

LITERATURE REVIEW**Cough: A protective reflex and herbal therapies****Imran Ozdemir¹**, **Nuray Bayar Muluk²**, **Oguzhan Oguz^{3,4}**, **Zeynel Ozturk^{5,6}**, **Cemal Cingi⁷**¹Department of Pulmonology, Turkiye Private Hospital, Istanbul, Turkey²Department of Otorhinolaryngology, Kırıkkale University, Faculty of Medicine, Kırıkkale, Turkey³Department of Audiology, Istanbul Nisantasi University, Health Services Vocational School, Istanbul, Turkey⁴Dr.Oguzhan Oguz Wellnose Clinic, Istanbul, Turkey⁵Department of Otorhinolaryngology, Istanbul Nisantasi University, Faculty of Medicine, Istanbul, Turkey⁶Baypark Hospital, Otolaryngology Clinics, Istanbul, Turkey⁷Department of Otorhinolaryngology, Eskisehir Osmangazi University, Faculty of Medicine, Eskisehir, Turkey**ABSTRACT****OBJECTIVES.** In this paper, we reviewed cough and herbal therapies.**MATERIAL AND METHODS.** Research methods included searching online databases such as Google, Google Scholar, ProQuest Central, and PubMed at Kırıkkale University. We used terms like "cough", "herbal", "reflex", "Primula veris", "Primula elatior", "Thymus vulgaris", "Althea Officinalis", and "Mentha piperita" to find related articles.**RESULTS.** Coughing is a reflex that serves a legitimate physiological purpose by expelling fluids and debris from the lungs. Herbal teas and preparations with antioxidant and expectorant properties are made from medicinal herbs like Primula veris and Primula elatior. The phenolic monoterpene thymol, one of the primary components of thyme oil, is found primarily in thyme plants. Both thymol and thyme essential oil have lengthy histories of usage in conventional medicine, particularly for their upper respiratory system-targeted expectorant, anti-inflammatory, antiviral, antibacterial, and antiseptic properties. Historically, people have turned to the plant Althea officinalis for help with treating respiratory issues, like cough. Officinalis extracts alone for dry cough therapy, while A. officinalis was more effective when combined with Zataria multiflora, Zingiber officinale, or Helix hederata. Furthermore, all types of coughs benefited from officinalis. One of the most popular types of herbal tea, known as a tisane, is peppermint, or Mentha piperita. Peppermint essential oil and tea made from the plant's leaves have long histories of usage in alternative medicine. Some studies have found that peppermint may have antiallergenic properties in addition to its antibacterial, antiviral, antioxidant, and anticancer properties.**CONCLUSION.** Cough is a persistent symptom of many acute and chronic illnesses. Primula veris, Thymus vulgaris, Althea Officinalis, and Mentha piperita are some herbs used to treat cough. Cough patients can supplement their standard medical care with herbal remedies that contain these compounds.**KEYWORDS:** Primula veris, Primula elatior, thymol, thyme, peppermint (Mentha piperita), cough.**COUGH: OVERVIEW**

Clinicians often face difficulties while treating persistent coughing. Adults most frequently reported chronic cough, which has not improved after eight weeks of treatment^{1,2}. Up to 40% of the population may suffer from chronic cough^{3,4}.

Historically, otolaryngologists have been responsible for

the upper airway, and pulmonologists have been responsible for the lower airway. The "one airway" theory proposes that disorders that begin in the nose and mouth and extend to the most distal aspects of the lungs^{5,7} share a common mechanism: a continuum of inflammation that involves the entire airway. This theory was inspired by recent research showing that a large percentage of patients with asthma also suffer from allergic rhinitis.

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Patients with cough-variant asthma, postnasal drip syndrome, and gastroesophageal reflux disease (GERD) all have increased levels of inflammatory mediators in the lower airways. Due to the wide variety of possible causes, persistent cough generally requires a multidisciplinary approach, with the primary care physician acting as a treatment coordinator and referring the patient to an otolaryngologist, pulmonologist, or both. The workup also benefits from the attention of an allergist and immunologist, neurologist, speech therapist, and gastroenterologist⁸.

Using data from the Korea National Health and Nutrition Examination Survey 2010-2016 and the EuroQol five-dimension (EQ-5D) index score on a scale from 0 to 100, Won et al.⁹ found that adults with chronic cough have a lower quality of life (QoL) in terms of their health. Researchers found that 3.48 percent of people aged 40 and higher suffered from persistent cough. Overall, people with a chronic cough had a lower EQ-5D-3L index score than those without a chronic cough. This difference was most pronounced for women aged 65 and up. Anxiety, despair, and discomfort were reported to be more strongly linked to chronic cough than self-care or mobility⁹.

MATERIAL AND METHODS

For this research we used online databases such as Google, Google Scholar, PubMed, and ProQuest Central at Kirikkale University. We used terms like "cough", "herbal", "reflex", "Primula veris", "Primula elatior", "Thymus vulgaris", "Althea Officinalis", and "Mentha piperita" to find related articles. Review articles, randomized controlled trials, prospective studies, and retrospective research are all part of the data set pulled in by the search between the years 2024 to 1980.

IS IT A PROTECTIVE REFLEX TO CONTINUE?

In order to rid the pulmonary system of excess fluids and debris, coughing serves as a protective reflex. There are three parts to the cough reflex: the efferent limb³, the central processing centre, and the afferent sensory limb⁴. Cough receptors receive afferent pathways from the trigeminal, glossopharyngeal, and vagus nerves, with the vast majority coming from the vagus via its pharyngeal, superior laryngeal, and pulmonary branches⁵.

From the pharynx to the end of the bronchioles, the airway is lined with receptors; however, the larynx, carina, and bifurcation of the bigger bronchi contain the highest concentration of receptors¹⁰.

Primarily, there are three types of receptors^{8,11-13}:

- Rapid adapting receptors (RARs) – respond to mechanical stimulation: cigarette smoke; pulmonary congestion; atelectasis; bronchoconstriction; ammo-

nia; acidic and alkaline solutions; hypotonic and hypertonic saline;

- Slowly adapting receptors (SARs) – receptors that change very gradually;
- Inflammatory and immunological mediators like histamine, prostaglandins, bradykinin, capsaicin, substance P, and acidic pH are all detected by nociceptors on C-fibers, which also respond to chemical stimuli.

The nucleus tractus solitarius in the brainstem's medulla are the brain's cough centre, and it receives afferent impulses from the respiratory muscles.

The diaphragm, the intercostal muscles, the abdominal wall, and the pelvic floor are supplied by the phrenic and spinal motor neurons of C3 to S2. At the same time, efferent impulses leave the medulla and proceed to the larynx and tracheobronchial tree via the vagus¹⁰.

Because coughing causes prolonged irritation, inflammation, and tissue remodeling¹², it has been established that the cough reflex is neuroplastic, leading to a hypersensitive response over time. Exaggerated cough responses are common among patients and contribute further to the maintenance of chronic cough^{8,13}. This is partly due to peripheral (increased sensitivity of cough receptors) and central (changes in central processing in the brainstem) sensitization.

Patients with chronic cough hypersensitivity syndrome experience a tickling or itching feeling in the throat and are sensitive to cold air, food, and odors^{8,14}, but they do not respond to standard therapies and have a negative workup. Because an overly sensitive cough reflex is the underlying abnormality leading to persistent coughing, chronic cough hypersensitivity syndrome has been recommended as the new method to name chronic cough¹⁴⁻¹⁶. "Vanilloid 1 (TRPV1)" and "ankyrin 1 (TRPA1) channels", both of which are part of the family of transient receptor potential (TRP) ion channels, have been proposed as receptors that trigger cough¹⁷.

CAUSES OF CHRONIC COUGH

Among immunocompetent, nonsmoking patients with normal chest radiograph findings¹⁸, 92-100% have a chronic cough that can be attributed to one of three diseases, according to retrospective research. Here they are, in descending order of frequency⁸:

1. The postnasal drip syndrome (PNDS) has been renamed the upper airway cough syndrome (UACS)
2. Asthma
3. Acid reflux in the stomach (also known as GERD).

The pathogenic trio of persistent cough consists of these three factors.

Non-asthmatic eosinophilic bronchitis (NAEB) is a fourth possible cause that should be considered immediately because it is expected, simple to detect, and well-treated.

Differentiating between cough caused by eosinophilic airway illnesses (asthma and NAEB) and non-eosinophilic chronic cough is another technique to classify the causes¹⁹. High amounts of exhaled nitric oxide and elevated induced sputum eosinophil counts are diagnostic of eosinophilic airway disorders, which cause inflammation of the airways. They are also linked to a healthy response to steroids¹⁹.

Upper airway cough syndrome

In addition to nasal discharge and constant throat clearing, PNDS is characterized by a feeling of secretions draining from the nose or sinuses into the pharynx. Regrettably, this relies heavily on patients' subjective complaints, sometimes unsubstantiated by objective measures. Twenty percent of people who cough due to postnasal drip syndrome (PNDS) are uninformed that their cough is caused by postnasal drip²⁰. Oropharyngeal mucus and cobblestoning of the mucosa are merely suggestive of this being the underlying cause. However, these results need more specificity^{8,18}.

HERBAL REMEDIES FOR COUGH RELIEF AND PREVENTION

Many acute and chronic illnesses feature coughing as a persistent symptom. Because of the disruption it causes, many people seek medical attention, and the market for OTC treatments is worth millions of dollars²¹. Acute cough symptoms can be brought on by an upper respiratory tract infection (URTI), the common cold, or exposure to smoke and/or allergens in the surrounding environment. Most people will cough at least once in their lives, but how often you cough depends on things like your gender and how sensitive you are to allergens^{22,23}. Neither N-acetyl cysteine (NAC) nor any other traditional mucolytic has been shown to reduce patient discomfort by facilitating mucus expectoration²⁴. Over-the-counter medicines have also failed to show consistent, objective advantages in clinical trials²⁵. This includes cough syrups and cough suppressants. Phytotherapies, hydro therapies, and Traditional Chinese Medicine (TCM) are only a few examples of the many alternative treatments available, yet orthodox medicine rarely uses them. Although herbal remedies have been used for a long time in many different cultures, there needs to be more data from RCTs²⁶⁻²⁸. Due to their efficacy, Ivy, primrose, and thyme-based medicines are indicated as expectorants in current European guidelines²⁹ for treating coughs.

According to Wagner et al.³⁰, there is solid proof that *Andrographis paniculata* and ivy/primrose/thyme-based products are considerably superior to placebo in reducing the frequency and severity of cough symptoms in patients, and moderate evidence that *Pelargonium sidoides* is similarly effective.

Primula veris

The effects of Primula veris and Primula elatior on cough

The true primrose, *Primula L.* Herbal teas, and other preparations derived from medicinal herbs such as *Primula elatior* (L.) Hill are known for their antioxidant and expectorant properties. Both the flowers and the roots of these plants have similar biological properties. This work used a quick and easy HPLC-DAD method (high-performance liquid chromatography with diode-array detection) to assess the phenolic component concentration and composition of raw materials from wild-grown *P. veris* and *P. elatior*. The research confirmed that both kinds of blooms contain high levels of flavonoids. Isorhamnetin-3-O-glucoside, astragaloside, and (+)-catechin were all found in greater concentration in the flowers of *P. veris*, while rutoside and isorhamnetin-3-O-rutinoside were found in greater concentration in the flowers of *P. elatior*. Only *P. elatior* flowers contained the hyper side. Only the roots contained phenolic glycosides (primverin and primulaverin). *P. veris* had almost ten times as much of them as *P. elatior* did in its subsurface organs. The results demonstrate significant differences between the *Primula* species regarding phenolic component concentration and composition³¹.

Small, long-lived perennials from the family "Primulaceae, cowslip (*Primula veris* L., syn. *P. officinalis* Hill) and oxlip (*Primula elatior* (L.) Hill)" are native to the temperate regions of Europe and Asia³¹. Cowslip can be found in herb-rich meadows, nutrient-poor grasslands, and the margins and openings of sunny, warm forests. Although oxlip is mostly home in damp, shady woodlands, you can also find it in mountain meadows^{32,33}. A rosette of leaves and flower stalks up to 20-30 cm in height are produced by both species. Cowslip blossoms are orange dots on a bright yellow background. They develop into an umbel-shaped inflorescence at the very tips of the stems. In turn, oxlip produces pale yellow, nearly odourless flowers on their stems. An orange ring can be seen in the middle of these blossoms^{32,34}. Grayish-brown rhizomes (*P. veris*) or brown (*P. elatior*) roots (also termed roots) make up the underground organs^{31,34,35}.

Primarily used for making herbal teas and other preparations regarded as dietary supplements³⁴, *Primula veris* and *P. elatior* have been widely cultivated. Pharmacological effects such as pectolytic, expectorant, anti-inflammatory, diuretic, antibacterial, antifungal, and sedative are indicated. *Primula* flowers and roots are used to cure a variety of ailments, including nervousness, headaches, and rheumatism³⁶⁻³⁹, as reported by the European Medicines Agency (EMA). Historically, people have consumed both the leaves and blooms of the primula plant, either raw or cooked, when they were in season around the end of winter⁴⁰. Other *Primula* species are described as showing some therapeutic potential in addition to *P. veris* and *P. elatior*. Demir et al.⁴¹ has reported antioxidant activity in *P. vulgaris*. Cytostatic characteristics have been seen in *P. den-*

ticulata extracts, and antifungal qualities have been observed in *P. macrophylla* extracts^{31,42,44}.

Triterpene saponins and phenolic compounds such as flavonoids (approximately 3% in flowers), phenolic acids, and phenolic glycosides^{36,37} are the primary active components found in *Primula* flowers and roots. The pectolytic and expectorant effects of plants are due to saponins. Phenolic chemicals, found primarily in *Primula* flowers, have been found to have antioxidant, antibacterial, and cytostatic effects^{31,41,42}.

Clinical studies on Primula veris and Primula elatior

The presence of hyperoside indicates anti-inflammatory and antioxidant properties, as reported by Kim et al.⁴⁵. Antiviral action was found by Wu et al.⁴⁶, and Kohlmanzer⁴⁷ noted diuretic and hypotensive effects. Furthermore, rutoside has been shown to have antioxidant, antibacterial, and anti-inflammatory properties⁴⁸. This could account for the use of flowers from both *Primula* species as a remedy for coughs and other respiratory system disorders. This research demonstrates that hyperoside and rutoside significantly split the species under study. Therefore, the increased pharmacological activity that may be indicated by *P. elatior* flowers (which are rich in hyperoside and characterized by a larger quantity of rutoside than *P. veris*) is not surprising. Both species had isorhamnetin-3-glucoside in their blossoms, contradicting the findings published by Wichtl³⁴. Both isorhamnetin derivatives shared hyperoside's extremely varied composition. While *P. elatior* showed a more significant variation in isorhamnetin-3-O-glucoside (CV 43.31%), *P. veris* showed a more significant variation in isorhamnetin-3-O-rutinoside (CV 45.54%). Isorhamnetin aglycon displays cytotoxic action for human hepatocellular carcinoma cells, as reported by Teng et al.⁴⁹. One phenolic acid (chlorogenic acid) was also found to be present in both species of *Primula* flowers in our research; its concentration was identical in *P. veris* and *P. elatior* (72.84 and 55.38 mg/100 g DW, respectively).

Primverin and primulaverin are two phenolic glycosides commonly found in *P. veris* and *P. elatior* subsurface parts. Müller et al.⁵⁰ earlier established these compounds' existence in *Primula*'s roots. There is a wide range of possible concentrations of EMA37 in both species, with some estimates going as high as 2.3%. They cause the raw material's characteristic odor to become noticeable after drying^{31,34}.

The flowers only detected two anthocyanins, malvidin, and petunidin glycosides. In contrast, three flavonol glycosides, including quercetin and kaempferol derivatives, were found in the flowers and the leaves of *P. sieboldii*⁵¹. The phenolic acid content of *P. vulgaris* flowers was evaluated by Ozkan et al.⁵² using high-performance liquid chromatography (HPLC) for the determination of catechin, rutin, "gallic, protocatechuic, p-OH benzoic, vanillic, and p-coumaric acids". This study concluded that rutin and "p-coumaric acid" constituted the primary phe-

nolic compounds in this raw material. "Primetin (5,8-dihydroxyflavone)", responsible for high sensitizing capabilities, was also detected^{31,53} in several *Primula* species, including *P. denticulata*, *P. auricular*, *P. Haller*, *P. malachites*, and *P. marginata*.

Thymus vulgaris

Coughs caused by infections are often treated with herbal remedies to speed healing or fortify the immune system. Extracts of thyme and primrose, or both in combination with thymol, are an example of such a preparation. In addition to its antioxidant and anti-inflammatory properties, thymus vulgaris can help reduce muscle spasms and regulate the immune system. Thymol, found in thyme oil, is the active ingredient responsible for thyme's medicinal properties. In addition to its expectorant and pectolytic properties, primrose has spasmolytic, anti-inflammatory, and antibacterial properties as a saponin agent. The extracts mentioned above are frequently utilized as a combination medication due to their synergistic effects and diverse activity profile. We evaluated the efficacy of this combination in treating upper respiratory infections (URI) by measuring its ability to reduce symptoms like coughing and shorten the duration of the illness. It has been proven that the medicine made from thyme and primrose extracts with the addition of thymol is both practical and safe⁵⁴.

Many species belong to the genus *Thymus* in the family Lamiaceae. These plants are native to the Mediterranean region and are used in cooking, cosmetics, and medicine⁵⁵. Herb of the thyme family, whose source is *Thymus vulgaris* L. and *Thymus signs* L. is the most widely recognized natural component in modern medicine. These days, pharmaceutical manufacturers employ only standardized formulations of thyme herb and essential oil that comply with national pharmacopoeias or European Pharmacopoeia X (Ph. Eur. X)⁵⁶.

The phenolic monoterpene thymol (2-isopropyl-5-methylphenol) is found primarily in thyme plants, and it is one of the primary components of thyme oil. Both thymol and thyme essential oil have lengthy histories of usage in conventional medicine, particularly for their upper respiratory system-targeted expectorant, anti-inflammatory, antiviral, antibacterial, and antiseptic properties. Essential oils like thyme and a compound called thymol are among the natural plant compounds being studied for their potential biological or medicinal properties⁵⁶.

The plant thyme and its volatile oil have been used for centuries to alleviate the symptoms of bronchitis, colds, parasite infections, rashes, sprains, and bruises. It has found widespread application as an expectorant for cold-related coughs and a dental disinfectant⁵⁷. Antiviral (herpes simplex virus type I, influenza viruses, and human rhinoviruses), antifungal, anti-inflammatory, antioxidant, and spasmolytic activity; antibacterial effect on

Gram-positive and Gram-negative bacteria. No toxicity has been recorded at widely used levels. Therefore, volatile thyme oil can be considered a safe medicine even though it has cytotoxic effects in high concentrations and may induce intestinal cell damage when supplied orally. High quantities applied to the skin may be irritating. Skin rash, bronchospasm, asthma attacks, and anaphylaxis are some of the symptoms of a severe allergic reaction. Since there may be cross-reactivity between thyme and other members of the Lamiaceae family, people who are sensitive to thyme should not use this essential oil (EO)^{56,58-60}.

According to Kowalczyk et al.⁵⁶, thymol and thyme EO have various biological and therapeutic properties. Bacteria, like *Escherichia coli*, are targeted by antibiofilm strategies. Thyme essential oil and extracts have broad antiviral action, inhibiting the replication of many different viruses. Thymol's anti-SARS-CoV-2 action has also shown great promise in vitro and computer simulation tests.

Althaea officinalis

Historically, people have turned to the plant *Althaea officinalis* for help with treating respiratory issues like a cough. *A. officinalis* extracts alone proved their efficiency for dry cough therapy, while *A. officinalis* combined with *Zataria multiflora*, *Zingiber officinale*, or *Helix hederata* was effective on all types of cough⁶¹.

The polysaccharide rhamnogalacturonan found in *Althaea officinalis* reduces the cough reflex in unsensitized guinea pigs dose-dependently. At the same time, testing showed that the antitussive action of a plant polysaccharide wore off faster under inflammatory settings. Both sensitized and unsensitized animal groups showed no change in airway responsiveness to rhamnogalacturonan under in vivo settings measured by specific resistance values. The duration of guinea pigs' coughing fits is reduced by rhamnogalacturonan, isolated from *Althaea officinalis* mucilage, and has an extreme cough suppressive effect⁶².

The biological effects of rhamnogalacturonan, derived from the roots of the medicinal plant *Althaea officinalis* L., on the citric acid-induced cough reflex and reactivity of airway smooth muscle were studied in vitro and in vivo. It had a dose-dependent cough-suppressing action, just like the opioid agonist codeine. However, rhamnogalacturonan had no discernible influence on airway smooth muscle responsiveness when examined in both vitro and in vivo. This suggests that bronchodilatory activity did not affect the cough-suppressing effect of the polysaccharides evaluated. Activation of K+ATP ion channels is likely not implicated in the mechanism of rhamnogalacturonan's cough suppressive capacity since the polymer's cough suppression action was not significantly altered by pretreatment with selective antagonists. However, when rats were pretreated with a selective 5-HT₂ receptor antagonist, rhamnogalacturonan's antitussive effectiveness was drastically reduced⁶³.

Mentha piperita

Peppermint is a hybrid of water mint and spearmint, two species of mint that can be found naturally occurring in both Eurasia and North America. The leaves of the peppermint plant and the oil extracted from them have both been used medicinally. Peppermint essential oil is extracted from the plant's leaves and flowers. Essential oils are highly concentrated oils containing aromatic or flavourful compounds that give a plant its unique identity. Peppermint oil is a popular scent additive in soaps and cosmetics, and it is also widely used as a flavouring enhancer in meals and drinks. People have relied on peppermint for its medicinal properties for thousands of years. The ancient Greeks, Romans, and Egyptians all documented its use for gastrointestinal and other ailments. Today, peppermint is touted as a treatment for various ailments, including irritable bowel syndrome (IBS), indigestion, the common cold, sinus infections, and headaches. For headaches, muscular aches, joint discomfort, and itching, peppermint oil is advised for topical therapy (applied to the skin). Peppermint oil has several uses in aromatherapy, including curing cold and flu symptoms, relieving discomfort, enhancing concentration, and calming the nerves⁶⁴.

One of the most popular types of herbal tea, known as a tisane, is peppermint (*Mentha piperita* L.). Peppermint essential oil and tea made from the plant's leaves have long histories of usage in alternative medicine. The bioactivity of this herb is discussed in light of the available scientific evidence. In addition to eriocitrin, luteolin, and hesperidin, rosmarinic acid is also present in the leaves as a phenolic compound. Menthol and menthone are the essential oil's primary volatile components. Peppermint has shown promising antibacterial, antiviral, antioxidant, anticancer, and even antiallergenic properties in vitro. Animal studies have shown anti-inflammatory, analgesic, anaesthetic, immunomodulatory, and cancer-preventive properties and a relaxing impact on gastrointestinal (GI) tissue. Peppermint oil and its components have shown gastrointestinal, respiratory, and analgesic benefits in human studies⁶⁵.

Plants belonging to the genus *Mentha* (peppermint) in Lamiaceae (mint family) can be found in nearly every temperate zone on Earth. Peppermint essential oil (PEO) and non-essential components are found in mentha. Anti-inflammatory, antibacterial, antiviral, suicidal, immunomodulatory, anticancer, neuroprotective, antifatigue, and antioxidant actions are all present in PEO, which is composed primarily of menthol, menthone, neo menthone, and iso-menthone. Growing research suggests that PEO may have hypoglycemic and hypolipidemic effects and protect the gastrointestinal, liver, renal, skin, respiratory, brain, and neurological systems. PEO has a wide range of clinical applications, including treating gastrointestinal and dermatological disorders and surgical adjuvant therapy⁶⁶.

There are numerous chemical compounds in mentha, including steroids, flavonoids, triterpenoids, phenolic acids, etc., in addition to the essential oil known as peppermint essential oil (PEO). There are a variety of biologically active secondary metabolites in PEO, including menthol, menthone, neo menthone, and iso-menthone, which have anti-inflammatory, antibacterial, antiviral, suicidal, immunomodulatory, anticancer, neuroprotective, antifatigue, and antioxidant properties. PEO has been shown to have hypoglycemic and hypolipidemic effects, as well as to protect the gastrointestinal, liver, renal, skin, respiratory, brain, and neurological systems, according to the available research. PEO is a postoperative adjuvant therapy for various conditions, including those affecting the digestive tract and the skin⁶⁷.

Anti-inflammatory activity

In the case of the transient receptor potential melastatin 8 (TRPM8) channel, menthol acts as an agonist. Menthol's ability to activate the TRPM8 channel, block the chemical and mechanosensory responses of nociceptive the transient receptor potential (TRP) channels, and reduce the release of pro-inflammatory mediators from nerve endings⁶⁸ makes it a promising treatment for irritable bowel syndrome (IBS). PEO can control IBS symptoms by decreasing the production of pro-inflammatory cytokines and increasing the production of anti-inflammatory cytokines. PEO has been shown to reduce intestinal inflammation caused by xylene in mice and acetic acid in rats⁶⁹ when given orally. Prostaglandin E2 (PGE2) synthesis, activation of K⁺-ATP channels, and an antisecretory effect are all linked to mucus secretion, which is why menthol has a gastroprotective impact through anti-inflammatory action⁷⁰.

There is evidence that by blocking the Extracellular signal-regulated kinase - nuclear factor kappa B (ERK-NF-B) pathway⁷¹, PEO can reduce inflammation and the resulting atopic dermatitis-like lesions. Furthermore, menthol has been shown to lessen oxidative stress and inflammation^{71,72}. In particular, PEO's anti-inflammatory and analgesic actions in respiratory disease⁷³ are noteworthy. PEO also inhibits carbachol-induced muscular contraction involving the autonomic ganglia. In addition to its analgesic⁷⁴ and anti-inflammatory properties, PEO is effective against croton oil-induced mouse ear edema by suppressing nitric oxide and prostaglandin E2 production^{66,75}.

Antibacterial activity

PEO has potent antimicrobial action, as mounting research shows⁷⁶. One of the *Staphylococcus* superbugs, *Staphylococcus aureus*, has emerged as a problematic bacterial strain in modern invasive medicine⁷⁷. *Pseudomonas aeruginosa*, *Escherichia coli*, *Neisseria gonorrhoeae*, and *Staphylococcus aureus* are just a few of the human pathogenic bacteria that peppermint essential oil 7 (PEO7) inhibits^{78,79}. Peppermint essential oil (PEO) has a powerful antibacterial impact on *Staphylococcus aureus*, *Listeria monocytogenes*, *Bacillus cereus*, and *Escherichia coli*, as

shown by broth microdilution and disc diffusion technique analyses^{66,80}.

Antiviral activity

PEO treatment of virus particles used in fusion experiments showed a significant reduction in virus entry into cells and a subsequent decrease in viral replication efficiency. Research shows that at non-cytotoxic concentrations, PEO rapidly reduces HIV-1 virions' infectious potential. Infectious respiratory illness is caused by a syncytial virus called the human respiratory syncytial virus (RSV). It is shown that PEO has potent anti-RSV action⁸¹.

Immunomodulatory activity

Macrophages and other phagocytes function as the primary effectors of the innate immune system, clearing the body of invading pathogens. Recognition of a pathogen-associated molecular pattern (PAMP) triggers the activation of macrophages. PEO is discovered to regulate immunological activity by phagocytosis in vitro research⁸².

In addition to lowering IL-6 via regulating phosphorylation of Janus kinase 2 (JAK2) and signal transducer and activator of transcription 3 (STAT3), PEO can reduce airway epithelial hyperplasia, collagen deposition, and goblet cell activation in asthmatic mice⁸³.

CONCLUSIONS

Many acute and chronic disorders have the persistent symptom of cough⁸⁴. *Primula veris*, *Thymus vulgaris*, *Althaea officinalis*, and *Mentha piperita* are some herbs used to treat coughs. Herbal therapies like Otatusin® (Otacı, Kurtsan İlaçları, İstanbul, Turkey)⁸⁵ and Otabron (Otacı, Kurtsan İlaçları, İstanbul, Turkey)⁸⁵, which can be found in Turkey and include these compounds, can be used to supplement standard medical care for patients with cough.

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