in patients already receiving fish oil (PUFAs). Olive oil appears to act synergistically with omega-3 fish oils to improve the symptoms of RA; the benefits are thought to be exerted through the oleic acid component. Oleic acid is converted to eicosatrienoic acid (ETA) and then leukotriene A₃ (LTA₃). LTA₃ is a potent inhibitor of proinflammatory leukotriene B₄ synthesis and decreases the risk of developing RA.^[39,40]

3. Numerous other applications of perilla oil

PUFAs (ω -3 and ω -6), MUFAs (ω -9), plus multi-vitamins and minerals or placebo supplementation is useful in children with learning and behavioral problems. ω -3 Fatty acids exerts neuroprotective action in Parkinson's disease, exhibit a protective effect (Alzheimer's disease as well). The high doses of ω -3 FAs prevented the neurotoxin-induced decrease of dopamine that ordinarily occurs. Since Parkinson's is a disease caused by disruption of the dopamine system, this protective effect exhibited could show promise for future research in the prevention of Parkinson's disease^[41,42]. Not only does Perilla contain the PUFAs, but it also a rich source of phenolic compounds, flavanoids and anthocyanins known for their antioxidant properties. Rosemarinic acid, luteolin, chrysoeriol, quercetin, catechin and apigenin, etc., found in Perilla seeds. These antioxidants may also be involved in allergy, antimicrobial, cardiovascular and cancer prevention along with the ω -3 fatty acids. The polyphenol luteolin showed the strong antimicrobial effect than other phenolic compounds^[43,44]. Perilla oil can be used as a tasty addition to salad dressings, hot cereal, blender drinks and other foods. Many individuals enjoy the flavor of perilla oil by taken orally at teaspoonful.

4. Discussion

Research showed that the low incidence of heart attacks even their diet was so high in fat when the fats in the diet have high amount of PUFAs, MUFAs, especially ω -3 fatty acids. These PUFAs provided protection from heart diseases. ALA or ω -3 fatty acids *In-vivo* decreases the blood pressure, cholesterol and glyceride contents in the blood. It also controls hematoblastic aggregation and thrombi reduction.^[45-47] ω -3 fatty acids has inhibitory action on the growth and metabolism of breast and colon cancer. The higher intakes of ω -3 FAs ALA, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) may afford some degree of protection against coronary heart diseases. The physiological potency of EPA and DHA is much greater than that for ALA^[28-30]. Many health issues depend on a proper balance of ω -3 and ω -6 fatty acids. While ω -6 fatty acids are necessary for normal immune function and clotting, too much ω -6 fatty acid may promote abnormal clotting and an overactive immune system. It is believed that our ancestors evolved on a diet where these two omega fatty acids were approximately equal. Considerable evidence indicates the unsaturated fatty diet is linked to a decreased incidence of cardiovascular disease and certain cancer types, despite the fact that this diet is higher in fat than other saturated fatty diets. Since previous research concludes fat intake has a positive correlation with the risk of CHD and cancer. Saturated fatty acids have been linked to unfavorable health outcomes; whereas, MUFAs have been found to be beneficial. The studies provide good evidence perilla oil may be beneficial for reducing high blood pressure and preventing breast and colon cancer. There is, however, evidence that the active compounds in perilla oil are capable of distribution throughout the body. However, it seems safe to assume the benefits of perilla oil also apply to consumption of whole perilla because the therapeutic components of the oil are also found in the whole perilla. Regarding breast cancer, the protective effect of perilla oil was seen in women with respect to blood pressure reduction, respectively.^[48-50] Although the PUFAs diet consumed is thought to be a significant, if not the primary, contributor to the reduced incidence of CHD and certain cancers seen in these populations, it may not be the only factor. Perilla oil is also not the only component of the diet that has been found to have biological benefits. The evidence indicates, however, that perilla oil and its components contribute significantly to the health benefits, with more of an effect on prevention than treatment. Perilla oil to be potentially benefits to prevent and cure different ailments

like cardiovascular diseases, allergy, asthma, antioxidant, pain reliever, anti-inflammatory, constipation, etc, but little health risk was also reported.

Conclusion

Perilla oil is a viable source of vegetarian ω -3 fatty acids for nutrition and health. Perilla oil to be potentially benefits for protecting the heart diseases, allergy, asthma, pain and inflammation, intestinal dryness, constipation and stimulate immune functions also. The increase intake of ω -3 fatty acids prevent inflammation or increase the production of anti-inflammatory substances. Most important the ω -3 fatty acids have been shown to improve cardiovascular activity to regulate and control of heart functions like blood pressure, vascular resistance, lower triglycerides, abnormal heart rhythm, sudden cardiac death, and may reduce the risk of heart attack. Perilla seeds also contain various polyphenols, mainly luteolin and rosmarinic acid. These polyphenols have powerful impact on decreasing allergy symptoms and free radicals scavenging activity.

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Table 1: Some Saturated and Unsaturated Fatty Acids

Type of fatty acids	Molecular formula
Saturated fatty acid	
Palmitic acid	CH ₃ (CH ₂) ₁₄ COOH
Stearic acid	CH ₃ (CH ₂) ₁₆ COOH
Monounsaturated fatty acids	
Oleic acid	CH ₃ (CH ₂) ₇ CH=CH (CH ₂) ₇ COOH
Polyunsaturated fatty acids	
Linoleic acid	CH ₃ (CH ₂) ₄ CH=CHCH ₂ CH=CH-(CH ₂) ₇ COOH
Linolenic acid	CH ₃ CH ₂ CH=CHCH ₂ CH=CHCH ₂ CH=CH(CH ₂) ₇ COOH
Arachidonic acid	CH ₃ (CH ₂) ₃ (CH ₂ CH=CH) ₄ (CH ₂) ₃ COOH

Table 2: Different components of perilla seed oil

Serial No.	Component	No. of double bonds
1	Palmitic acid	Saturated (0)
2	Stearic acid	Saturated (0)
3	Oleic acid	Monounsaturated (1)
4	Linoleic acid	Polyunsaturated (2)
5	Linolenic acid	Polyunsaturated (3)