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LITERATURE REVIEW

Cough: A protective reflex and herbal therapies

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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 Kirikkale 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 Althaea 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 hedera. 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, Althaea 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 gastroenterologist[8].

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 mobility[9].

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 limb[3], the central processing centre, and the afferent sensory limb[4]. 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 branches[8].

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 receptors[10].

Primarily, there are three types of receptors[8,11-13]:

- Rapid adapting receptors (RARs) – respond to mechanical stimulation: cigarette smoke; pulmonary congestion; atelectasis; bronchoconstriction; ammonia; 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 solitaries 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 vagus[10].

Because coughing causes prolonged irritation, inflammation, and tissue remodeling[12], 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 cough[14-16]. “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 cough[17].

CAUSES OF CHRONIC COUGH

Among immunocompetent, nonsmoking patients with normal chest radiograph findings[18], 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 frequency[8]:

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 causes[19]. 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 steroids[19].

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 drip[20]. 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 dollars[21]. 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 expectoration[24]. Over-the-counter medicines have also failed to show consistent, objective advantages in clinical trials[25]. 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 RCTs[26-28]. Due to their efficacy, Ivy, primrose, and thyme-based medicines are indicated as expectorants in current European guidelines[29] 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, astragalin, 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 composition[31].

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 Asia[31]. 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 supplements[34], *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 rheumatism[36-39], 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 winter[40]. 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 Kohlmnzer[47] noted diuretic and hypotensive effects. Furthermore, rutoside has been shown to have antioxidant, antibacterial, and anti-inflammatory properties[48]. 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 Wichtl[34]. 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 phenolic 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 safe[54].

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 medicine[55]. 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 properties[56].

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 disinfectant[57]. 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 hedera* was effective on all types of cough[61].

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 effect[62].

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 reduced[63].

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 nerves[64].

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 studies[65].

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 therapy[66].

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 skin[67].

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 endings[68] 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 rats[69] 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 action[70].

There is evidence that by blocking the Extracellular signal-regulated kinase - nuclear factor kappa B (ERK-NF-B) pathway[71], 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 disease[73] are noteworthy. PEO also inhibits carbachol-induced muscular contraction involving the autonomic ganglia. In addition to its analgesic[74] 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 shows[76]. One of the Staphylococcus superbugs, Staphylococcus aureus, has emerged as a problematic bacterial strain in modern invasive medicine[77]. 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 action[81].

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 research[82].

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 mice[83].

CONCLUSIONS

Many acute and chronic disorders have the persistent symptom of cough[84]. *Primula veris*, *Thymus vulgaris*, *Althaea officinalis*, and *Mentha piperita* are some herbs used to treat coughs. Herbal therapies like Otatusin® (Otacı, Kurtsan Ilaçları, Istanbul, Turkey)[85] and Otabron (Otacı, Kurtsan Ilaçları, Istanbul, 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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REFERENCES

1. Palombini BC, Villanova CA, Araújo E, Gastal OL, Alt DC, et al. A pathogenic triad in chronic cough: asthma, postnasal drip syndrome, and gastroesophageal reflux disease. Chest. 1999;116(2):279-84. DOI: 10.1378/chest.116.2.279.
2. Song WJ, Chang YS, Faruqi S, Kang MK, Kim JY, Kang MG, et al. Defining chronic cough: a systematic review of the epidemiological literature. Allergy Asthma Immunol Res. 2016;8(2):146-55. DOI: 10.4168/aair.2016.8.2.146.
3. Nasra J, Belvisi MG. Modulation of sensory nerve function and the cough reflex: understanding disease pathogenesis. Pharmacol Ther. 2009;124(3):354-75. DOI: 10.1016/j.pharmthera.2009.09.006.
4. Andersson C, Bonvini SJ, Horvath P, Marquez E, Satia I, Kirkham P, et al. Research highlights from the 2017 ERS International Congress: airway diseases in focus. ERJ Open Res. 2018;4(1):00163-2017. DOI: 10.1183/23120541.00163-2017.
5. Cruz AA. The 'united airways' require an holistic approach to management. Allergy. 2005;60(7):871-4. DOI: 10.1111/j.1398-9995.2005.00858.x.
6. de Benedictis FM, Bush A. Rhinosinusitis and asthma: epiphenomenon or causal association? Chest. 1999;115(2):550-6. DOI: 10.1378/chest.115.2.550.
7. Grossman J. One airway, one disease. Chest. 1997;111(2 Suppl):11S-16S. DOI: 10.1378/chest.111.2_suppliment.11s.
8. Chen HH. Chronic Cough. [Internet]. Medscape. [updated Jun 18, 2023]. Available from: https://emedicine.medscape.com/article/1048560-overview?form=fpf. Accessed May 6, 2024.
9. Won HK, Lee JH, An J, Sohn KH, Kang MG, Kang SY, et al. Impact of chronic cough on health-related quality of life in the Korean adult general population: The Korean National Health and Nutrition Examination Survey 2010-2016. Allergy Asthma Immunol Res. 2020;12(6):964-79. DOI: 10.4168/aair.2020.12.6.964.
10. Simpson CB, Amin MR. Chronic cough: state-of-the-art review. Otolaryngol Head Neck Surg. 2006;134(4):693-700. DOI: 10.1016/j.otohns.2005.11.014.
11. Millqvist E, Bende M. Role of the upper airways in patients with chronic cough. Curr Opin Allergy Clin Immunol. 2006;6(1):7-11. DOI: 10.1097/01.all.0000199796.64304.ca.
12. Chung KF, Pavord ID. Prevalence, pathogenesis, and causes of chronic cough. Lancet. 2008;371(9621):1364-74. DOI: 10.1016/S0140-6736(08)60595-4.
13. Chung KF. Chronic cough: future directions in chronic cough: mechanisms and antitussives. Chron Respir Dis. 2007;4(3):159-65. DOI: 10.1177/1479972307077894.
14. Birring SS. New concepts in the management of chronic cough. Pulm Pharmacol Ther. 2011;24(3):334-8. DOI: 10.1016/j.pupt.2011.01.005.
15. Birring SS. Controversies in the evaluation and management of chronic cough. Am J Respir Crit Care Med. 2011;18396):708-15. DOI: 10.1164/rccm.201007-1017CI.
16. Chung KF. Chronic 'cough hypersensitivity syndrome': a more precise label for chronic cough. Pulm Pharmacol Ther. 2011;24(3):267-71. DOI: 10.1016/j.pupt.2011.01.012.
17. Geppetti P, Patacchini R, Nassini R, Materazzi S. Cough: the emerging role of the TRPA1 channel. Lung. 2010;188 Suppl 1:S63-8. DOI: 10.1007/s00408-009-9201-3.
18. Pratter MR. Overview of common causes of chronic cough: ACCP evidence-based clinical practice guidelines. Chest. 2006;129(1 Suppl):59S-62S. DOI: 10.1378/chest.129.1_suppl.59S.
19. Pavord ID, Chung KF. Management of chronic cough. Lancet. 2008;371(9621):1375-84. DOI: 10.1016/S0140-6736(08)60596-6.
20. Pratter MR, Bartter T, Akers S, DuBois J. An algorithmic approach to chronic cough. Ann Intern Med. 1993;119(10):977-83. DOI: 10.7326/0003-4819-119-10-199311150-00003.
21. Morice AH. Epidemiology of cough. Pulm Pharmacol Ther. 2002;15(3):253-9. DOI: 10.1006/pupt.2002.0352.
22. Barbee RA, Halonen M, Kaltenborn WT, Burrows B. A longitudinal study of respiratory symptoms in a community population sample. Correlations with smoking, allergen skin-test reactivity, and serum IgE. Chest. 1991;99(1):20-6. DOI: 10.1378/chest.99.1.20.
23. McGarvey LP, Heaney LG, Lawson JT, Johnston BT, Scally CM, Ennis CM, et al. Evaluation and outcome of patients with chronic non-productive cough using a comprehensive diagnostic protocol. Thorax. 1998;53(9):738-43. DOI: 10.1136/thx.53.9.738.
24. Rubin BK. Mucolytics, expectorants, and microkinetic medications. Respir Care. 2007;52(7):859-65.
25. Schroeder K, Fahey T. Systematic review of randomized controlled trials of over the counter cough medicines for acute cough in adults. BMJ. 2002;324(7333):329-31. DOI: 10.1136/bmj.324.7333.329.
26. Brendler T, van Wyk BE. A historical, scientific, and commercial perspective on the medicinal use of Pelargonium sidoides (Geraniaceae). J Ethnopharmacol. 2008;119(3):420-33. DOI: 10.1016/j.jep.2008.07.037.
27. Kindscher K. Ethnobotany of purple coneflower (Echinacea angustifolia, Asteraceae) and other Echinacea species. Econ Bot. 1989;43:498-507. DOI: 10.1007/BFO2935924.
28. Singh AK, Raghubanshi AS, Singh JS. Medical ethnobotany of the tribals of Sonaghati of Sonbhadra district, Uttar Pradesh, India. J Ethnopharmacol. 2002;81(1):31-41. DOI: 10.1016/s0378-8741(02)00028-4.
29. Kardos P, Berck H, Fuchs KH, Gillissen A, Klimek L, Morr H, et al. Guidelines of the German Respiratory Society for diagnosis and treatment of adults suffering from acute or chronic cough. Pneumologie. 2010;64(11):701-11. DOI: 10.1055/s-0030-1255526.
30. Wagner L, Cramer H, Klose P, Lauche R, Gass F, Dobos G, et al. Herbal medicine for cough: a systematic review and meta-analysis. Forsch Komplementmed. 2015;22(6):359-68. DOI: 10.1159/000442111.
31. Baczek K, Przybyl JL, Mirgos M, Kosakowska O, Szymborska-Sandhu I, Węglarz Z. Phenolics in Primula veris L. and P. elatior (L.) Hill raw materials. Int J Anal Chem. 2017;2017:2871579. DOI: 10.1155/2017/2871579.
32. Kalman K, Medvegy A, Penzes Z, Mihalik E. Morph-specific variation of

floral traits associated with reciprocal herkogamy in natural populations of Primula vulgaris and Primula veris. Plant Syst Evol. 2007;268:15-27. DOI: 10.1007/s00606-007-0575-5.
33. Brys R, Jacquemyn H. Biological flora of the British Isles: Primula veris L. Journal of Ecology. 2009;97:581-600. DOI: 10.1111/j.1365-2745.2009.01495.x.
34. Wichtl M, editor. Herbal drugs and phytopharmaceuticals: A handbook of practice on a scientific basis. 3rd. Stuttgart, Germany: CRC Press; 2004.
35. European Pharmacopoeia. Primula root (Primulaeradix). European Directorate for the Quality of Medicines and Health Care (EDQM) 5th. Strasbourg, France: Council of Europe; 2006, p. 2310-11.
36. European Medicines Agency. Committee on Herbal Medicinal Products (HMPC). Assessment report on Primula veris L. and/or Primula elatior (L.) Hill, flos. EMA/HMPC/136583/2012. 19 September 2012. Available from: https://www.pharmacompass.com/pAssets/pdf/pubchem/primula-veris-l.pdf.
37. European Medicines Agency. Committee on Herbal Medicinal Products (HMPC). Assessment report on Primula veris L. and/or Primula elatior (L.) Hill, radix. EMA/HMPC/113577/2012. 19 September 2012. Available from: https://www.ema.europa.eu/en/documents/herbal-report/final-assessment-report-primula-veris-l-and-or-primula-elatior-l-hill-radix_en.pdf.
38. Zielinska-Pisklak M, Szeleszczuk L. Pierwiosnek, nie tylko zwiastun wiosny, drug in Poland. Farmakot. 2013;23:1-4.
39. Basbulbul G, Ozmen A, Biyik HH, Sen O. Antimitotic and antibacterial effects of the Primula veris L. flower extracts. Caryologia. 2008;61(1):88-91. DOI: 10.1080/00087114.2008.10589614.
40. Wiersema JH, Leon B. World Economic Plants: A Standard Reference. 1st Edition. CRC Press; 1999.
41. Demir N, Gungor AA, Nadaroglu H, Demir Y. The antioxidant and radical scavenging activities of Primrose (Primula vulgaris). Eur J Exp Biol. 2014;4:395-401.
42. Tokalov SV, Kind B, Wollenweber E, Gutzeit HO. Biological effects of epicuticular flavonoids from Primula denticulata on human leukemia cells. J Agric Food Chem. 2004;52(2):239-45. DOI: 10.1021/jf0347160.
43. Najmus-Saqib Q, Alam F, Ahmad M. Antimicrobial and cytotoxicity activities of the medicinal plant Primula macrophylla. J Enzyme Inhib Med Chem. 2009;24(3):697-701. DOI: 10.1080/14756360802333406.
44. Aslam K, Nawchoo IA, Ganai BA. In vitro antioxidant, antibacterial activity, and phytochemical studies of Primula denticulate - an important medicinal plant of Kashmir Himalaya. Int J Pharmacol Research. 2015;5(3):49-56. DOI: 10.7439/ijpr.v5i3.1699.
45. Kim SJ, Um JY, Lee JY. Anti-inflammatory activity of hyperoside through the suppression of nuclear factor-κB activation in mouse peritoneal macrophages. Am J Chin Med. 2011;39(1):171-81. DOI: 10.1142/S0192415X11008737.
46. Wu LL, Yang XB, Huang ZM, Liu HZ, Wu GX. In vivo and in vitro antiviral activity of hyperoside extracted from Abelmoschus manihot (L) media. Acta Pharmacol Sin. 2007;28(3):404-9. DOI: 10.1111/j.1745-7254.2007.00510.x.
47. Kohlműnzer S. Farmakognozja, Wydawnictwo Lekarskie PZWL. 5th. Warsaw, Poland; 2013.
48. Chua LS. A review on plant-based rutin extraction methods and its pharmacological activities. J Ethnopharmacol. 2013;150(3):805-17. DOI: 10.1016/j.jep.2013.10.036.
49. Teng BS, Lu YH, Wang ZT, Tao XY, Wei DZ. In vitro anti-tumor activity of isorhamnetin isolated from Hippophae rhamnoides L. against BEL-7402 cells. Pharmacol Res. 2006;54(3):186-94. DOI: 10.1016/j.phrs.2006.04.007.
50. Muller A, Ganzera M, Stuppner H. Analysis of phenolic glycosides and saponins in Primula elatior and Primula veris (primula root) by liquid chromatography, evaporative light scattering detection and mass spectrometry. J Chromatogr A. 2006;111291-2):218-23. DOI: 10.1016/j.chroma.2005.10.067.
51. Hashimoto N, Ohsawa R, Kitajima J, Iwashina T. New flavonol glycosides from the leaves and flowers of Primula sieboidii. Nat Prod Commun. 2015;10(3):421-3.
52. Ozkan TM, Aliyazicioglu R, Demir S, Misir S, Turan I, Yildirmis S, et al. Phenolic characterization and antioxidant activity of Primula vulgaris and its antigenotoxic effect on fibroblast cell. Jundishapur Journal of Natural Pharmaceutical Products. 2016;12(1):e40073.
53. Aslam K, Nawchoo IA, Bhat MA, Ganie AH, Aslam N. Ethno-pharmacological review of genus Primula. IJAR. 2014;2:29-34.
54. Schonknecht K, Krauss H, Jambor J, Fal AM. Treatment of cough in respiratory tract infections - the effect of combining the natural active compounds with thymol. Wiad Lek. 2016;69(6):791-8.
55. Ghasemi G, Alirezalu A, Ghosta Y, Jarrahi A, Safavi SA, Abbas-Mohammadi M, et al. Composition, antifungal, phytotoxic, and insecticidal activities of Thymus kotschyanus essential oil. Molecules. 2020;25(5):1152. DOI: 10.3390/molecules25051152.
56. Kowalczyk A, Przychodna M, Sopata S, Bodalska A, Fecka I. Thymol and Thyme essential oil-new insights into selected therapeutic applications. Molecules. 2020;25(18):4125. DOI: 10.3390/molecules25184125.
57. Thosar N, Basak S, Bahadure RN, Rajurkar M. Antimicrobial efficacy of five essential oils against oral pathogens: An in vitro study. Eur J Dent. 2013;7(Suppl 1):71-7. DOI: 10.4103/1305-7456.119078.
58. European Medicines Agency. Committee on Herbal Medicinal Products (HMPC). Assessment report on Thymus vulgaris L., Thymus zygis L., aetheroleum. EMA/HMPC/52980/2017. 8 July 2020. Available from: https://www.ema.europa.eu/en/documents/herbal-report/final-assessment-report-thymus-vulgaris-l-thymus-zygis-l-aetheroleum-revision-1_en.pdf.
59. Walther C, Schmidtke M. Anti-rhinovirus and anti-influenza virus activities of mucoactive secretolytic agents and plant extracts – a comparative in vitro study. Research Square. 2020. DOI: 10.21203/rs.2.23461/v1. Available from: https://www.researchsquare.com/article/rs-14028/v1. [Preprint].
60. Lenz E, Muller C, Mostafa A, Dzieciolowski J, Kanrai P, Dam S, et al. Authorised medicinal product Aspecton® Oral Drops containing thyme extract KMTv24497 shows antiviral activity against viruses which cause respiratory infections. J Herb Med. 2018;13:26-33. DOI: 10.1016/j.hermed.2018.02.003.
61. Mahboubi M. Marsh Mallow (Althaea officinalis L.) and its potency in the treatment of cough. Complement Med Res. 2020;27(3):174-83. DOI: 10.1159/000503747.
62. Sutovska M, Capek P, Franova S, Joskova M, Sutovsky J, Marcinek J, et al. Antitussive activity of Althaea officinalis L. polysaccharide rhamnogalacturonan and its changes in guinea pigs with ovalbumin-induced airways inflammation. Bratisl Lek Listy. 2011;112(12):670-5.
63. Sutovska M, Nosalova G, Sutovsky J, Franova S, Prisenznakova L, Capek P. Possible mechanisms of dose-dependent cough suppressive effect of Althaea officinalis rhamnogalacturonan in guinea pigs test system. Int J Biol Macromol. 2009;45(1):27-32. DOI: 10.1016/j.ijbiomac.2009.03.008.
64. National Center for Complementary and Integrative Health. Peppermint Oil. [Internet]. Available from: https://www.nccih.nih.gov/health/peppermint-oil.
65. McKay DL, Blumberg JB. A review of the bioactivity and potential health benefits of peppermint tea (Mentha piperita L.). Phytother Res. 2006;20(8):619-33. DOI: 10.1002/ptr.1936.
66. Zhao H, Ren S, Yang H, Tang S, Guo C, Liu M, et al. Peppermint essential oil: its phytochemistry, biological activity, pharmacological effect and application. Biomed Pharmacother. 2022;154:113559. DOI: 10.1016/j.biopha.2022.113559.
67. Bardaweel SK, Bakchiche B, ALSalamat HA, Rezzoug M, Gherib A, Flamini G. Chemical composition, antioxidant, antimicrobial and Antiproliferative activities of essential oil of Mentha spicata L. (Lamiaceae) from Algerian Saharan atlas. BMC Complement Altern Med.

2018;1891):201. DOI: 10.1186/s12906-018-2274-x.

68. Peiris M, Weerts ZZRM, Aktar R, Masclee AAM, Blackshaw A, Keszthelyi D. A putative anti-inflammatory role for TRPM8 in irritable bowel syndrome - An exploratory study. Neurogastroenterol Motil. 2021;33(9):e14170. DOI: 10.1111/nmo.14170.
69. Azad AK, Doolaanea AA, Al-Mahmood SMA, Kennedy JF, Chatterjee B, Bera H. Electro-hydrodynamic assisted synthesis of lecithin-stabilized peppermint oil-loaded alginate microbeads for intestinal drug delivery. Int J Biol Macromol. 2021;185:861-75. DOI: 10.1016/j.ijbiomac.2021.07.019.
70. Rozza AL, Hiruma-Lima CA, Takahira RK, Padovani CR, Pellizzon CH. Effect of menthol in experimentally induced ulcers: pathways of gastroprotection. Chem Biol Interact. 2013;206(2):272-8. DOI: 10.1016/j.cbi.2013.10.003.
71. Kim SY, Han SD, Kim M, Mony TJ, Lee ES, Kim KM, et al. Mentha arvensis essential oil exerts anti-inflammatory in LPS-stimulated inflammatory responses via inhibition of ERK/NF-κB signaling pathway and anti-atopic dermatitis-like effects in 2,4-dinitrochlorobezene-induced BALB/c mice. Antioxidants (Basel). 2021;10(12):1941. DOI: 10.3390/antiox10121941.
72. Alliger K, Khalil M, Konig B, Weisenburger S, Koch E, Engel M. Menthacarin attenuates experimental colitis. Phytomedicine. 2020;77:153212. DOI: 10.1016/j.phymed.2020.153212.
73. de Sousa AAS, Soares PMG, de Almeida ANS, Maia AR, de Souza EP, Assreuy AMS. Antispasmodic effect of Mentha piperita essential oil on tracheal smooth muscle of rats. J Ethnopharmacol. 2010;130(2):433-6. DOI: 10.1016/j.jep.2010.05.012.
74. Mogosan C, Vostinaru O, Oprean R, Heghes C, Filip L, Balica G, et al. A comparative analysis of the chemical composition, anti-inflammatory, and antinociceptive effects of the essential oils from three species of Mentha cultivated in Romania. Molecules. 2017;22(2):263. DOI: 10.3390/molecules22020263.
75. Sun Z, Wang H, Wang J, Zhou L, Yang P. Chemical composition and anti-inflammatory, cytotoxic, and antioxidant activities of essential oil from leaves of Mentha piperita grown in China. PLoS One. 2014;9(12):e114767. DOI: 10.1371/journal.pone.0114767.
76. Zouari-Bouassida K, Trigui M, Makni S, Jlaiel L, Tounsi S. Seasonal variation in essential oils composition and the biological and pharmaceutical protective effects of Mentha longifolia leaves grown in Tunisia. Biomed Res Int. 2018;2018:7856517. DOI: 10.1155/2018/7856517.
77. Uzair B, Niaz N, Bano A, Khan BA, Zafar N, Iqbal M, et al. Essential oils showing in vitro anti MRSA and synergistic activity with penicillin group of antibiotics. Pak J Pharm Sci. 2017;30(5(Supplementary)):1997-2002.
78. Metin S, Didinen BI, Telci I, Diler O. Essential oil of Mentha suaveolens Ehrh., composition and antibacterial activity against bacterial fish pathogens. An Acad Bras Cienc. 2021;93(suppl 3):e20190478. DOI: 10.1590/0001-3765202120190478.
79. Valkova V, Duranova H, Galovicova L, Vukovic NL, Vukic M, Kacaniova M. In vitro antimicrobial activity of lavender, mint, and rosemary essential oils and the effect of their vapours on growth of Penicillium spp. in a bread model system. Molecules. 2021;26(13):3859. DOI: 10.3390/molecules261133859.
80. Shahbazi Y. Chemical composition and in vitro antibacterial activity of Mentha spicata essential oil against common food-borne pathogenic bacteria. J Pathog. 2015;2015:916305. DOI: 10.1155/2015/916305.
81. Li YX, Liu YB, Ma AQ, Bao Y, Wang M, Sun ZL. In vitro antiviral, anti-inflammatory, and antioxidant activities of the ethanol extract of Mentha piperita L. Food Sci Biotechnol. 2017;26(6):1675-83. DOI: 10.1007/s10068-017-0217-9.
82. Lang M, Ferron PJ, Bursztyka J, Montjarret A, Duteil E, Bazire A, et al. Evaluation of immunomodulatory activities of essential oils by high content analysis. J Biotechnol. 2019;303:65-71. DOI: 10.1016/j.jbiotec.2019.07.010.
83. Kim MH, Park SJ, Yang WM. Inhalation of essential oil from Mentha piperita ameliorates PM10-exposed asthma by targeting IL-6/JAK2/STAT3 pathway based on a network pharmacological analysis. Pharmaceuticals (Basel). 2020;14(1):2. DOI: 10.3390/ph14010002.
84. Kolarov V, Kotur Stevuljevic J, Ilic M, Bogdan M, Tusek B, Agic A, et al. Factorial analysis of N-acetylcysteine and propolis treatment effects on symptoms, life quality and exacerbations in patients with Chronic Obstructive Pulmonary Disease (COPD): a randomized, double-blind, placebo-controlled trial. Eur Rev Med Pharmacol Sci. 2022;26(9):3192-9. DOI: 10.26355/eurrev_202205_28737.
85. Otacı. Kurtsan Ilaçları. [Internet]. Available from: https://otacigidatakviyeleri.com/urunler/otatusin/. Accessed May 6, 2023.