Arh. farm. 2025; 75: 408 – 422 *Professional paper/Stručni rad*

Herbal medicinal products for respiratory infections in the pediatric population

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Received: 26 August 2025; Revised in revised form: 01 October 2025; Accepted: 02 October 2025

Abstract

Cough and cold represent some of the most prevalent indications for using herbal medicinal products in pediatric care across European countries. These herbal medicines are generally regarded as safe, with their efficacy predominantly classified as good to very good. Traditional herbal medicinal products based on mucilaginous herbal drugs like *Althaeae radix, Malvae folium, Lichen islandicus* and *Plantaginis lanceolatae folium* are used in the treatment of oral and pharyngeal inflammations and associated dry cough. For productive coughs, herbal medicinal products with well-established use, based on *Hederae folium*, or a range of traditional herbal medicinal products containing *Primulae radix*, *Thymi herba*, and other aromatic drugs and essential oils are administered. It is important to note that products containing essential oils and certain aromatic herbal drugs are contraindicated in children under 2 to 2.5 years of age due to the risk of laryngospasm. In the pediatric population, products derived from *Matricariae flos*, *Pelargonii radix*, *Tiliae flos* and *Sambuci flos* are used to relieve various cold symptoms. Use is restricted to children over a certain age, mostly due to lack of safety data, and in some cases due to the possibility of certain adverse effects.

Key words: herbal drugs, cough and cold, children, demulcent, expectorant

https://doi.org/10.5937/arhfarm75-61085

Introduction

Herbal drugs have been used for centuries to treat various ailments in patients of all ages. Their popularity is increasing, especially in industrialised countries. In underdeveloped countries, they are part of primary health care, as material resources are limited and other medicines are expensive and unavailable. If they are regulated and of good quality, such as herbal medicinal products, they are generally considered safe and a good alternative to conventional medicines. The herbal medicinal products are mostly used for minor ailments and in the form of self-medication (1–3).

Although often used in children and adolescents, herbal medicinal products (HMPs) as part of official pediatric medicine are mainly represented in some European countries (Germany, Austria, Switzerland). In Germany, 85% of children have used HMPs once or twice a year (4, 5). In Spain, on the other hand, 40% of pediatricians prescribe food supplements based on medicinal herbs for mild disorders, 31% as a first choice and 22% at the request of parents (6).

A large pharmaco-epidemiological study on the use of HMPs (PhytoVIS project, 2014–2016) was performed to generate data on the therapeutic usefulness of HMPs in the general population, including special patient groups like children. Overall, 2063 datasets from the pediatric population were evaluated, and mostly the indication was the treatment of cough and cold (68%), followed by gastrointestinal complaints (14%), skin diseases (5%), sleep disturbances and anxiety (4%). Their effect was mostly classified as very good (48% of patients), good to moderate (37%), while only 4% of the patients did not notice any effect. Ninety-four per cent of all patients did not experience any adverse effects (4, 5). The study shows that the HMPs in pediatrics can be considered effective and safe, but the special needs of children must be considered (5, 7).

One of the main problems with the use of HMPs in pediatrics is the dosage: more than 50% of the medicines used in children have not been tested for the specific age group (1, 7). Commission E, ESCOP (European Scientific Cooperative on Phytotherapy) and WHO (World Health Organization) monographs list specific doses for children for only a small number of herbal drugs/preparations. Herbal medicines are available and widely used, but many of them have not been tested for efficacy and safety in clinical studies. In addition, clinical trials involving children are rare and raise complex ethical issues.

The European Medicines Agency (EMA) does not consider the use of many herbal medicines suitable for children and adolescents due to lack of data. In many monographs of the HMPC/EMA (Committee on Herbal Medicinal Products / European Medicines Agency), the use of HMP is limited to the age of 12 or 18 years and older. There is a lack of dosage recommendations for the pediatric population in many countries. In order to provide evidence for the use of traditional HMPs in children, some possibilities arise: the generation of datasets from real-world data and real-world evidence, and extrapolating dosages for children based on pharmacokinetic and clinical data from adults (5, 8, 9).

Children may be more susceptible to adverse effects associated with the use of HMPs due to the specificity of their physiology and metabolism. Adverse effects may

also occur due to interactions with conventional medicinal products, contamination with pollutants (e.g. heavy metals, pesticides), the presence of adulterants (e.g. other plant species), and additives (10).

In a systematic review (128 case studies) of possible side effects associated with the use of medicinal plants, 38% of cases were observed in children aged 2–8 years and 37% involved children younger than 2 years. Reported side effects included neurological disorders (35%, convulsions, CNS depression and lethargy), gastrointestinal problems (14%, nausea, vomiting, diarrhea), hepatotoxicity (11%) and cardiovascular disorders (10%, hypertension). Of the reported effects, 36% were the result of accidental ingestion. It should be noted that these are very often not HMPs, but poorly characterised products from traditional Chinese and Ayurvedic medicine or dietary supplements (11).

The HMPC/EMA issued monographs of herbal drugs and herbal preparations that can be used in respiratory infections in the pediatric population. Two herbal preparations have a well-established use status, whereas evidence for 28 herbal drugs is based on traditional use (Table I) (12).

Table I The use of HMPs in respiratory infections in pediatrics according to HMPC/EMA (12)

Tabela I Primena biljnih lekovitih proizvoda (BLP) kod respiratornih infekcija u pedijatriji prema HMPC/EMA (12)

Well-established use **Expectorant for productive coughs**	**Traditional use** **Treatment of coughs and cold**
Hederae helicis folium (alcoholic extract)	*Anisi fructus* *Echinaceae angustifoliae radix*
Well-established use **Prevention and treatment of common cold**	*Echinaceae pallidae radix*
Echinaceae purpureae herba (expressed juice)	*Eucalypti folium, E. aetheroleum* *Foeniculi amari fructus, F. dulcis fructus*
Traditional use **Treatment of oral and pharyngeal inflammations**	*Marrubii herba*
Agrimoniae herba *Althaeae radix* *Calendulae flos* *Lichen islandicus* *Malvae folium, Malvae sylvestris flos* *Matricariae flos* *Plantaginis lanceolatae folium* *Polygoni avicularis herba* *Rosae flos* *Sisymbrii officinalis herba*	*Matricariae flos* *Menthae piperitae aeth.* *Pelargonii radix* *Polypodii rhizoma* *Primulae flos, P. radix* *Sambuci flos* *Thymi herba, T. aetheroleum* *Thymi herba / Primulae radix* *Tiliae flos* *Verbasci flos*

Herbal medicinal products for the treatment of oral and pharyngeal inflammations

Traditional HMPs based on mucilage-containing herbal drugs for the treatment of oral and pharyngeal inflammations and associated dry cough

Mucilage creates a protective layer on the mucous membranes and reduces cough irritation. (13). According to HMPC/EMA, HMPs with herbal drugs with mucilage include products based on marshmallow root, *Althaeae radix,* mallow leaf and flower, *Malvae folium, Malvae sylvestris flos,* Iceland moss, *Lichen islandicus* and ribwort plantain leaf, *Plantaginis lanceolatae folium* (12). They are used as demulcent preparations for the symptomatic treatment of oral or pharyngeal irritation and associated dry cough. The duration of use is one week and if the symptoms persist longer, a doctor should be consulted.

Mucilage can influence the absorption of nutrients and medicines. The absorption of simultaneously administered medicinal products may be delayed, so the product should not be taken less than half to 1 hour before or after the intake of other medicinal products. If dyspnea, fever or purulent sputum occur or the symptoms worsen during the use of the medicinal product, a doctor should be consulted.

Marshmallow root, *Althaeae radix*, (*Althaea officinalis* L., Malvaceae), contains mucilage (5–11.6%), starch, pectins and flavonoids. Colloid polysaccharides in mucilage that swell in water, cover the mucosa with a protective layer and consequently reduce the cough reflex. Aqueous marshmallow root extract also shows anti-inflammatory activity on irritated areas and stimulates tissue regeneration (14). Marshmallow root is commonly utilised as comminuted herbal substance for macerate preparation or as syrup made from macerate, but also as liquid or dry extract in liquid and solid dosage forms. Macerate should be applied fresh, immediately after preparation. It can be used for adolescents and children older than 3 years, but the use in children under 3 years of age is not recommended because of concerns requiring medical advice.

Use is contraindicated if hypersensitivity to the active substance occurs. Undesirable effects are not known (15).

The mallow leaf, *Malvae folium (Malva sylvestris* L., *M. neglecta* Wallr., Malvaceae) and the mallow flower, *Malvae sylvestris flos (M. sylvestris)*, also contain mucilage (flowers 10%, leaf 6–8%) (16). They are used comminuted for the preparation of infusion or decoction for oral or oromucosal use. It can be used for one week in children older than 12 years (17, 18).

Similar to marshmallow and mallow, Iceland moss, *Lichen islandicus* (*Cetraria islandica* (L.) Acharius s.l., Parmeliaceae), also has a high mucilage content (25–50%) with a demulcent effect. It contains usnic acid, which has antimicrobial effect and bitter lichen acids, which stimulate the appetite. The aqueous extract of *Lichen islandicus* showed an anti-inflammatory and immunomodulatory activity (19). Comminuted herbal substance as herbal infusion or macerate for oral use, can be utilized in children above 12

years of age. On the other hand, soft extracts in solid dosage form can be used for oromucosal application in younger children, over 6 years of age (20).

Mucilage, iridoid glycosides and flavonoids are the main constituents of ribwort plantain, *Plantaginis lanceolatae folium* (*Plantago lanceolata* L., Plantaginaceae). It not only soothes throat irritation and dry coughs, but also has a bronchospasmolytic and mild expectorant effect (21). Oral use of herbal tea (infusion) in children under 12 years of age is not recommended. Other HMPs that contain liquid, soft or dry extracts and fresh juice can be utilised for oral or oromucosal use in children over 3 years of age (22).

Other traditional HMPs for the treatment of oral and pharyngeal inflammations associated with the common cold

Matricaria flower, *Matricariae flos (Matricaria recutita* L., syn. *M. chamomilla* L., Asteraceae), is a well-known herbal drug used in various countries worldwide. The main constituents are: essential oil with proazulenes (matricin), flavonoids (apigenin) and phenolic acids. It has an anti-inflammatory, anti-edematous and moderate antimicrobial effect. The matricaria flower also promotes tissue regeneration and wound healing (23). It is used to relieve symptoms of common cold, in the form of inhalation. The comminuted herbal substance can be used in hot water for inhalation for children over 6 years of age, and liquid extracts for adolescents over 12 years of age. It is also suitable for the treatment of minor ulcers and inflammations in the mouth and throat. These HMPs based on comminuted herbal substance or liquid extract are used for rinsing and gargling for adolescents or children over 6 years of age (liquid extract (DER 1:1), extraction solvent: ethanol 55% V/V). The use of comminuted herbal substance or liquid extracts as steam inhalation, as mouth washes or for gargling in children under 6 (inhalation) or 12 years of age (gargling) has not been established due to lack of adequate data. They are contraindicated in cases of hypersensitivity to the active substance and to other plants of the Asteraceae (Compositae) family. Undesirable effects of unknown frequency have been reported, hypersensitivity reactions including severe allergic reactions (dyspnoea, Quincke's disease, vascular collapse, anaphylactic shock), occurred after mucosal contact with liquid chamomile preparations (24).

Traditional HMPs based on Calendula flower, *Calendulae flos,* (*Calendula officinalis* L., Asteraceae), agrimony herb, *Agrimoniae herba* (*Agrimonia eupatoria* L., Rosaceae) and knotgrass herb, *Polygonii avicularis herba* (*Polygonum aviculare* L., Polygonaceae), are also utilised as gargles for the symptomatic relief of mild inflammations of the mouth and throat. Their anti-inflammatory effect is based on triterpene saponins and alcohols (*Calendulae flos*) or tannins (*Agrimoniae herba, Polygonii avicularis herba*) and also flavonoids. They are used as comminuted herbal substance for tea preparation (infusion, decoction) in adolescents over 12 years of age for oromucosal use (25–27). Herbal tea based on infusion of *Polygonii aviculare herba* can also be administered orally to relieve the symptoms of a common cold in children over 12 years of age.

Furthermore, traditional HMP based on the dry extract of hedge mustard, *Sisymbrii herba* (*Sisymbrium officinale* (L.) Scop., Brassicaceae), may be recommended for the relief of throat irritations such as hoarseness and dry cough in children over 6 years of age in solid dosage form for oromucosal use and in children over 3 years of age in liquid dosage form for oral use. *Sisymbrii herba* contains glucosinolates (minimum 0.3%), mucilage and flavonoids, but may also comprise cardenolide glycosides. Caution is advised and the content of cardenolides has to be specified in the herbal preparations and should be less than or equal to 1 ppm (28, 29).

Herbal medicinal products with expectorant activity

Expectorant effect of herbal drugs is based on the presence of either saponin compounds or essential oils. It has been hypothesized that saponins, present in herbal preparations such as those of ivy leaf or primula root, stimulate secretion from the serous bronchial glands via a reflex mechanism which involves an initial local irritation of the gastric mucosa, which in turn activates the parasympathetic nervous system. Other pathways are believed to be involved as well, such as the activation of β-adrenergic receptors and the resulting bronchodilation as observed with α-hederin from ivy leaf (30). Due to the irritant effect of the saponins on the gastric mucosa, these preparations should be used with caution in patients with gastritis or gastric ulcers, although this is rare in the pediatric population (31–34). Essential oils act through local irritation and direct stimulation of bronchial gland cells, affecting serous cells more than mucus cells, and thereby promoting a greater volume of thinner, more fluid secretions (30). In pediatric practice, the use of herbal expectorants encompasses both of these product groups. Medicines derived from saponin-containing herbal drugs are intended exclusively for oral administration, whereas those based on aromatic herbal drugs and essential oils may also be formulated for cutaneous application, as bath additives or inhalation. Among these, certain ivy leaf preparations have demonstrated good clinical efficacy in the pediatric population and are recognised as medicines with well-established use. In daily practice, several other herbal preparations based on primula root, primula flower, thyme herb, mullein flower, aniseed, fennel, eucalyptus leaf, or on thyme, peppermint and eucalyptus essential oils are also employed under traditional use status. In general, the use of these herbal medicines should be limited to one week. If dyspnea, fever, or purulent sputum develops, or if symptoms worsen during treatment, medical advice should be sought.

HMPs based on saponin-containing herbal drugs with expectorant activity

The primary constituents of ivy leaf, *Hederae folium* (*Hedera helix* L., Araliaceae), are triterpene saponins, among which the most relevant are the hederacoside C and, despite being present in smaller amounts, α-hederin, which is of particular pharmacological importance (activator of β-adrenergic receptors). In addition to saponins, ivy leaf contains flavonoids, phenolic acids, as well as polyacetylenes (falcarinone, falcarinol, and 11,12-dihydrofalcarinol) which have allergenic potential (35). The efficacy of certain aqueous-alcoholic and alcoholic extracts of ivy leaf as expectorants in the symptomatic treatment of productive cough has been demonstrated

in clinical studies, supporting their well-established use in both children and adults. However, liquid extract is not recommended for children under 6 years of age because of the alcohol content, while dry and soft extracts are indicated for use in children over 2 years of age, as well as in adolescents. Syrup formulations are the most commonly used dosage form in pediatric practice, although other dosage forms are also available (31). Ivy leaf preparations are contraindicated in children under 2 years of age due to the general risk of aggravating respiratory symptoms associated with the use of secretolytic agents. Hypersensitivity to the active substance or to other members of the Araliaceae family (e.g., ginseng) also precludes their use (31). Adverse effects may include gastrointestinal symptoms as well as allergic reactions, ranging from urticaria and skin rash to dyspnea and anaphylaxis. Falcarinol and dehydrofalcarinol are considered the principal allergens responsible for the frequently observed allergic contact dermatitis following direct contact with ivy leaf. Analyses of ivy leaf extracts obtained in different seasons and from localities have demonstrated considerable variation in the concentrations and ratios of these allergenic compounds (31, 35).

Another herbal drug whose expectorant effect is based on the presence of saponins is primula root, *Primulae radix* (*Primula veris* L., *P. elatior* (L.) Hill, Primulaceae), whose efficacy and safety are based on data from traditional long-term use. It contains 3–10% triterpene saponins, as well as up to 2.3% of the phenolic glycosides (primverin and primulaverin), which transform into fragrant aglycones with a methyl salicilate-like odour when dried. For children aged 4 years and over, a liquid extract, a tincture, and a soft extract are mainly used in liquid formulations for oral administration. For children over the age of 12, there are several more preparations, including herbal tea prepared from comminuted herbal substance. Use in children under 4 years of age is not recommended and a medical doctor should be consulted. Use is contraindicated if there is a history of allergic reactions to the herbal substance. The undesirable effects are not known (32, 36). Apart from products based exclusively on primula root preparations, extracts are used in combination with other herbal substances or herbal preparations. The combination with preparations of thyme herb is particularly widespread (34).

Similarly to the root, the primula flower, *Primulae flos* (*Primula veris* L., *P. elatior* (L.) Hill, Primulaceae), contains up to 2% triterpene saponins, which contribute to its expectorant activity. Based on long-standing traditional use, primula flower preparations, such as comminuted herbal material for infusion or liquid extracts, are indicated as expectorants in the treatment of cough associated with the common cold in adolescents over 12 years of age. The primula flower is commonly used in combination with other herbal substances in the formulation of herbal teas, liquid preparations, and solid dosage forms (33, 37). In contrast to the underground parts, the aerial parts of *Primula* species may contain primin and other quinoid compounds, which are responsible for the contact-allergenic properties observed in some representatives of this genus. Consequently, the use of primula flower–based preparations may cause allergic reactions and is contraindicated in individuals with a history of hypersensitivity to *Primula* species (33, 37).

Due to its saponin content, mullein flower, *Verbasci flos* (*Verbascum thapsus* L., *V. densiflorum* Bertol., *V. phlomoides* L., Plantaginaceae), has been traditionally used as an expectorant (38). In addition to saponins, key constituents include iridoid glycosides, flavonoids, phenylethanoid glycosides, and mucilaginous polysaccharides, which contribute to its anti-inflammatory and demulcent properties (39). Herbal medicines derived from mullein flower hold traditional use status and are indicated for the relief of sore throat associated with dry cough, administered as a herbal infusion in adolescents over 12 years of age. Use is contraindicated in individuals with known hypersensitivity to the herbal substance. No adverse effects have been reported to date (40).

HMPs based on aromatic herbal drugs and essential oils with expectorant activity

Thyme herb, *Thymi herba* (*Thymus vulgaris* L., *T. zygis* L., Lamiaceae), contains not less than 1.2% essential oil, with the phenolic monoterpenes thymol and carvacrol as the predominant constituents (41). Other important components include phenolic acids and flavonoids. The comminuted herbal substance is used for preparing herbal tea for oral administration, while various extracts are formulated into liquid or solid dosage forms. For children over 4 years of age, liquid extract (DER 1:2–2.5; extraction solvent: ammonia solution 10%, glycerol 85%, ethanol 90%, and water [1:20:70:109]) or so-called "expressed juice" – a liquid water extract from fresh herb (DER 1:1.5–2.4), can be used. For adolescents over 12 years of age, additional products are available, including those based on a broader range of extracts as well as herbal tea prepared from the comminuted substance. The addition of ammonia solution to the extraction mixture, enhances the yield of phenolic monoterpenes from thyme herb. Comparative *ex vivo* studies have shown that extracts with higher thymol content demonstrate greater efficacy than those with very low thymol levels, both as a relaxant and as an antispasmodic compound, as well as in ciliary transport experiments (42). Thyme herb-based products are contraindicated in individuals with a known hypersensitivity to the active substance or to other plants of the Lamiaceae family. Gastrointestinal disorders may occur as adverse reactions (43).

Several fixed combinations of extracts of primula root and thyme herb are available as expectorants for coughs associated with the common cold based on their complementary activities that together result in a synergistic effect. Due to limited efficacy data for the well-established use combinations, only those with traditional use status are recommended in children. At present, only three fixed preparations are approved for use in children aged 4 years and older, while several additional combinations are available for adolescents over 12 years of age. Owing to the saponin content of primula root, gastrointestinal disturbances such as nausea may occur during treatment (34).

Herbal medicines containing isolated thyme essential oil, *Thymi aetheroleum* (*Thymus vulgaris* L., *T. zygis* L., Lamiaceae), are available in liquid dosage forms for oral use or as liquid or semi-solid preparations for cutaneous application or as bath additives. However, in children, thyme essential oil is approved only for use as a bath additive,

specifically for those over 3 years of age. The prescribed amount of thyme essential oil is added per liter of bath water, with a recommended duration of 10–20 minutes every other day for one week. Full hot baths are contraindicated in cases of extensive skin injuries, acute skin diseases, high fever, severe infections and significant circulatory disturbances. Hypersensitivity reactions and skin irritation, with unknown frequency, have been reported as undesirable effects (44).

Bitter fennel, *Foeniculi amari fructus* (*Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, Apiacae), sweet fennel, *Foeniculi dulcis fructus* (*F. vulgare* Miller subsp. *vulgare* var. *dulce* (Mill.) Batt. & Trab., Apiacae), and aniseed, *Anisi fructus* (*Pimpinella anisum* L., Apiaceae), are marketed as traditional herbal medicines as expectorants in cough associated with cold. Their activity is mainly attributed to essential oils, which share a similar qualitative composition, with quantitative differences in key constituents. The major compound in all three oils is *trans*-anethole, responsible for their sweet taste, while fenchone contributes to the bitterness of fennel fruits. A constituent of concern is estragole, a phenylpropanoid with genotoxic and carcinogenic metabolites (45). Owing to safety concerns, of the three oils, only aniseed essential oil remains approved by the HMPC/EMA, although its use is contraindicated in children and adolescents under 18 years of age (46–48). Aniseed fruits may be used in patients over 12 years, while sufficient long-standing use data exist for bitter and sweet fennel fruits, which may be used in children over 4 years of age. Crushed fruits are prepared as herbal tea, with recommended use up to two weeks in adolescents and one week in children. Use is contraindicated in individuals allergic to the herbal substance, to anethole, or to other Apiaceae plants (e.g., caraway, celery, coriander, dill). Reported adverse effects include allergic reactions affecting the skin or respiratory system (48–50).

Herbal medicinal products based on the eucalyptus leaf, *Eucalypti folium* (*Eucalyptus globulus* Labill., Myrtaceae), as well as on the essential oil obtained from several oil-rich species of eucalyptus, eucalyptus oil, *Eucalypti aetheroleum* (*E. globulus* Labill., *E. polybractea* R.T. Baker, *E. smithii* R.T. Baker, Myrtaceae), hold traditional use status for the relief of cough associated with the common cold. The eucalyptus dried leaf contains at least 2% essential oil, whose major constituent, 1,8-cineole (eucalyptol), is considered the principal active component. In adolescents over 12 years of age, eucalyptus leaf infusion may be taken orally or by inhalation, while eucalyptus oil products may be applied to the chest and back or used as bath additives. In children aged 3–12, oral use is not recommended, but eucalyptus oil may be applied topically, by inhalation, or as a bath additive. The use of the eucalyptus leaf and oil is contraindicated in individuals with hypersensitivity to the herbal substance and in children under 30 months of age, owing to the risk of laryngospasm caused by essential oil and 1,8-cineole (41, 51, 52).

Essential oil obtained from peppermint, peppermint oil, *Mentae piperitae aetheroleum* (*Mentha x piperita* L., Lamiaceae), is characterized by its major constituents menthol (30–55%) and menthone (14–32%). Menthol acts as an agonist of the transient receptor potential melastatin 8 (TRPM8) receptor, which mediates the sensation of cold

on the mucous membranes and subsequently stimulates the swallowing reflex and inhibits the cough reflex (53). The essential oil also contains small amounts of the potentially hepatotoxic compounds pulegone and menthofuran. In children, daily exposure to pulegone is limited to 0.75 mg/kg body weight (54). For patients aged 12 years and older, peppermint oil-based herbal medicines for the relief of cough are available as lozenges or oral sprays, liquid forms for inhalation, and liquid or semi-solid preparations for cutaneous or transdermal use, applied in a thin layer to the chest, back, or around the nostrils. In children aged 4–11, use is restricted to cutaneous preparations applied around the nostrils. Oral use is not recommended in individuals with heartburn, hiatal hernia, gastric or duodenal ulcers, or biliary disorders. Peppermint oil is contraindicated in children under 2 years of age (risk of menthol-induced reflex apnea and laryngospasm), in children with a history of seizures, and in individuals hypersensitive to peppermint oil or menthol. Undesirable effects, largely attributed to menthol, may include bronchospasm, laryngospasm, headache, bradycardia and contact sensitivity. Cases of overdose have been reported with both oral and inhaled use (55).

In addition, colds and respiratory infections can be facilitated by the application of HMPs with immunomodulatory activity. Herbal medicinal products with well-established use containing expressed juice of *Echinaceae purpureae* herba recens (*Echinacea purpurea* (L.) Moench, Asteraceae), or traditional herbal medicinal products containing preparations of narrow-leaved coneflower root (*E. angustifolia* DC.) and pale coneflower root (*E. pallida* (Nutt.) Nutt.), are used in children over 12 years of age for 10 days (56–58).

Furthermore, traditional HMPs based on pelargonium root, *Pelargonii radix* (*Pelargonium sidoides* DC., *P. reniforme* Curt., Geraniaceae), can be administered in liquid or solid dosage forms for oral use in the treatment of common cold for children aged 6 years and older (59, 60).

Finally, traditional HMPs based on the lime flower, *Tiliae flos* (*Tilia cordata* Mill., *Tilia platyphyllos* Scop., *Tilia x vulgaris* Hayne, Malvaceae) and elder flower, *Sambuci flos* (*Sambucus nigra* L., Viburnaceae), should not be forgotten. According to the HMPC/EMA, they can be used as a comminuted herbal substance as herbal tea, liquid extract or tincture for the relief of the symptoms of cold for children over 12 years of age and lime flowers as infusion for children over 4 years of age (61, 62).

Conclusion

A wide range of herbal medicines is available for the treatment of upper respiratory tract infections in the pediatric population. In addition to their generally favourable risk-benefit profile, these medicines are well accepted and perceived as effective by patients and caregivers. Their use is mainly symptomatic, encompassing herbal drugs with mucilaginous (e.g. *Althaeae folium, Plantaginis lanceolatae folium*), anti-inflammatory (e.g. *Matricariae flos*), and expectorant properties (e.g. *Hederae folium, Primulae radix, Thymi herba, Thymi aetheroleum*), as well as agents with immunomodulatory activity (e.g. *Echinaceae* spp.), which provide a broader relief of respiratory tract symptoms. The majority of herbal medicinal products used in children are authorised under traditional

use status, while only a limited number of herbal substances or preparations have evidence of efficacy and safety from clinical studies, and are classified as products with well-established use.

Acknowledgements

This research was funded by the Ministry of Science, Technological Development and Innovation, Republic of Serbia through two Grant Agreements with University of Belgrade – Faculty of Pharmacy No 451-03-136/2025-03/ 200161 and No 451-03-137/2025-03/ 200161.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

MM: Conceptualization, Writing – original draft, Writing – review & editing, Visualization, Supervision; JA: Writing – original draft, Writing – review & editing, Visualization.

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Biljni lekoviti proizvodi kod respiratornih infekcija u pedijatrijskoj populaciji

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Kratak sadržaj

Najčešće indikacije za upotrebu biljnih lekovitih proizvoda u pedijatriji u evropskim zemljama su kašalj i prehlada. Ovi biljni proizvodi se generalno smatraju bezbednim i njihov efekat se uglavnom klasifikuje kao dobar ili veoma dobar. Tradicionalni biljni lekovi na bazi biljnih droga sa sluzima poput *Althaeae radix*, *Malvae folium*, *Lichen islandicus* i *Plantaginis lanceolatae folium* koriste se u lečenju upala usne duplje i ždrela i pratećeg suvog kašlja. Kod produktivnog kašlja primenjuju se biljni lekovi na bazi *Hederae folium*, ili niz tradicionalnih biljnih lekova na bazi *Primulae radix, Thymi herba*, i drugih aromatičnih droga i etarskih ulja. Važno je napomenuti da su proizvodi na bazi etarskih ulja, kao i nekih aromatičnih droga, kontraindikovani kod dece mlađe od 2 ili 2,5 godina, zbog rizika od laringospazma. U pedijatrijskoj populaciji, za ublažavanje različitih simptoma prehlade, primenjuju se i proizvodi na bazi *Matricariae flos*, *Pelargonii radix*, *Tiliae flos* i *Sambuci flos*. Primena je ograničena na decu određenog uzrasta, najčešće zbog nedostatka dokaza o bezbednosti, a u pojedinim slučajevima zbog mogućnosti pojave određenih neželjenih efekata.

Ključne reči: biljne droge, kašalj i prehlada, deca, demulcent, ekspektorans