Medicinal Plants for Treatment of Common Colds

Subjects: Infectious Diseases

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The common cold is generally considered a usually harmless infectious disease of the upper respiratory pathway, with mostly mild symptoms. However, it should not be overlooked, as a severe cold can lead to serious complications, resulting in hospitalization or death in vulnerable patients. The treatment of the common cold remains purely symptomatic. Analgesics as well as oral antihistamines or decongestants may be advised to relieve fever, and local treatments can clear the airways and relieve nasal congestion, rhinorrhea, or sneezing. Certain medicinal plant specialties can be used as therapy or as complementary self-treatment.

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1. *Allium sativum* L.

Garlic *Allium sativum* L. (*A. sativum*) has been widely known for centuries to influence health and to provide benefits to almost all physiologic systems including immunity. The antioxidant properties of *A. sativum* have also been also studied for their impact on human health, especially against tissue damage and inflammation [1]. Garlic is considered an antimicrobial and antiviral product that could relieve common cold viruses such as the human rhinovirus. A bibliometric study was performed to determine the effect of *A. sativum* on either the prevention or treatment of the common cold. However, data are limited to one clinical trial. The trial reported 24 occurrences of the common cold in the garlic intervention group (allicin content) compared with 65 in the placebo group ($p < 0.001$), resulting in fewer days of illness in the garlic group compared with the placebo group (111 versus 366). The authors of the clinical trial suggest that using garlic as a supplement to allicin can prevent the onset of common cold infections. However, the clinical data published in the bibliometric study were insufficient to validate the effect of garlic in the prevention or treatment of the common cold [2][3].

2. *Echinacea angustifolia* DC., *Echinacea pallida (*Nutt.*)* Nutt., *Echinacea purpurea* (L.) Moench

The medicinal herbal echinacea species have clinical properties essentially as an immune-modulator in the case of common colds and respiratory infections [4]. The immunological effects of echinacea have been investigated extensively in vitro and in vivo. Echinacea products are made from the roots, the whole plant, or aerial parts of *Echinacea angustifolia* (*E. angustifolia*), *Echinacea pallida* (*E. pallida*), or *Echinacea purpurea* (*E. purpurea*) [4][5].

The *E. purpurea* has been recommended as a medicinal plant for the treatment of the common cold, cough, bronchitis and upper respiratory infections [6]. In vitro experiments with human macrophages found that fresh-pressed juice and dried juice from the aerial parts of *E. purpurea* stimulated the production of cytokines including IL-1, IL-10, and TNF-α [7]. In addition, evidence pointed out the effective activity of *E. purpurea* towards Coronavirus disease 2019 (COVID-19) in an organotypic cell culture model [8][9][10].

The effectiveness of *E. purpurea* against colds was investigated by a randomized clinical trial performed on a total of 79 healthy children, designed to treat upcoming cold episodes with either 3 or 5 Echinaforce Junior tablets (EFJ) (contains the same herbal extract of freshly harvested *E. purpurea*) daily for up to 10 days. A total of 130 cold episodes were reported in 68 children overall during the 5.3 months of observation, encompassing a full cold and flu season. Results showed the treatment with EFJ had an excellent safety profile for the acute treatment of common cold symptoms [11]. In addition, in a randomized, double-blind, placebo-controlled trial, 282 subjects aged 18–65 years with a history of 2 or more colds in the previous year were recruited to evaluate the benefits of the treatment against cold symptoms. Among people who developed a cold, a significant decrease in symptoms was observed in the group that was under *Echinacea* treatment compared to the placebo group [12]. These findings confirmed the results of a randomized, double-blind, placebo-controlled clinical trial realized on 80 volunteers who had experienced the first symptoms of a cold. After a period of treatment with *E. purpurea* herb, this plant remains clinically efficient to relieve symptoms faster than a placebo [13]. However, *Echinacea* therapy represents an effective alternative to standard symptomatic medications in the acute treatment of the common cold [14].

3. *Eucalyptus globulus* Labill.

Evidence has been shown that a selection of natural herbs improves the relief of symptoms of upper respiratory tract infections and that their inhalation has antitussive and expectorant effects [15].

The genus *Eucalyptus* encompasses more than 900 species and subspecies. Different species of *Eucalyptus* are used in alternative medicine as antiseptics due to their antimicrobial and antioxidant properties to treat the common cold and respiratory infections [16][17][18]. In addition, a recent study was able to determine that a formula containing hyaluronic acids, *Eucalyptus* oil, copper, and manganese salts is effective for safe nasal irrigation and therefore for alleviating symptoms associated with the common cold such as nasal congestion [19]. Additionally, the *Eucalyptus* plant is often used as a compound in an ointment containing camphor, menthol, and *Eucalyptus* oils for topical application, which lessens the symptoms of colds [20][21]. A meta-analysis published in 2022 was able to synthesize the clinical trials that demonstrate the effectiveness of *Eucalyptus* in relieving cough. However, six studies have been published. Four randomized controlled trials have shown that *Eucalyptus globulus* Labill. (*E. globulus*) used in a formula significantly reduces cough compared to the placebo group. This study supports the idea of using the medicinal plant *Eucalyptus* as a remedy for cold symptoms primarily for cough and runny nose [22].

4. *Grindelia robusta* Nutt./*Grindelia squarrosa* (Pursh) Dunal, *Grindelia humilis* Hook. et Arn., *Grindelia camporum* Greene

EMA has pointed to the non-pharmaceutical value of several conger herbs in post-viral infection cough. The *Grindelia* plant is one of them [23]. However, it has been shown that *Grindelia squarrosa (G. squarrosa)* has an anti-inflammatory effect in inhibiting proinflammatory cytokines such as IL-8, TNF-α, IL-1β, and IL-6 in culture cells such as macrophage, neutrophil, and respiratory epithelial cell line [24][25]. The researchers suggest that the anti-cold activity of *Grindelia* comes down to the composition of the medicinal plant formula used, and that *G. squarrosa* could have an essential effect on the treatment of inflammatory diseases of the respiratory tract [24][25]. Moreover, *G. robusta* has been demonstrated to be effective as an expectorant, antitussive, and anti-inflammatory remedy in children, but no clinical trial has confirmed its efficiency [26].

5. *Glycyrrhiza glabra* L., *Glycyrrhiza inflata* Bat., *Glycyrrhiza uralensis* Fisch

The *Glycyrrhiza* plant is known for its anti-inflammatory and immunomodulatory properties during upper respiratory infections, targeting respiratory symptoms such as sore throat or cough. Its action is mediated by interfering with the Toll-like receptor 4 (TLR4) signaling and decreased production of pro-inflammatory cytokines including nuclear factor-κB, tumor necrosis factor, IL-1, and IL-6 [27].

The effect of *Glycyrrhiza* alone as an herbal remedy in the treatment of common colds is not yet clear, but several herbal preparations containing *Glycyrrhiza* have long been used to treat upper respiratory tract infections. In contrast, there are herb mixes containing *Glycyrrhiza*: Siji-kangbingdu, Maxing Shigan decoction, Lianhua-Qingwen capsules, and Macmoondongtang, which are used in China and Korea to treat upper respiratory tract infections [28][29].

A mixture of ASMATUSTM herbs has been used to relieve symptoms of asthma in children, and its activity has been evaluated as a remedy for colds. For example, a study has been conducted on 46 children with asthma and onset of cold symptoms. Patients received either the herbal mixture (composed of *Matricaria chamomilla* L., *Althaea officinalis* L., *Malva sylvestris* L., *Hyssopus officinalis* L., *Adiantum capillus-veneris* L., *G. glabra* and *Ziziphus jujube* Mills), or a placebo daily for 5 days. Indeed, the herbal mixture significantly decreased the severity of coughing and nocturnal awakenings compared to the placebo [30].

6. *Mentha × piperita* L.

Mentha × piperita L. (*M. × piperita*) is one of the herbs most widely used as a remedy for common colds [31][32]. The antiviral and anti-inflammatory activities of *M. × piperita* leaves have been investigated in the case of respiratory infection. In the in vitro model, *M. piperita* decreases the production of proinflammatory cytokines such as TNF-α, IL-6, and PGE2, and has antiviral activity against the respiratory syncytial virus (RSV) [33].

According to EMA, *M. × piperita* essential oil (inhalation) could be used as a treatment of cough and cold symptoms by stimulating cold receptors in the respiratory tract [34][35]

A prospective randomized double-blind controlled trial was assessed to investigate the effects of essential oils in patients with upper respiratory tract infections based on a sore throat, hoarseness, or cough. *Mentha* × *piperita* was investigated in an herbal mixture containing *E. citriodora, E. globulus*, *Origanum syriacum* L., and *Rosmarinus officinalis* L. A spray containing essential oils of plant mixture was applied five times a day for 3 days and compared with a placebo spray. Spray application reported an immediate improvement in the symptoms of upper respiratory ailments [36].

7. *Origanum dictamnus* L.

As noted in the previous section, *Origanum dictamnus* L. (*O. dictamnus)* was used among the herbal mixture that showed an effect on improving symptoms of upper respiratory infections [36][37]. EMA announced in its report related to this plant that the Committee on Herbal Medicinal Products stated that it can be used as a remedy for the symptoms of the common cold, but no clinical trial has been published to date [38].

8. *Pelargonium sidoides* DC, *Pelargonium* reniforme Curt

Pelargonium sidoides DC (*P. sidoides*) (family *Geraniaceae*) is a plant native to South Africa whose roots have been used as herbal remedies for respiratory and gastrointestinal infections for many centuries by the local South African populations [39]. A number of studies highlighted the activity of the proanthocyanidin-rich extract EPs 7630 from the roots of *P. sidoides.* It is considered effective against a variety of respiratory viruses such as HCoV (HCo-229E), influenza A virus (H1N1, H3N2), respiratory syncytial virus (RSV), and parainfluenza virus by limiting the symptom severity and disease duration of these infections [40][41].

A total of 120 patients with a common cold and at least 2 out of 10 common cold symptoms received one film-coated 20 mg tablet of EPs 7630 thrice daily for 10 days in an uncontrolled, interventional multicenter trial (ISRCTN65790556). Common-cold-associated symptoms and treatment satisfaction were evaluated after 5 days and at the treatment end. In 61 patients, viral nucleic acids were detected. Of these, 23 (37.7%) tested positive for at least 1 HCoV (HCoV subset) and 38 (62.3%) for other viruses only (non-HCoV subset). Patients of both subsets showed a significant improvement in common cold symptoms already after 5 days of treatment. EPs 7630 treatment outcomes of common cold patients with confirmed HCoV infection were as favorable as in patients with other viral infections [40]. Another clinical trial has evaluated the efficacy of EPs 7630, compared with the placebo for the treatment of the common cold. Of 207 patient participants, 103 were included in the standard dose of EPs 7630 (received 3 × 30 drops per day), 104 participated in the high dose group (received treatment with 3 × 60 drops per day), and the control group received a placebo. The study was conducted over a period of 10 days. The active EPs 7630 is an effective, well-tolerated, and safe treatment for the common cold. It significantly reduced the severity of symptoms [42]. The effectiveness of the extract roots of *P. sidoides* was also evaluated and confirmed by Lizogub [43] and Ross [44].

9. *Pimpinella anisum* L.

The Committee on Herbal Medicinal Products and EMA suggest that *Pimpinella anisum* L. *(P. anisum)* can be used as an expectorant (a medicine that helps bring up phlegm) for coughs associated with colds [45]. This evidence could be reinforced by the study of Iannarelli et al. [46]. The authors of this study evaluated the anti-inflammatory activity and the effect on mucin secretion of *P. anisum* essential oil in primary airway bronchial and tracheal epithelial cells (HBEpC and HTEpC, respectively). The data indicated that *P. anisum* essential oil showed a significant anti-inflammatory effect on both HBEpC and HTEpC cells together with mucus hypersecretion, which indicates that *P. anisum* could be used as an expectorant during cold periods [46]; however, on the other hand, there is no published clinical trial which confirms the expectorant effect of this plant.

10. *Primula elatior* (L.) Hill, *Primula veris* L.

Official therapeutic indications are based on traditional use and include use as an expectorant in the cough due to a cold for both the preparations from flower and roots [47][48].

Parts of the plant used in official phytotherapy are flowers and/or roots. Flowers can be dried whole or cut and can or cannot include calyx [49]. The main constituents in flowers are triterpenic saponins, which are predominantly present in the sepals (up to 2%); flavonoids, which are predominantly present in the petals (up to 3%); carotenoids; essential oil (trace amounts); rosmarinic acid; d-volemitol; and other saccharide alcohols [49]. Roots may be whole or cut and dried [50]. The main constituents in roots are triterpenic saponins (3–12%), phenolic glycosides, saccharides, and d-volemitol (primulitol) [50].

According to the European Union herbal monograph, flowers are used as a herbal substance, comminuted and prepared as tea, or a liquid extract (prepared with 25% ethanol) [48][49]. The roots may be used as a herbal substance for the production of herbal preparations: dry extract (prepared with 40–50% ethanol), liquid extract (prepared with 70% ethanol), tincture (prepared with 70% ethanol), soft extract (prepared with water; 20–55% ethanol; 50% methanol; or a mixture of methanol, water, and ammonia), and comminuted herbal substance [47].

Since *Primula* flowers are usually used in combinations with other herbal substances (*Primula* content in teas is typically 10–30%, 1% in liquid, and 8% in solid dosage forms), assessing their effectiveness in the treatment of cough is challenging [49]. There are no clinical trials published in which only *Primula* flower or root preparation are used in the treatment group. However, combinations with thyme preparations show effectiveness on cough in clinical trials [51].

Primula preparations are generally safe to use, but their effectiveness in the treatment of cough is questionable. The mechanism of action for this indication is unclear and there is a lack of relevant clinical studies.

11. *Sambucus nigra* L.

Sambucus nigra or elderberry belongs to the family *Adoxaceae* [52].

The part of elderberry used in traditional and rational phytotherapy is the flower. Elderberry flowers are used dried and the herbal substance contains at least 0.80% flavonoids according to the European Pharmacopoeia [53]. Flavonoid content may be up to 3%. Other important compounds are triterpenes essential oil, 3% caffeic acid derivatives, 0.11% sterols, 8–9% minerals (especially potassium), and other (e.g., tannins, mucilages, pectins and saccharides, plastocynin) [53][54].

According to the European Union herbal monograph, elderberry flowers are used as an herbal substance and herbal preparations, i.e., comminuted, as a liquid extract (25% ethanol used as an extraction solvent) or as a tincture (25% ethanol used as extraction solvent). These can be further processed into tea or liquid oral dosage formulations. The EMA has approved the indication for “the relief of early symptoms of common cold”, which is based solely on traditional use [55].

In some cases, fruit is also used. Dried, ripe berries are the herbal substance, but fresh berries are also used in some preparations [56]. Fresh fruits contain anthocyanins and flavonoids. The dried seeds contain hemagglutinin (lectins, e.g., *S. nigra* agglutinin III), while *S. nigra* agglutinin Vf lectin is present in fresh fruits. Other constituents are essential oil (trace amounts), vitamins, minerals, and saccharides [56]. The seeds of the unripe fruits also contain cyanogenic glycosides, sambunigrin, prunasin, zierin, and holocalin [57]. Other traditional uses of elderberry fruit preparations are as a laxative, diaphoretic, diuretic, analgesic, and sedative, to alleviate headache, dental, heart, nerve pain and neuralgia, and against cough and cold, to name a few [56]. However, the EMA monograph on elderberry fruit is not available yet.

To conclude, the data from clinical studies and mechanistic studies are too scarce to unambiguously support the evidence-based use of elderberry preparations for the relief of the symptoms of the common cold. However, the use of flower preparations is safe and has an approved indication based on long-standing use. Elderberry fruit, although safe to consume if ripe, was not granted an indication by the EMA due to the lack of relevant data.

12. *Sideritis scardica* Griseb./*Sideritis clandestina (*Bory and Chaub.*)* Hayek./*Sideritis raeseri* Boiss./and Heldr., *Sideritis syriaca* L.

The Committee on Herbal Medicinal Products and EMA reported that the three species are used as a remedy for cold symptoms and primarily for cough prevention in Albania, Greece, and Bulgaria [58]. Other evidence noted that *Sideritis scardica* Griseb (*S. scardica)* has been used in traditional medicine as a remedy for improving symptoms during respiratory infections such as bronchitis and bronchial asthma. Additionally, this plant is known for its effectiveness against colds and coughs [59][60], but there is no published clinical trial which confirms these effects.

13. *Thymus vulgaris* L., *Thymus zygis* L.

The genus *Thymus* or thyme (family *Lamiaceae*) numbers about 400 species. This species is a common perennial shrub, native to southern Europe and the western Mediterranean.

Thyme is a traditional Mediterranean aromatic plant used for centuries in cooking, medicine, and perfume preparations. Consequently, thyme has spread worldwide, as has its uses, and this has led to many varieties. Nowadays, thyme cultivation is economically important to producing essential oils for the perfume industry, monoterpene production, and medicinal use. Thyme could also be used as a preservative for food products. Thyme leaves are also used as a fresh or dry condiment. The EMA published two monographs about the use of thyme for cough and cold, one for the herb and the second for the essential oil. The herbal substances and the herbal preparation(s) are composed of the leaves and/or flowers separated from the dried stems of the plant. The essential oil is obtained by steam distillation from fresh flowering aerial parts of *T. vulgare* or *T. zygis* [61][62].

As a member of the *Lamiaceae* family, essential oil production by thyme is important [63][64][65] To date, six main chemotypes have been described with main constituents: [63][64][66]: chemotype geraniol, terpineol, thuyanol-4, linalool, carvacrol, and thymol. EMA herbal monograph lists 10 chemotypes, underlying the chemical diversity of this plant [61].

In the recent article by Silva et al. on phenolic acids, tannins, rosmarinic and salvianolic acid, flavonoids, and polyphenols also enter frequently the chemical composition of *Thymus*.

Its therapeutic properties derive mainly from the essential oil with antitussive, expectorant, antiseptic, antimicrobial, and anthelmintic properties. Traditional uses also report hepatoprotective properties. No genotoxicity has been reported. However, considering the growth area of the plant, it could be contaminated with pollutants such as trace metals such as lead (Pb). Additionally, the chemical stability of essential oils is low [63]. Flavonoids from thyme do not seem to have a strong pharmacological potential [63].

Leaves are mostly used as an infusion, or as tea, ointment, and syrup. The reported properties of thyme infusion are as a general stimulant, anti-flatulent, cough depressant, common cold treatment, and antibacterial [63][65][67]. The anti-microbial properties are used in mouth, gastrointestinal, and urinary tract infections, as well as respiratory diseases (cough, bronchitis, asthma). The most important medicinal use relies on thymol, *p*-cymene, and carvacrol.

Almost all medicinal applications are due to the antioxidant, anti-inflammatory (anti-TNFα et IL-1β), and antimicrobial activities (antibacterial including antibiofilm activity, fungicidal, virucidal) [66][67][68][69][70][71][72]. Kowalsky et al. suggested that the use of thymol in combination with an antibiotic may lead to reduced antibiotic concentration in therapeutic use against planktonic and biofilm-forming bacteria [68].

It is suggested that thymol antiviral activity may occur at a different level of the viral cycle, from cell penetration and viral envelope interference to protein inhibition [68].

Boskabady et al. [73] described a relaxant effect on the tracheal chain on guinea pigs as efficient as theophylline, and Wienkotter et al. [74] described a β_2 agonist activity (molecular binding and biological effects), suggesting an interesting therapeutic activity at both symptomatic and viral levels in the case of upper respiratory tract infections such as the common cold and flu. Additional anti-inflammatory activities lead *Thymus* sp. to have strong potential in

upper respiratory tract viral infections. Patil et al. [65] reported an inhibition of the 5-lipooxygenase at a low concentration of thyme essential oil (IC_{50} at 0.005 µg/mL), suggesting the latter could reduce leukotrienes synthesis during inflammation.

Lenz et al. [75] also showed antiviral activity of thyme extract (in a commercial preparation, where the active compound is thymol according to the authors) against the human rhinovirus 1a (HRV1a, MDCK/A549 cells, MOI 1).

From a clinical point of view, Kemmerich et al. [76] published a clinical trial (doubled blind, placebo controlled, multicenter, with 363 patients including 182 with herbal treatment and 181 in the placebo group) which showed the efficacy and tolerability of a fluid extract of thyme herb (mixed with Ivy) on acute bronchitis. The herbal treatment significantly reduced cough compared to placebo (77.6% vs. 55.9%; $p < 0.0001$) after 9 days and reduced the severity of bronchitis (evaluated with BSS score). The authors also reported the superiority of the herbal treatment on sleep disturbance, and general well-being. They also reported that adverse effects were low and similar to those in the placebo group (3.8% and 4.5% respectively). All adverse effects had been resolved at the end of the study and the authors concluded the very good tolerability of the treatment [76].

Thymol is the most studied essential oil constituent from thyme and show good activity against several viruses (rhinoviruses, influenza viruses) in vitro, in vivo, and in clinical trials. The latter also shows the efficiency as well as the safety of thyme extracts in symptom reduction. The mechanism of action is not yet fully understood. However, several studies showed that thyme could reduce inflammation, enhance bronchodilatation via β2 agonism, and directly reduce viral replication. Thus, finally, thyme showed a direct and indirect strong potential in upper viral tract infections [77][78].

According to https://clinicaltrials.gov (accessed on 21 September 2022) and Silva et al. (2021), two clinical studies are still undergoing so as to better evaluate thyme, thyme extracts, or essential oils in upper respiratory tracts infections (NCT03218696 [79], NCT02981147 [63][80]).

To conclude, regarding the safe traditional use of thyme herbal preparation and essential oils in productive cough and common cold associated with in vitro, in vivo, and clinical data, common thyme is safe and efficient in this indication, as mentioned in the revised final opinion of the EMA.

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