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A Review of Phytochemical and Pharmacological Activity of *Perilla frutescens* (L.) Britton

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ABSTRACT

Perilla frutescens is a medicinal, aromatic, edible, and aesthetically pleasing plant that belongs to the Lamiaceae family of mints. Perillas are native to East Asian nations (China, Taiwan, Vietnam Japan, Korea, and India) and they have long been valued for their culinary and traditional medicinal properties. P. frutescens leaves, seeds, and stems are utilized for a number of medicinal purposes. The main phytochemicals found in this species are flavonoids (luteolin, apigenin), phenolic compounds (rosmarinic acid, caffeic acid, and ferulic acid), phytosterols, tocopherols, policosanols, and fatty acids. Perilla seed oil contains one of the highest percentages of omega-3 (ALA) fatty acids (56–64%) when compared to other plant oils. Around 14% of perilla oil contains omega-6 (linoleic acid) and omega-9 (oleic acid). These polyunsaturated fatty acids are extremely beneficial to human health and help prevent a number of diseases, including rheumatoid arthritis, cancer, heart disease, and inflammation. Perilla has long been used to treat depression-related disorders, anxiety, asthma, chest stuffiness, vomiting, coughs, colds, flus, phlegm, tumors, allergies, intoxication, fever, headache, stuffy nose, constipation, stomach discomfort, and indigestion. It is also widely used as an analgesic, anti-abortive, and sedative. Despite promising preclinical (in vitro and in vivo) results, clinical trials are insufficient; further study is necessary to confirm its therapeutic effects and ensure its safety and effectiveness.

Keywords ; *Perilla frutescens*, essential oils, rosmarinic acid, pharmacology, preclinical.

INTRODUCTION [1-7]

Perilla frutescens L. is a member of the Lamiaceae family, which has over 7000 species and 236 genera. The annual herb P. frutescens, sometimes referred to as perilla, is found in China, Korea, Japan, and the Himalayan regions of India and Nepal. Due to its increasing economic significance, some western nations, including the United States, Russia, and Europe, are now also cultivating it [1]. Uttarakhand, Kashmir, Himachal Pradesh, Sikkim, Manipur, Mizoram, and Meghalaya are among the Indian states where it can be found. Perilla frutescens is used medicinally and traditionally in Garhwal Himalaya for a variety of purposes, including medicine, edible oil, garnish, flavoring, and other traditional foods [2]. In northern India the stem of the plant is traditionally used as an analgesic and anti-abortive agent. The leaves are said to helpful for asthma, colds and flu's and regulate stomach function The seed oil of P. frutescens is also used as a substitute for hydrogenated oil or cream in baking pastries. The medicinal use of P. frutescens was first recorded in Miscellaneous Records of Famous Physicians (Mingyi Bielu in Chinese), which is a collection of successive generations of materia medica, covered a total of 730 kinds of drugs in this ancient book. The plants of P. frutescens were grouped into two species in the ancient book; those with green leaves on the upper and lower surfaces classified to Baisu, and those with red or purple on the lower of the leaves classified to Zisu [3,4]. Numerous significant phytochemicals, including rosmarinic acid, luteolin, chrysoeriol, quercetin, catechin, caffeic acid, and ferulic acid, are found in perilla plants. Perilla seeds have also been found to include phytosterols, tocopherols, squalene, and polyunsaturated fatty acids. The perilla plant exhibited antimicrobial, antiallergic, anticancer, antitumor, antidepressant, antiviral, anti-asthmatic, and antioxidant properties, according to biological investigation [5]. Globally, it is used as a functional food, but in some regions, it is not grown systematically, and despite its many uses and advantages, it is still a crop that is underutilized [6]. This review aims to give comprehensive information on perilla botany, applications, phytochemistry, pharmacological studies, and nutrition, with a focus on perilla seed and perilla seed oil. Additionally, this study would highlight scientific gaps in the present understanding and provide a methodical foundation for further Perilla research [7].

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BOTANICAL DESCRIPTION OF PERILLA PLANT [8]

Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Spermatophyta
Superdivision	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Lamiales
Family	Lamiaceae – Mint Family
Genera	Perilla

VERNACULAR NAMES OF PERILLA [8-10]

Perilla has a variety of synonyms and regionally specific colloquial names. It is called Shiso in Japan [8], Zisu in China, Deulkkae or Tilkae in Korea [9], and Silam in Nepal. It goes by a number of names in India, including Bhanjeer or Banjiraa in Uttarakhand, Hanshi or thoiding in Manipur, and chhawhchhi in Mizoram [10].

PLANT DESCRIPTION [11-12]

Perilla is an annual plant with downy-haired, oblong to round, shiny green or purple leaves, a square stem, and tiny tubular, purplish to white blooms that can reach a height of 150 cm. 3–4 mm in length, the flower stalks are 1.5 mm long, and the calyx, which has brown seeds, is roughly 3 mm long. Perilla seeds are tiny and weigh roughly 4 grams per 1000. Its seeds are sown in May, and depending on the region, harvesting takes place between September and October. It is cultivated using mixed cropping; it needs soil that can absorb moisture but isn't particularly productive. The leaves and seeds of the perilla plant are useful elements [11, 12].

CHEMICAL COMPONENTS OF *Perilla frutescens* [13-20]

The seeds, leaves, and aerial parts of P. frutescens have been reported to contain a variety of phytoconstituents, such as alkaloids, phenylpropanoids, terpenoids (monoterpenes, diterpenes, and triterpenoids), phenolic acids, flavonoids (flavones, flavonols, flavanones, isoflavanones, aurones, and chalcones), neolignans, fatty acids, policosanols, tocopherols, sitosterols, glycosides, glucosides, peptides, and benzoxipen derivatives.

Alkaloids, Phenylpropanoids, and Terpenoids

Neoechinulin A, a significant alkaloid found in P. frutescens' aerial portions, prevents the phosphorylation of mitogen-activated protein kinase (MAPK). The aerial parts also include indole-3-carboxaldehyde and 1H-indole-3-carboxylic acid, among other alkaloids. The shikimate route uses phenylalanine or tyrosine to biosynthesize phenylpropanoids, which are chemical molecules primarily found in plants. Numerous phenylpropanoids also serve as building blocks or precursors for the production of lignins, flavonoids, and coumarins. Several significant phenylpropanoids, including elemicin, isoelemicin, myristicin, and methylisoeugenol, are found in P. frutescens' leaves and other aerial parts. Myristicin and Elemicin are well-known psychotropic substances. Methylisoeugenol and isoelemicin have antiplasmodial properties against strains of Plasmodium falciparum. Dillapiole, nothoapiole, perilloside E (phenylpropanoid glucoside), and allyltetramethoxybenzene are among the antidepressant and antioxidant phenylpropanoids found in the leaves. During lung inflammation, it has also been discovered that phenylpropanoids, including elemicin, isoelemicin, dillapiole, nothoapiole, and allyltetramethoxybenzene, efficiently suppress proinflammatory cytokines. The

leaves and other aerial portions of P. frutescens contain a variety of terpenoids, including triterpenoids, sesquiterpenoids, and monoterpenoids. P.frutescens contains monoterpenoids of the perilla-ketone and perillaldehyde types. By preventing the production of proinflammatory cytokines, perilla-ketone-type monoterpenoids such as frutescenone A, frutescenone B, frutescenone C, isoegomaketone, and 9-hydroxyisoegomaketone [have anti-inflammatory properties [13,14]. 3-hydroxyperillaldehyde and perillic acid are examples of monoterpenoids of the perillaldehyde class [15]. Acyclic, monocyclic, and bicyclic monoterpenoids are also present in P. frutescens leaves and other aerial components. β-myrcene, geraniol, β-citronellene, nerol, linalool, and ocimene are examples of acyclic monoterpenoids. Terpineol, thymol, phellandrene, 1,8-cineole, damascenone, terpinene, carvacrol, carvone, piperitone, piperitenone, limonene, menthone, carveole, and pulegone are examples of monocyclic monoterpenoids [16,17,18]. The leaves include bicyclic monoterpenoids such as verbenol, camphene, sabinene, and δ-2-carene. Sesquiterpenoids, including acyclic, monocyclic, bicyclic, and tricyclic forms, are abundant in P. frutescens leaves. Nerolidol, farnesene, and farnesol are examples of acyclic sesquiterpenoids. α-humulene, bisabolene, germacrene, elemene, and β-ionone are examples of monocyclic sesquiterpenoids [19]. Particularly abundant in bicyclic and tricyclic sesquiterpenoids are the leaves. α-pinene, β-pinene, β-caryophyllene, ε-muurolene, α-cadinene, β-cadinene, α-santalol, α-bulnesene, β-gurjunene, β-selinene, α-fenchene, eremophilene, calarene, and valencene are examples of bicyclic sesquiterpenoids. Spathulenol, viridiflorene, cubebene, alloaromadendrene, patchoulane, α-copaene, longifolen, and ylangene are examples of tricyclic sesquiterpenoids. The leaves and aerial portions of P. frutescens have yielded only one diterpenoid phytol to date. The leaves and other aerial parts of P. frutescens have been found to contain over 200 different kinds of volatile components. Ursolic acid, corosolic acid, 3-epicorosolic acid, pomolic acid, tormentic acid, hyptadienic acid, oleanolic acid, augustic acid, and 3-epimaslinic acid are among the pentacyclic triterpenoids found in P. frutescens leaves. These compounds have been shown to be cytotoxic against a variety of cancers, including leukemia, breast, and hepatic carcinomas [20].

POLYPHENOLIC COMPOUNDS [21-22]

P. frutescens has a high content of various phenolic chemicals in its leaves, stems, and seeds. Rosemary, methylrosmarinic acid, caffeic acid, and its derivatives, such as vinyl, ethyl, and methyl caffeate, trans-p-menthenyl caffeate, caffeic acid-3-O-glucoside, and (Z, E)-2-(3,4-dihydroxyphenyl)ethenyl ester of caffeic acid and (Z,E)-2-(3,5-dihydroxyphenyl)ethenyl ester of caffeic acid, are all present in the leaves [21]. Additionally, 4-coumaric acid, coumaroyl tartaric acid, 4-hydroxyphenyl lactic acid, sagerinic acid, p-hydroxybenzoic acid, isovanillic acid, sinapic acid, gallic acid, ferulic acid, 4-hydroxyphenyl lactic acid, and hydroxytyrosol are present in the leaves. Rosemary, methyl rosmarinic acid, rosmarinic acid-3-O-glucoside, 3′-dihydroxyl-rosmarinicacid-3-O-glucoside, caffeic acid, caffeic acid-3-O-glucoside, vanillic acid, ferulic acid, and cimidahurinine are among the phenolic chemicals found in P. frutescens seeds [22]. The stems of P. frutescens contain derivatives of caffeic acid, vinyl caffeate, protocatechuic aldehyde, primarily ethyl and methyl caffeates.

Flavonoids [23-28]

P. frutescens produces a variety of flavonoids, including as flavones, flavanones, chalcones, and aurones, in its leaves, stems, fruits, and seeds. Flavones found in P. frutescens leaves include luteolin, apigenin, scutellarein, negletein, vicenin-2, and catechin [23,24,25]. Additionally, several derivatives of luteolin, apigenin, and scutellarein [26] are present, such as luteolin-7-O-glucuronide, luteolin-7-O-diglucuronide, luteolin 7–0–glucuronide -6″-methyl ester, luteolin-7-O-glucoside, apigenin 7–O-caffeoylglucoside ,apigenin-7-O-glucuronide, , scutellarein-7–O-glucuronide, and scutellarein 7–O–diglucuronide. Flavones found in P. frutescens fruits include luteolin, apigenin, and chrysoeriol; flavones found in seeds include diosmetin, chrysoeriol, luteolin, luteolin-5-O-glucoside, luteolin-7-O-glucoside, apigenin, and apigenin-7-O-glucoside [27]. Shisoflavanone A, liquiritigenin, 5,8-dihydroxy-7-methoxyflavanone, (2S)-5,7-dimethoxy-8,4′-dihydroxy flavanone, and 8-hydroxy-5,7-dimethoxyflavanone are among the flavanones found in P. fritescens leaves. Two chalcones, 2′,4′-dimethoxy-4,5′,6′-trihydroxychalcone and 2′,3′-dihydroxy-4′,6′-dimethoxychalcone, as well as an aurone, (Z)-4,6-dimethoxy-7,4′-dihydroxyaurone, are found in P. frutescens leaves [28].

Anthocyanins, Coumarins, Carotenoids, and Neolignans [29-30]

Anthocyanins and their glucosides are found in the leaves of P. frutescens. These anthocyanins include peonidin 3-O-malonyl glucoside-5-O-p-coumarylglucoside, cyanidin 3-O-feruloyl glucoside-5-O-glucoside, cyanidin 3-O-caffeoyl glucoside-5-O-glucoside, and shisonin, cis-shosinin, malonyl shisonin, and cis-malonyl shisonin [29]. The compounds esculetin and 6,7-dihydroxycoumarin found in P. frutescens leaves have anti-inflammatory and xanthine oxidase (XO)-inhibitory properties. Lololiolide and isololiolide, two carotenoids found in leaves, have the ability to inhibit Magnosalin and amanicin, two neolignans found in P. frutescens leaves, have the ability to cure inflammation and endotoxemia [30].

Fatty Acids, Policosanols, Tocopherols, and Sitosterols [31]

About 40% of the total weight of the seeds is made up of perilla seed oil. Saturated fatty acids, including stearic acid, arachidic acid, palmitic acid, lauric acid, myristic acid, pentadecanoic acid, palmitic acid, and heptadecanoic acid, are present in P. frutescens seed oil. The seeds contain polyunsaturated fatty acids (PUFAs) such as linoleic acid (18:2 cis-9,12), α-linolenic acid (18:3 cis-9,12,15), eicosadienoic acid (20:2 cis-11,14), and eicosatrienoic acid (20:3 cis-11,14,17) as well as monounsaturated fatty acids (MUFAs) like palmitoleic acid (16:1 cis-7), oleic acid (18:1 cis-9), and eicosenoic acid (20:1 cis-11). With 54-64% α-linolenic acid, 14-23% oleic acid, 11-16% linoleic acid, and 7-8% saturated fatty acids, perilla seed oil is mostly rich in unsaturated fatty acids. Eicosanol, heneicosanol, docosanol, tricosanol, tetracosanol, pentacosanol, hexacosanol, heptacosanol, octacosanol, nonacosanol, and triacontanol are among the policosanols found in P. frutescens seed. Eighty-eight percent of policosanols are composed of tetracosanol, hexacosanol, and octacosanol. Important vitamin-E-related antioxidant chemicals called tocopherols, such as δ-tocopherol, γ-tocopherol, β-tocopherol, and α-tocopherols, are also present in P. frutescens seeds. Perilla seeds contain 70–80% of the total tocopherol content as γ-tocopherol, which is roughly equivalent to α-linolenic acid in concentration. Phytosterols such campesterol, stigmasterol, β-sitosterol, β-amyrin, β-cholestanol, and 5α-cholestane are also present in the seeds [31].

Glucosides, Peptides, Benzoxepin Derivatives, and Other Constituents [32]

P. frutescens leaves contain a variety of glucosides, such as monoterpene glucosides including dehydrovomifoliol, perillanolide A, B, and perilloside A, B, C, and D Loganin, also known as iridoid glucoside, 5′-β-D-glucopyranosyl oxyjasrnonic acid, 3-β-D-glucopyranosyl-3-epi-2-isocucurbic acid, n-octanoyl-β-D-fructofuranosyl-α-D-glucopyranoside, 4-(3,4-Dihydroxybenzoyloxymethyl)phenyl-O-β-d-glucopyranoside (polyphenolic glucoside) and 3-β-D-glucopyranosyloxy-5-phenylvalericacid. Additionally, the leaves have methyl-α-D-galactoside and five β-D-glucosides (eugenyl-β-D-glucoside, benzyl-β-D-glucoside, β-sitosteryl-β-D-glucoside, prunasin, and sambunigrin). Oligopeptides (PSO) and dipeptides like Tyr-Leu and Phe-Tyr are found in the seeds. It has also been found that P. frutescens leaves contain the glycoprotein Pf-gp6. Benzoxepin derivatives, including perilloxin and dehydroperilloxin, are found in P. frutescens stems. P. frutescens leaves have been found to contain other components, including trans-p-hydroxycinnamic acid, p-hydroxyacetophenone, p-hydroxybenzaldehyde, and 3,4,5-trimethoxycinnamyl alcohol [32].

PHARMACOLOGICAL ACTIVITIES

Modern studies on P. frutescens' pharmacology and biology reveal that this medicinal plant has a wide range of biological properties, such as anti-inflammatory, antibacterial, antifungal, antidepressant, anticancer, anti-obesity, antioxidant, anti-microbial and anti-ulcer properties.

ANTIOXIDANT ACTIVITY [33-39]

Using DPPH, researchers examined the antioxidant qualities of perilla seed, leaf, and stalk extract as well as their capacity to scavenge free radicals, reduce power, and chelate metals. They found that 50% of the methanol leaf extract had the potential to be employed as a novel functional food [33]. Using the ABTS, DPPH, and FRAP tests, perilla seeds were found to have greater antioxidant activity than chia and flax seeds [34] Compared to a number of other seed oil crops, including linseed (83.0 mg/kg), mustard (69.0 mg/kg), and sesame (100.0 mg/kg), perilla seed (152.1 mg/kg) has a greater average tocopherol content [35] Isolated from Perilla extract, four antioxidant components were discovered as luteolin, apigenin, chrysoeriol, and rosmarinic acid [36] Rosmarinic acid shields MES23.5 cells against the neurotoxicity caused by 6 hydroxydopamine because of its antioxidant properties [37]. In addition, luteolin, which was separated from Perilla seed methanol extract, lessened the cytotoxicity that hydrogen peroxide caused in primary neurons from neonatal rat cortex [38] In a more recent work, Tyyr-Leu (YL) and Phe-Tyr (FY), two antioxidant peptides, were discovered from enzyme hydrolysates of defatted Perilla seed protein. It was discovered that these peptides prevented HepG-2 cells from being harmed by hydrogen peroxide and decreased lipid peroxidation in the rat liver [39].

ANTI-INFLAMMATORY ACTIVITY [40-41]

The substantial anti-inflammatory effect of P. frutescens was largely attributed to the anti-inflammatory activity of PK-type monoterpenoids, alkaloids, and glycoglycerolipids through their inhibition of pro-inflammatory cytokines and inflammatory mediators (tumor necrosis factora, interleukin-1b, and interleukin-6) in lipopolysaccharide-stimulated RAW264.7 cells. Leaf extracts from P. frutescens were effective in treating respiratory conditions such allergic airway irritation and chronic obstructive pulmonary disease [40]. The mice's colitis was lessened and pro-inflammatory gene expression was regulated by adding the essential

oil that was extracted from P. frutescens to their food. It was discovered that the radiation-induced mutant of P. frutescens significantly reduced arthritic symptoms compared to the wild-type plants [41].

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES [42-43]

It has been demonstrated that the natural antibacterial agent PA is incorporated into the gelatin/zein polymer to increase the shelf life of frozen chicken. PA has been shown to lower oral inflammation and Candida albicans levels in mice with oropharyngeal candidiasis, as well as to prevent normal cell death and increase mice survival rates [42] Because P. frutescens essential oil damaged Enterococcus faecalis' cell membrane, it hindered bacterial reproduction and stopped food from deteriorating [43].

ANTIMICROBIAL [44-45]

In a study, it was discovered that oral pathogenic bacteria (Porphyromonas gingivalis strains and oral streptococci) could be effectively inhibited by the ethyl acetate extract of perilla seeds and the polyphenols extracted from this extract (luteolin) [44]. Similarly, Nisin and Perilla seed oil work together to have bactericidal effects on S. aureus and L. monocytogenes [45].

ANTIDEPRESSANT ACTIVITY [46-48]

Depression is a prevalent illness that affects roughly 3.8% of people worldwide. In the rat model of chronic unexpected mild stress (CUMS), long-term PA treatment decreased the amount of inflammatory mediators by controlling the expression of TXNIP/TRX/NLRP3 in the hippocampus CA4, thereby mitigating the depressive behavior brought on by CUMS [46]. In order to improve the stress-coping and depression-like behaviors brought on by sleep loss, luteolin7-O-glucuronide was utilized [47]. P. frutescens seed oil was investigated for antidepressant properties based on the enhancement of brain-derived neurotrophic factors expression in the rats [48].

ANTICANCER ACTIVITY [49-51]

Hela cells underwent dose-dependent apoptosis due to P. frutescens' anthocyanins [49]. The anti-cancer action of P. frutescens leaf extracts was demonstrated in vitro by their effective inhibition of human colon and lung cancer cell growth, colony formation, adhesion, and metastasis [50]. It has been demonstrated that PA inhibits PC-3 prostate cancer cells' ability to proliferate, invade, and migrate as well as RAW264.7 cells' ability to differentiate osteoclasts and undergo bone metastases. According to a prior study, PA can also raise the amount of autophagy-related proteins and stop stomach cancer from growing [51].

ANTI-DIABETIC [52-54]

A study using a type 2 diabetes mice model examined the anti-diabetic properties of perilla seed sprouts. Perilla seed sprouts supplemented at 100, 300, and 1,000 mg/kg of body weight reduced body weight and blood triacylglyceride levels; enhanced insulin resistance, glucose tolerance, and hyperglycemia; activated AMP-activated protein kinase (AMPK); and controlled gluconeogenesis [52]. In a different study, an ethyl acetate soluble fraction of the methanol extract of Perilla contains the Aldose reductase enzyme inhibitors chlorogenic acid and rosmarinic acid, which lower the problems associated with diabetes [53]. Furthermore, a 12-week study was conducted on the impact of Perilla oil supplementation on the intestinal microbiota of diabetic KKAy mice. Perilla oil supplementation was found to significantly increase the microfora Lactobacillus, which is thought to be a beneficial bacteria because it converts sugars to lactic acid, and significantly decrease the Microfora Blautia, a gram positive anaerobe bacterium that causes disruptions in glucose metabolism [54].

EFFECT ON GASTROINTESTINAL SYSTEM [55-56]

Ileum contraction is the source of gastrointestinal discomfort, and daily stress, dietary sensitivities and allergies, infections, and genetic predisposition are risk factors. Research on the impact of perilla seed oil on gastrointestinal motility revealed that supplementing albino rats with 5ml/kg, 7.5ml/kg, and 10ml/kg of perilla seed oil enhanced motility and had a laxative effect; loperamide was discovered to be the cause of constipation in rats [55]. Similarly, in wister strain albino rats, intraperitoneal treatment of Perilla seed oil (1, 2 and 3 ml/kg) significantly protects against reflux esophagitis by decreasing the amount of gastric juice, raising the pH of the stomach, and suppressing the esophagitis index [56].

NEUROPROTECTIVE [57-63]

Perilla seed's active ingredient, α-linolenic acid, has been shown to have neuroprotective properties by preventing apoptosis and reducing inflammation in mice brain cells when fed an atherogenic diet [57]. Fish oil may not be the only option for supporting

neuroprotective and mitochondrial processes in the brain; perilla seed oil, with its high α-linolenic acid content, may be a good substitute [58]. Recent research has demonstrated that perilla seed oil is a safe and useful antioxidative therapy for people suffering from mild to moderate dementia [59]. Perilla cold-pressed seed oil defended PC12 rat pheochromocytoma cells from beta-amyloid-induced neurotoxicity and has potential use as a functional diet for Alzheimer's patients [60]. In an elderly population with mild cognitive impairment, a 6-month randomized, placebo-controlled trial found that supplementing Perilla seed oil with brain training increased plasma and erythrocyte plasma membrane α-linolenic acid levels, as well as improving cognitive function as measured by Frontal Assessment Battery (FAB) score [61]. Adult male rats were given a diet high in seed oil during a forced swim test, which altered their fatty acid profiles and the expression of brain-derived neurotrophic factor (BDNF) in the brain [62]. This suggests that the oil from PF seeds may have antidepressant qualities. Furthermore, by generating new hippocampus neuronal membrane structures and inducing specific protein creation, ω-3 fatty acid-rich perilla seed oil improved rats' cognitive performance [63].

OTHER PHARMACOLOGICAL ACTIVITY [64-66]

The hepatoprotective properties of the primary phenolic components found in cold-pressed Perilla frutescence seed flour (CP-PFSF) following oil extraction were studied both in vitro and in vivo. These components are rosmarinic acid and caffeic acid. RA-rich extract treatment decreased H2O2-induced cytotoxicity in vitro. Oral administration of RA-rich extract in vivo significantly decreased hepatocyte degeneration and neutrophilic infiltration caused by tert-butyl hydroperoxide, as well as the levels of aspartate and alanine aminotransferases [64]. It has been demonstrated that perilla oil has the same anti-inflammatory cytokine effects as fish oil. Specifically, mice fed a high-fat diet showed significantly lower levels of IL-1β, TNF-α, and IL-6. Additionally, both perilla oil and fish oil supplementation showed lower levels of Gram-negative Prevotella, which may be a factor in the development of non-alcoholic fatty liver disease [65]. Perilla frutescense modulates endometrial receptivity by upregulating the cytokine LIF (leukemia inhibitory factor). Enhancing endometrial receptivity is necessary for successful embryo implantation, hence Perilla may help women who have had improper implantation [66].

TOXICITY [67-69]

Perilla is often avoided by cattle; however, it has been linked to cattle poisoning in the past. Late in the summer, when seed production is at its highest, is when plants become most toxic when cut and dried for hay. Pneumonia (fluid in the lung cavity) is caused by perilla ketone in a number of animal species, excluding dogs and pigs [67]. Perillaldehyde exposure causes dermatitis on the hands in 20–50% of long-term perilla workers in Japan [68]. In 1993, Brenner examined the toxicity of gorillas. Through an IgE-mediated mechanism, occupational asthma was caused by inhaling smoke from roasting perilla seeds. There is also a single recorded case of anaphylaxis brought on by perilla seeds [69].

CONCLUSION

The current review paper gathers data on the chemical makeup of perilla, its potential applications, and the potential biological impacts of the plant's numerous sections, including the seeds and seed oil. Cultivars of P. frutescens L. are utilized today in many Asian countries, where they have been for a very long time. The plant has been grown for its many uses, including treating depression-related illnesses, tumors, asthma, allergies, coughs, colds, fever, chills, headaches, stuffy noses, and a host of digestive problems. It is also used as an antioxidant. It has been utilized as a beautiful plant in gardens due to genetic variances. Due to their high levels of fatty acid oils and carotenoids, respectively, the leaves and seeds have substantial nutritional value. They may also be used in the food business as functional dietary supplements. This review's presentation of the pharmacological effects of P. frutescens ingestion suggests that it has a higher therapeutic value. Its pharmacological activity, availability of diverse phytochemicals, and active ingredients demonstrate this plant's potential for application in the upcoming development of novel, highly effective formulations.

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