Arh. farm. 2022; 72: 320 – 339 *Review article/Pregledni rad*

Phytotherapy of acute upper respiratory tract infections in children

Tatjana Kundaković[1], Zoran Maksimović[1,*]

[1]University of Belgrade - Faculty of Pharmacy, Department of Pharmacognosy, Vojvode Stepe 450, 11221 Belgrade, Serbia

*Corresponding author: Zoran Maksimović, e-mail: maksim1@pharmacy.bg.ac.rs

Abstract

Acute upper respiratory tract infections (URIs) are the most common infections in the population, especially in children. URIs are mostly of viral origin and tend to resolve spontaneously in approximately one week. Bacterial URIs are less common, and come mostly as superinfections of acute viral diseases. The therapy is symptomatic and aimed at alleviating cough, maintaining the patency of airways and preventing disease progression. If there are no reasons to see a doctor, parents should be advised to apply general measures and give herbal medicinal products to their children, in an attempt to relieve cough, sore throat and nasal symptoms. In productive cough, herbal expectorants, such as, for example, *Hederae helicis folium* extracts, are used to facilitate the elimination of mucus. On the other hand, demulcents (*Althaeae radix*, *Plantaginis lanceolatae folium*) alleviate dry cough by reducing local irritation. Honey also significantly reduces the frequency and severity of acute cough episodes. Extracts of *Sisymbrii officinalis herba* and *Pelargonii radix* are useful for the alleviation of nasal symptoms and sore throat. If the application of the proposed herbal products does not resolve the symptoms within a week, advice of a medical doctor should be sought.

Key words: phytotherapy, herbal medicinal products, acute upper respiratory infections, children

https://doi.org/10.5937/arhfarm72-37803

Introduction

Acute upper respiratory tract infections (URIs) are among the most frequent infections in the general population, and are recognized as one of the main causes of work or school absenteeism (1). Certain risk factors that could be seen as inevitabilities of a modern lifestyle, such as high population density in cities, long stays indoors with an insufficient quantity of fresh air (offices, kindergartens, schools, theaters, gatherings, public transport), as well as smoking, including second-hand smoking, etc., significantly contribute to their high frequency (2). Adults contract 3-5 URI episodes per year; children contract them even more often, as many as 4-7 episodes on average, regardless of where they live or what their economic situation is (3, 4). URIs cover a wide span from a mild, catarrhal syndrome of the nasopharynx that tends to resolve spontaneously (common cold), to epiglottitis which is a life-threatening illness (1-3).

Viruses cause most URIs, as about 25-30% of these illnesses are caused by one of more than a hundred rhinovirus serotypes (5). Respiratory syncytial viruses (RSVs), influenza and parainfluenza viruses, human metapneumovirus, and adenoviruses account for another 25-35%; coronaviruses for 10 %, and other viruses (such as enteroviruses and herpes simplex viruses) for the rest (4-6). Because most URIs tend to run a definite course without treatment, their aggravation is more important than the infections themselves, as acute viral infections make children vulnerable to bacterial infections of the middle ear and sinuses, as well as the development of lower respiratory tract illnesses (LRIs) (4). Considering bacterial URIs, they are usually the result of β-hemolytic streptococcal A invasion, while *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis* have been identified as the most common microorganisms that cause bacterial superinfections (1, 2).

Nevertheless, URIs are the most common reason for prescribing antibiotics in medical practice, and are one of the main causes of their irrational use and increase in the resistance of bacterial strains (7-9). Antibiotic treatment is prescribed to as many as 85-98% of patients with rhinosinusitis, 70% of patients with a sore throat, and 60% of patients with the common cold (9).

Herbal medicinal products (HMPs) are the drugs of choice in the treatment of uncomplicated URIs in children (10). They are used in different ways and are usually given by patients' parents, mostly by their own choice and decision. However, the success and adequacy of URIs adjuvant therapy largely depend on their ability to distinguish between viral/bacterial infections and allergic rhinitis, i.e. harmless colds on the one hand and the initial stages of a process with complications requiring medical care on the other. These facts, as well as the position and role of pharmacists in contemporary pharmacy practice, speak in favor of providing responsible expert information about the medically justified use of HMPs, the possibilities of their application and the realistic scope of the therapy (10).

Therefore, the main goal of this review is presenting current facts related to the possibilities of using HMPs in the treatment of URIs in children.

Symptoms of acute upper respiratory tract infections

The main symptoms of URIs are a consequence of the immune response to infection, which includes a complex interplay of the effects of cytokines (interleukins, tumor necrosis factor, interferons) and local mediators (bradykinin, histamine, prostaglandins). The same mechanisms are activated in viral, bacterial or fungal infections and this is the reason for the intertwining of clinical signs and symptoms caused by different infectious agents (6).

After a short incubation period (usually 24-72 h), URI symptoms begin with pain in the throat, sneezing, rhinorrhea and nasal obstruction; sometimes, malaise (1). The body temperature is seldom elevated, except in flu cases (exceeding 38 °C), which are usually followed by chills and shivering, fever and muscle aches (1, 6, 11). Nasal secretions are usually ample and watery in the beginning, but later become more mucoid and purulent (in this case, mucopurulent secretions do not indicate a bacterial superinfection) (1). Cough is usually moderate but often continues for as long as two weeks (1). Most symptoms of uncomplicated URIs usually cease within a week (1, 6, 11).

Therapeutic options

Unless the reasons for seeing a physician have been identified (such as a frontal headache, persistent temperature and productive cough, presence of blood in sputum, ear or chest pain, chronic bronchitis, diabetes, asthma, etc.), symptomatic therapy should be introduced as soon as possible (11).

Pharmacological therapy is aimed at alleviating the symptoms of the disease, maintaining the patency of airways, eradicating pathogens (antibiotic therapy), as well as preventing complications and disease progression (12). The use of HMPs in the treatment of URIs is analogous, having basically the same aims, with one important exception: the use of HMPs generally cannot lead to the eradication of pathogens.

The Committee on Herbal Medicinal Products of the European Medicines Agency (EMA/HMPC) lists 40 monographs of herbal substances, herbal preparations and fixed combinations for use in medical treatment of URIs, in the therapeutic area “Cough and Cold” (Table I). These herbal substances and preparations can be roughly classified into the groups of analgoantipyretics, diaphoretics, those intended for inhalation, dermal and oromucosal application, cough-relieving agents (demulcents, expectorants), and herbal immunomodulators.

Of the 40 herbal substances and preparations listed, only a limited number of HMPs are considered suitable for use in children, mostly due to a lack of adequate safety data, or because physician’s advice should be sought, as well as for contraindications for use in specific age groups (Table I).

Only three HMPs from the list presented in Table I – fresh purple coneflower herb (*Echinaceae purpureae herba recens*), common ivy leaves (*Hederae helicis folium*), and some preparations of the fixed combination of thyme herb (*Thymi herba*) and

primula root (*Primulae radix*) are products with well-established use (WEU); the others have a record of traditional use (TU).

Table I Herbal substances and preparations with Final European Union herbal monographs in the therapeutic area "Cough and Cold", and their suitability for use in children1

Tabela I Droge i preparati biljnih droga sa finalnim monografijama Evropske Unije u terapijskoj oblasti „Kašalj i prehlada" i podesnost za primenu kod dece

Herbal substance	Biological source (species and family)	Therapeutic use	Suitability for use in children
Allii sativi bulbus	*Allium sativum* L., Amaryllidaceae	Traditional herbal medicinal product used for relief of the symptoms of common cold.	Use in children under 12 years of age has not been established due to lack of adequate data.
Althaeae radix	*Althaea officinalis* L., Malvaceae	Traditional herbal medicinal product used as a demulcent preparation for symptomatic treatment of oral or pharyngeal irritation and associated dry cough.	Use in children under 3 years of age is not recommended.
Anisi aetheroleum	*Pimpinella anisum* L., Apiaceae	Traditional herbal medicinal product used as an expectorant in cough associated with cold.	Use in children and adolescents under 18 years of age is contraindicated.
Anisi fructus			Use in children under 12 years of age has not been established due to a lack of adequate data.
Echinaceae angustifoliae radix	*Echinacea angustifolia* DC., Asteraceae	Traditional herbal medicinal product for supportive treatment of common cold.	Use in children under 12 years of age is not recommended.
Echinaceae pallidae radix	*Echinacea pallida* (Nutt.) Nutt., Asteraceae	Traditional herbal medicinal product for relief of symptoms of common cold.	Use in children under 12 years of age is not recommended.
Echinaceae purpureae herba recens	*Echinacea purpurea* (L.) Moench, Asteraceae	Herbal medicinal product for short-term prevention and treatment of common cold.	Use in children under 12 year of age is not recommended.
Echinaceae purpureae radix		Traditional herbal medicinal product for relief of symptoms of common cold.	
Eucalypti aetheroleum	*Eucalyptus globulus* Labill.; *E. polybractea* R.T. Baker; *E. smithii* R.T. Baker., Myrtaceae	Traditional herbal medicinal product used for relief of cough associated with cold.	In general, use is contraindicated in cases of hypersensitivity to eucalyptus oil or 1,8-cineol, in children with a history of seizures (febrile or not), and in children under 30 months of age, due to a risk that 1,8-cineole containing preparations can induce laryngospasm. Full hot baths are contraindicated in cases of large skin injuries and open wounds, acute skin diseases, high fever, severe infections, severe circulatory disturbances and cardiac failure. Oral use in children under 12 years of age is not recommended. Cutaneous use, and use as bath additive or inhalation, are not recommended in children between 2.5 and 4 years of age.

[1] Compiled from: European Medicines Agency website. Herbal medicinal products: European Union herbal monographs. https://www.ema.europa.eu/en/medicines

Eucalypti folium	*Eucalyptus globulus* Labill., Myrtaceae	Traditional herbal medicinal product used for relief of cough associated with cold.	Use is generally contraindicated in children under 30 months of age, as well as in cases of hypersensitivity to the active substance. Oral use of comminuted herbal substance or as for inhalation is not recommended for children under 12 years of age, due to a lack of adequate data. Oral use of eucalyptus leaf tincture in children and adolescents under 18 is not recommended.
Filipendulae ulmariae flos *Filipendulae ulmariae herba*	*Filipendula ulmaria* (L.) Maxim. (= *Spiraea ulmaria* L.)., Rosaceae	Traditional herbal medicinal product for supportive treatment of common cold.	Use in children and adolescents under 18 years of age is not recommended.
Foeniculi amari fructus	*Foeniculum vulgare* Miller *subsp. Vulgare var. vulgare*, Apiaceae	Traditional herbal medicinal product used as an expectorant in cough associated with cold.	Use in children and adolescents under 18 years of age is not recommended due to a lack of adequate data and because pediatrician advice should be sought.
Foeniculi amari fructus aetheroleum			Use in children and adolescents under 18 years of age is contraindicated.
Foeniculi dulcis fructus	*Foeniculum vulgare* Miller *subsp. Vulgare var. dulce*, Apiaceae	Traditional herbal medicinal product used as an expectorant in cough associated with cold.	Use in children and adolescents under 18 years of age is not recommended due to a lack of adequate data and because pediatrician advice should be sought.
Grindeliae herba	*Grindelia robusta* Nutt., *G. squarrosa* (Pursh) Dunal, *G. humilis* Hook. Et Arn., Asteraceae	Traditional herbal medicinal product for relief of cough associated with cold.	Use in children and adolescents under 18 years of age is not recommended.
Hederae helicis folium	*Hedera helix* L., Araliaceae	Herbal medicinal product used as an expectorant in case of productive cough.	Use in children under 2 years of age is contraindicated because of the general risk of aggravation of respiratory symptoms through secretolytic drugs.
Lichen islandicus	*Cetraria islandica* (L.) Acharius s.l. , Parmeliaceae	Traditional herbal medicinal product used as a demulcent for symptomatic treatment of oral or pharyngeal irritation and associated dry cough.	**Oral use** in children under 12 or 18 years of age is not recommended, depending on the product. **Oromucosal use** in children under 6 years of age is not recommended.
Liquiritiae radix	*Glycyrrhiza glabra* L., *G. inflata* Bat., *G. uralensis* Fisch., Fabaceae	Traditional herbal medicinal product used as an expectorant in cough associated with cold.	Use in children and adolescents under 18 years of age is not recommended.
Malvae folium	*Malva sylvestris* L.; *Malva neglecta* Wallr., Malvaceae	Traditional herbal medicinal product used as a demulcent preparation for symptomatic treatment of oral or pharyngeal irritation and associated dry cough.	Use in children under 12 years of age is not recommended.
Malvae sylvestris flos	*Malva sylvestris* L, Malvaceae	Traditional herbal medicinal product used as a demulcent preparation for symptomatic treatment of oral or pharyngeal irritation and associated dry cough.	Use in children under 12 years of age is not recommended.
Marrubii herba	*Marrubium vulgare* L., Lamiaceae	Traditional herbal medicinal product used as an expectorant in cough associated with cold.	Use in children under 12 years of age is not recommended.
Matricariae flos	*Matricaria recutita* L., Asteraceae	Traditional herbal medicinal product used for relief of symptoms of common cold.	Use of comminuted herbal substance for steam inhalation in children under 6 years of age is not established due to a lack of adequate data.

Menthae piperitae aetheroleum	*Mentha x piperita* L., Lamiaceae	Traditional herbal medicinal product used for relief of symptoms in coughs and colds.	Cutaneous and transdermal use in children under 2 years of age are contraindicated. Use in children between 2 to 3 years of age has not been established due to a lack of adequate data. Nasal application in children from 2 to 11 years of age has not been established due to a lack of adequate data.
Origani dictamni herba	*Origanum dictamnus* L., Lamiaceae	Traditional herbal medicinal product used for relief of cough associated with cold.	Use in children and adolescents under 18 years of age is not recommended.
Pelargonii radix	*Pelargonium sidoides* DC; *P. reniforme* Curt., Geraniaceae	Traditional herbal medicinal product for symptomatic treatment of common cold.	Use in children under 6 years of age is not recommended.
Plantaginis lanceolatae folium	*Plantago lanceolata* L., Plantaginaceae	Traditional herbal medicinal product as a demulcent for symptomatic treatment of oral or pharyngeal irritations and associated dry cough.	**Oral use** in children under 3 years of age is not recommended. **Oromucosal use** in children and adolescents under 18 years of age is not recommended.
Polygoni avicularis herba	*Polygonum aviculare* L., Polygonaceae	Traditional herbal medicinal product used for relief of symptoms of common cold.	Use in children under 12 years of age is not recommended.
Polypodii rhizoma	*Polypodium vulgare* L., Polypodiaceae	Traditional herbal medicinal product used as an expectorant in cough and cold.	Use is not recommended in children under 12 years of age.
Primulae flos	*Primula veris* L.; *P. elatior* (L.) Hill, Primulaceae	Traditional herbal medicinal product used as an expectorant in cough associated with cold.	Use in children under 12 years of age is not recommended.
Primulae radix			Use is not recommended in children under 4 or 12 years of age, depending on the product, because medical advice should be sought.
Salicis cortex	Different *Salix*-species, including *S. purpurea* L.; *S. daphnoides* Vill.; *S. fragilis* L., Salicaceae	Traditional herbal medicinal product used for relief of fever associated with common cold.	Use in children and adolescents under 18 years of age is contraindicated.
Sambuci flos	*Sambucus nigra* L., Adoxaceae	Traditional herbal medicinal product used for relief of early symptoms of common cold.	Use in children under 12 years of age is not recommended.
Sideritis herba	*Sideritis scardica* Griseb.; *S. clandestina* (Bory & Chaub.) Hayek; *S. raeseri* Boiss. & & Heldr.; *S. syriaca* L., Lamiaceae	Traditional herbal medicinal product used for relief of cough associated with cold.	Use in children and adolescents under 18 years of age is not recommended.
Sisymbrii officinalis herba	*Sisymbrium officinale* (L.) Scop., Brasicaceae	Traditional herbal medicinal product for relief the symptoms of throat irritation such as hoarseness and dry cough.	**Oromucosal use** in children under 6 years of age is not recommended. **Oral use** in children under 3 years of age is not recommended.
Thymi aetheroleum	*Thymus vulgaris* L.; *T. zygis* Loefl. Ex L., Lamiaceae	Traditional herbal medicinal product used as an expectorant in cough associated with cold. Traditional herbal medicinal product for relief of symptoms in coughs and colds.	**Oral use** in children and adolescents under 18 years of age is not recommended. **Cutaneous use** in children and adolescents under 18 years of age is not recommended. **Use as a bath additive** in children under 3 years of age is not recommended.
Thymi herba		Traditional herbal medicinal product used in productive cough associated with cold.	Use in children under 4 or 12 years of age is not recommended, depending on the product.

Tiliae flos	*Tilia cordata* Miller, *T. platyphyllos* Scop., *Tilia x vulgaris* Heyne or their mixture, Malvaceae	Traditional herbal medicinal product used for relief of symptoms of common cold.	Use in children under 4 years of age is not recommended.
Verbasci flos	*Verbascum thapsus* L.; *V. densiflorum* Bertol. (*V. thapsiforme* Schrad); *V. phlomoides* L., Schrophulariaceae	Traditional herbal medicinal product used to relieve symptoms of sore throat associated with dry cough and cold.	Use in children under 12 years of age is not recommended.
Fixed combination: *Thymi herba* and *Primulae radix*	*T. vulgaris* L./*T. zygis* L. and *P. veris* L./*P. elatior* (L.) Hill	**WEU:** Herbal medicinal product used as an expectorant in case of productive cough. **TU:** Traditional herbal medicinal product used as an expectorant in cough associated with cold.	**WEU:** Use in children and adolescents under 18 years of age is not recommended. **TU:** Use in children under 4 or 12 years of age is not recommended, depending on the product.

Cough therapy

HMPs used to relieve cough are classified into expectorants and demulcent agents.

Expectorants

The group of expectorants includes ivy leaf (*Hederae helicis folium*) (13), primula root (*Primulae radix*) (14), thyme herb and essential oil (*Thymi herba/aetheroleum*) (15, 16), as well as eucalyptus leaf (*Eucalypti folium*) (17) and eucalyptus essential oil (*Eucalypti aetheroleum*) (18). According to current EMA monographs, preparations of common ivy leaves, as well as some preparations of the fixed combination of thyme herb and primula root, have a WEU status based on appropriate clinical studies (indication: “Herbal medicinal product used as an expectorant in case of productive cough”) (Table II), while for all other herbal drugs and their preparations only a TU status has been documented (indication: “Traditional herbal medicinal product used as an expectorant in cough associated with cold”) (Table III) (13-24).

Hederae helicis folium. Safety studies on the use of HMPs based on ivy leaf have been performed on a large number of children aged 0-1; 1-3; and 1-5 years. Over 7,000 children participated in prospective clinical studies, and tolerability was described as “good” or “very good” in 90-98% of cases, according to both physicians and patients (25). In a 2004 retrospective study that included 52,478 children, it was concluded that the occurrence of side effects was age-related (25). From 115 adverse effects (0.22%) like diarrhoea (0.1%); enteritis (0.04%), allergic exanthema/ urticaria (0.04%), and vomiting (0.02%), the most frequent in children were gastrointestinal disturbances, 0.17% in total. Their incidents were age related: 0.4% in children aged 0-1 year and 0.13% children 2-9 years. In 2010, the French National Agency for the Safety of Medicines and Health Products (Agence nationale de sécurité du médicament et des produits de santé – ANSM) came to the decision that the use of mucolytics should be contraindicated in children under 2 years of age, due to the risk of respiratory congestion and bronchiolitis in babies (narrow bronchial diameter and underdeveloped bronchi reduce the capacity of their lungs to remove mucus). This has been accepted by

the Italian Medicines Agency (Agenzia Italiana del Farmaco – AIFA), as well as by the HMPC/EMA (25).

HMPs based on ivy leaf extracts are contraindicated in case of hypersensitivity to the constituents, or constituents of the other plants belonging to the Araliaceae family, as well as in children under 2 years. Their use is not recommended without consulting a physician in children between 2 and 4 years of age with persistent cough or cough that occurs frequently, as well as during pregnancy and lactation (13).

Caution is advised in patients with gastritis or gastric ulcer when using herbal expectorants containing saponosides (*Hederae helicis folium*, *Primulae radix*) because the presumed mechanism of action involves the irritation of gastric mucosa (13, 14). Therefore, side effects may include gastrointestinal symptoms (nausea, vomiting, diarrhea), but also allergic reactions due to the presence of polyacetylene falcarinol (urticaria, rash, dyspnea, anaphylactic reaction) (13).

Primulae radix. Controlled clinical studies of HMPs based on primula root as the only active ingredient are lacking; therefore, only the traditional use of primula root preparations as expectorants in cough associated with cold has been documented so far. Use in children under 4 years of age is not recommended without medical advice (14).

Fixed combinations of *Primulae radix* and *Thymi herba*. Unlike *Primulae radix* alone, the data from clinical studies for fixed combinations of primula root and thyme herb are evident. In the corresponding EMA monograph, 3 fixed combinations in total are recognized as WEU products for "use as expectorants in cases of productive cough". This indication is based on 3 clinical studies that did not include persons under 18 years of age; therefore, the use of WEU products in children and adolescents under 18 years of age is not recommended (26, 27).

On the other hand, traditional use for a number of combinations of dry, soft and liquid extracts of these drugs has been documented for the indication "expectorant in cough associated with cold." (26, 27). However, only three are found suitable for use in children aged 4 – 11 years:

- Liquid extract from thyme (DER 1:2-2.5; extraction solvent ammonia solution 10% m/m : glycerol 85% m/m : ethanol 90% V/V: water (1:20:70:109)) and soft extract from primula root (DER 1-2:1; extraction solvent ethanol 55% V/V);
- Liquid extract from thyme (DER 1:2-2.5; extraction solvent ammonia solution 10% m/m : glycerol 85% m/m : ethanol 90% V/V: water (1:20:70:109)) and tincture from primula root (ratio of herbal substance to extraction solvent 1:5; extraction solvent ethanol 50% V/V), and
- Liquid extract from thyme (DER 1:2-2.5; extraction solvent ammonia solution 10% m/m : glycerol 85% m/m : ethanol 90% V/V : water (1:20:70:109)) and liquid extract from primula root (DER 1:2-2.5; extraction solvent ethanol 70% m/m).

The use in children under 4 years of age is not recommended. If the symptoms persist longer than 1 week during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

***Thymi herba* / *Thymi aetheroleum*.** In an open multicenter study for Dentinox® (Dentinox Integrierter Abschlussbericht vom 4.12.1997 für Dentinox Gesellschaft KG, Berlin, as cited in ESCOP Herbal Monographs), a dose of 15-30 ml of the product (a syrup containing 10% of thyme liquid extract (DAB); 1 ml corresponds to 220 mg herbal substance) was administered during 7-14 days to 154 children aged 2 months to 14 years with diagnosed bronchial catarrh or bronchitis; 46 children did not receive any co-medication. As many as 93.5% of patients felt an improvement compared to the beginning of the medication, when it comes to relieving cough. However, this study had a number of shortcomings, as cited in ESCOP Hebal Monographs (27, 28).

For children aged 4 to 12 years, liquid extract of thyme herb can be used (DER 1 : 2-2.5; extraction solvent 10% ammonia (m/m) : 85% glycerol (m/m) : 90% ethanol (V/V) : water – 1 : 20 : 70 : 109) in a dose of 0.5 – 0.9 mL, 3-5 times a day, as well as liquid extract of fresh herb (DER 1 : 1.5-2.4; extraction solvent water), in a dose of 7-10 mL, 2-3 times a day for a week. Use in children under 4 years of age is not recommended. No or rare adverse effects can occur (allergic reaction, or stomachache and nausea) (15).

Thyme essential oil (*Thymi aetheroleum*) can be used in children (3-12 years) as a bath additive only (29).

***Eucalypti folium* / *Eucalypti aetheroleum*.** HMPs based on eucalyptus leaf are traditionally used to relieve cough associated with colds. However, clinical studies of HMPs based on eucalyptus leaf or eucalyptus essential oil, including special populations such as children under 12 years of age, have not been performed so far. Due to the specific odor of both the leaf and the essential oil that is strong and recognizable, it is almost impossible to mask it and to perform a double-blind study (30). Recent works, such as a review by Chandorkar et al. (2021), provided no further insight into the effects of eucalyptus leaf or essential oil. In this review, data from several clinical studies with eucalyptus essential oil (in combination with other ingredients) or 1,8-cineole were used (31).

The use of both eucalyptus leaf and essential oil is contraindicated in children under 30 months of age, due to possible reflex apnoea and laryngospasm that can be caused by cooling effect and strong odor (17, 18).

In Germany, HMPs with eucalyptus essential oil are registered for topical use in children older than 2 years of age, implying that the submitted documentation for registration had sufficient data on safety; however, it is publicly unavailable (30). Therefore, oral use in children between 2.5 and 4 years of age is not recommended without a medical doctor’s advice, due to the lack of clinical safety data.

Eucalyptus oil can be used in children between 4 and 12 years of age in the form of inhalation (2-4 drops per 250 mL of boiling water, 3 times a day), by applying on the

skin (liquid dosage forms: a few drops on the chest or back, 2-3 times a day; semi-solid dosage forms containing up to 10% of essential oil, applied in a thin layer on the chest and back, 2-3 times a day), and as a bath water additive (0.5-3 g of essential oil per 100 L of water, 3-4 times a week). Oral use of both leaf and oil is not recommended in children under 12 years of age, with the exception of eucalyptus leaf tincture, whose use is not recommended in children and adolescents under 18 years of age. If the symptoms persist longer than 1 week during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted (17, 18).

Table II Herbal medicinal products with well-established use, suitable for use in children, registered in Serbia

Tabela II Biljni lekoviti proizvodi sa dobro ustanovljenom primenom, podesni za primenu kod dece, registrovani u Srbiji

Name of herbal medicinal product and manufacturing site	Composition	Form	Indication
Hedelix®, Krewel –Meuselbach GmbH, Germany	Ivy (*Hedera helix* L.) leaves soft extract	Syrup; 8 mg/ml; glass bottle, 1x100 ml; 1x200 ml	Expectorant, used to alleviate productive cough in children older than 2 years of age, adolescents and adults (syrup, oral drops). Lozenges, oral solutions, effervescent tablets – in adults, adolescents and children older than 6 years of age.
Bronhoklir syrups® Ivy, Pharmanova d.o.o. Obrenovac, Serbia	Ivy (*Hedera helix* L.) leaves dry extract	Syrup; 7 mg/ml; glass bottle, 1x125 ml	
Prospan®, Engelhard Arzneimittel GmbH & Co. KG, Germany	Ivy (*Hedera helix* L.) leaves dry extract	Lozenge; 26 mg; blister, 2x10 pcs.	
		Syrup; 7 mg/ml; glass bottle, 1x100 ml; 1x200 ml	
		Effervescent tablets; 65 mg; strip, 5x20 pcs.	
		Liquid; oral solution; 35 mg/5 ml; sachet, 15x5 ml; 21x5 ml	
		Liquid; oral solution; 35 mg/5 ml; glass bottle, 1x100 mL; 1x 200 ml	
		Drops, oral solution; 20 mg/ml; glass bottle with a dropper, 1x20ml	
Tuspan®, Sopharma AD, Bulgaria	Ivy (*Hedera helix* L.) leaves dry extract	Syrup; 7 mg/ml; plastic bottle, 1x120 ml	
Herbion® Ivy Syrup, Krka Tovarna zdravil DD, Slovenia	Ivy (*Hedera helix* L.) leaves dry extract	Syrup; 7 mg/ml; glass bottle, 1x150 ml	
Herbion® Ivy Lozenges, Krka Tovarna zdravil DD, Slovenia		Lozenge; 35 mg; blister, 2x8 pcs; 3x8 pcs; 4x8 pcs.	
Mucoplant® Cough Syrup with Ivy Extract, Dr. Theiss Naturwaren GmbH, Germany	Ivy (Hedera helix L.) leaves dry extract	Syrup; 154 mg/100 ml; glass bottle, 1x100 ml; 1x250 ml	
Bronchipret®, Bionorica SE, Germany	Thyme (*Thymus vulgaris* L. and/or *Thymus zygis* L.) herb liquid extract; Ivy (*Hedera helix* L.) leaves liquid extract	Oral solution; 1,5g/10g + 0,15g/10g; glass bottle, 1x100 ml; 1x50 ml	Alleviation of acute bronchitis symptoms with productive cough, in children older than 6 years of age, adolescents and adults.
Sinupret® Syrup, Bionorica SE, Germany	Liquid extract (1:38,5) from 0,9 g of mixture of gentian root (*Gentiana lutea* L.), primrose flower with calyx (*Primula veris* (L.) and/or *Primula elatior* (L.) Hill.), sorrel herb (*Rumex acetosa* L.), elder flower (*Sambucus nigra* L.) and common vervain herb (*Verbena officinalis* L.) (1:3:3:3:3)	Syrup; 34.5g/100g; glass bottle, 1x100mL	To improve the symptoms of acute inflammations of the paranasal sinuses in adults, adolescents and children older than 2 years of age.

Demulcent agents

The group of demulcent agents includes mucilaginous herbal drugs, such as marshmallow root (*Althaeae radix*) (19), mallow leaf (*Malvae folium*) (20), mallow flower (*Malvae sylvestris flos*) (21), ribwort plantain leaf (*Plantaginis lanceolatae folium*) (22) and Iceland moss thallus (*Lichen islandicus*) (23). All demulcent herbal drugs and their preparations share a common indication: "Traditional herbal medicinal product used as a demulcent preparation for the symptomatic treatment of oral or pharyngeal irritation and associated dry cough", as well as the same duration of use: "If the symptoms persist longer than 1 week during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted" (19-23; Table I).

Herbal drugs containing mucilage (polysaccharides) are of great importance in the therapy of dry, irritating cough in children. Mucilage presumably prevents the activation of receptors and cough irritation by coating the mucous membrane of the pharynx, forming a kind of temporary protective coating. The effect is restricted to the throat only, because the mucilage cannot be absorbed after oral administration. This consideration is supported by the study of Schmidgall et al. (2000), which proved that marshmallow root heteropolysaccharides bind moderately to the buccal mucous membrane of laboratory animals in an *ex vivo* experiment, i.e. that they exert a moderate bioadhesive effect (32).

Althaeae radix. Marshmallow root, extracts and isolated heteropolysaccharides have been studied in several *in vitro* studies, as well as in animal studies, which support the use of marshmallow in dry cough and irritation of the oral and pharyngeal mucosa. (19).

The efficacy and tolerability of Phytohustil® marshmallow root syrup (aqueous extract of marshmallow root, 1 : 19.5 – 23.5; 2.5-10 mL depending on age, 4-6 times daily for not more than 3 days) were determined based on post-marketing observations in 313 children aging between 0 months and 12 years. The children had an irritation of the mucous membranes of the mouth and throat, as well as a dry cough as a consequence. The following symptoms were assessed by physicians, patients, or their parents:

- cough symptoms (intensity, frequency and length of cough periods during the day),
- symptoms associated with cough (sleep disturbance and sounds during the sleep, sore throat, chest pain), and
- accompanying symptoms (throat inflammation, fever).

The intensity and frequency of cough, as well as the symptoms associated with it, decreased after 3 days, and the tolerability of this syrup was assessed as good. However, it was found that, in some cases, serious side effects developed in the group of babies and toddlers, such as obstructive bronchitis and bronchopneumonia that required hospitalization, and the syrup based on marshmallow root cannot be recommended in children younger than 3 years of age (34).

In a retrospective observational study on 599 patients (children under 12 years of age) who used Phytohustil® syrup for irritation of mucous membranes of the mouth and throat accompanied by dry cough, a good or very good efficacy in all age groups was observed, without reported side effects. A dose of 1-5 ml of the product was administered depending on the age of patients, 1-6 times a day for 3 days to 2 weeks (7.5 days on average) (35). Although suggestive, the mentioned studies are not sufficient for laying a foundation to a WEU status for marshmallow root, but they support its traditional use. Long-term studies have shown that marshmallow root and its preparations are safe, but there are not enough data to recommend their use in children younger than 3 years of age. ***Plantaginis lanceolatae folium.*** In a post-marketing study that included 91 patients under 18 years of age (20 children under 7; 38 children between 8 and 12, and 33 children between 13 and 17 years of age), a dose of 22.4 ml of syrup (100 ml syrup contains 20 g fluid extract from *Plantago lanceolata* herb, DER 1:1, extraction solvent ethanol) was administered daily to patients for 9 days, and a 58% reduction in symptoms compared to baseline was observed (36). The available data are sufficient to support traditional use only and to indicate safety in children older than 3 years of age (37).

***Lichen islandicus*.** Thallus of Iceland moss contains hydrosoluble mucilage that coats the mucous membrane of the upper respiratory tract and relieves cough irritation. A multicenter post-marketing study on lozenges containing a soft aqueous extract (DER 0.4-0.8:1, and DER 2-4:1) of Iceland moss, which included data for 3,143 children aged 4-12 years with upper respiratory system disorders (irritating cough, inflammation of the mouth and throat, laryngitis, acute bronchitis) collected in 300 pediatric practices in Germany, showed that the tolerance to the medicinal product was good, with only 7 adverse reactions that may be associated to the active substance (38). Children between 6 and 12 years of age can use these HMPs for oromucosal use, 4 to 6 times a day (39).

Besides hypersensitivity, demulcent agents as HMPs seldom cause other side effects. However, the absorption of concomitantly administered medicines may be delayed. As a precautionary measure, the product should not be taken ½ to 1 hour before or after the intake of other medicinal products.

Table III Traditional herbal medicinal products registered in Serbia

Tabela III Tradicionalni biljni lekovi registrovani u Srbiji

Name of herbal medicinal product and manufacturing site	Composition	Form	Indication
Herbion® Iceland moss syrup, Krka Tovarna zdravil DD, Slovenia	Iceland moss (*Cetraria islandica*) thallus soft extract	Syrup; 6 mg/ml; glass bottle, 1x150 ml	Symptomatic alleviation of irritation of oral cavity and pharynx mucous membranes, as well as associated dry cough in adults and children older than 2 years of age; in children between 2 and 4 years of age, on advice of a medical doctor only.
Herbion® Ribwort Plantain syrup, Krka Tovarna zdravil DD, Slovenia	Ribwort plantain (*Plantago lanceolata*) leaves liquid extract; mallow (*Malva sylvestris*) flowers liquid extract; ascorbic acid	Syrup; 0,25 g/5 ml + 0,25 g/5 ml + 65 mg/5 ml; glass bottle, 1x150 ml	Symptomatic therapy of dry, irritating cough in children older than 4 years of age, adolescents and adults.
Mucoplant®, Dr. Theiss Naturwaren GmbH, Germany	Ribwort plantain (*Plantago lanceolata*) leaves liquid extract	Syrup; 5 g/100 g; glass bottle, 1x100 ml, 1x250 ml	Symptomatic therapy of oral cavity and pharynx mucous membranes irritation, associated with dry cough in chidren older than 3 years of age, adolescents, adults and elderly people.
Bronchicum® syrup S, A. Nattermann & Cie. GmbH, Germany	Thyme (*Thymus vulgaris* L. and/or *T. zygis* L.) herb liquid extract	Syrup; 150 mg/ml; glass bottle, 1x100 ml	Expectorant for cough associated with colds in children older than 4 years of age, adolescents, adults and elderly people.

Other symptoms

In addition to HMPs for relieving cough, other herbal substances and their preparations are used to alleviate the symptoms that accompany the URIs, such as a sore throat and nasal symptoms. Despite the fact that these are very well-known herbal substances and essential oils, their use is classified as traditional.

HMPs based on hedge mustard herb – *Sisymbrii officinalis herba* (40), South African geranium root or pelargonium root- *Pelargonii radix* (41), as well as marjoram herb – *Origani majoranae herba* are useful in the alleviation of the mentioned symptoms. (42).

Oromucosal application of products based on the hedge mustard herb, due to the presence of glucosinolates, can ease the symptoms of throat irritation, such as dry cough and hoarseness, in children aged 6 to 11 years. Tablets or lozenges containing a dry aqueous extract of the hedge mustard herb (10 mg) should be slowly dissolved in the mouth, without chewing, 5-6 times a day (40).

In the available literature, only 3 randomized, placebo-controlled, double-blind clinical studies on pelargonium root extract (43-45) were found. Out of these, one was comparative against acetylcysteine (45). This herbal medicinal product was found to be effective and safe for use in children older than 6 years of age. However, according to the EMA, these studies had several drawbacks. They were not conducted in the EU, but in Russia and Ukraine, and their design had some faults, such as the lack of homogeneity in groups considering the gender of subjects and the severity of symptoms, lack of the compliance to the instructions, and poor definition of which reduction in symptoms is considered clinically significant (46).

Hypersensitivity to the ingredients is a contraindication for use of HMPs based on pelargonium root. In addition, few cases of hepatotoxicity and hepatitis have been reported. If symptoms of hepatotoxicity occur, the product should be discontinued immediately and a physician should be consulted. Use during pregnancy and lactation is not recommended. Gastrointestinal disorders (epigastric discomfort, diarrhea, nausea, vomiting, and dysphagia), mild nasal bleeding and bleeding gums, as well as hypersensitivity reactions, have been also described (41).

An ointment containing the ethanol extract of marjoram herb (1:5) and paraffin in a ratio of 2:10 can be used to relieve skin irritation around the nostrils in rhinitis. It should be applied to the skin around the nostrils 2-4 times a day in children between 1 and 11 years. Use in children younger than one year of age is not recommended, as well as during pregnancy and breastfeeding. Contraindications for use are hypersensitivity to the constituents of *Origanum majorana* or other Lamiaceae species (42).

In addition to eucalyptus essential oil, the essential oil of peppermint (*Menthae piperitae aetheroleum*) can be used in children between 4 and 11 years of age, in the form of semi-solid (2-10%) preparations, by applying a thin layer on the chest or back, or around the nostrils in children (47). The use is contraindicated in children under 2 years of age (because menthol can induce reflex apnoea and laryngospasm), children with a history of seizures (febrile or not), and in cases of hypersensitivity to peppermint oil or menthol (47). If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Matricaria flower (*Matricariae flos*) can be used for inhalation in children between 6 and 12 years of age, as a traditional herbal medicinal product for the relief of symptoms of the common cold (2-5 g of chamomile flower in 100 mL of hot water, once or twice a day). Hypersensitivity to the active substance and to other plants of the Asteraceae (Compositae) family may occur (48).

In cases of the common cold accompanied with mild fever in children older than 4 years, lime flower (*Tiliae flos*) can be used as herbal tea for oral use (1 g of comminuted herbal substance in 150 mL of boiling water as a herbal infusion, 2–4 times daily) (49).

Addendum: honey in acute cough therapy

There was some evidence suggesting that honey reduced the frequency and severity of cough episodes in children and adolescents with an upper respiratory tract infection, based on a systematic review and meta-analysis of six randomised controlled trials involving 899 subjects (aging 12 months to 18 years) that were conducted in Brazil, Iran, Israel, Kenya and the USA (50, 51). In the mentioned studies, the influence of honey on cough was compared with no treatment, diphenhydramine, dextromethorphan, salbutamol, bromelin (a pineapple enzyme), and placebo (51).

The clinical significance of honey benefits on cough symptoms remains unclear, as this systematic review did not bring to light any strong arguments in favor or against the use of honey. It surely eases the severity of cough symptoms more than placebo, diphenhydramine or no treatment, and presumably reduces cough duration better than placebo or salbutamol, but makes not so convincing a difference if compared to dextromethorphan. Finally, most of the children received a dose of honey for one night only, which limits the results of this review (51).

Antitussive action may not be a specific feature of honey, because there is a possibility that any viscous, sweet liquid may increase salivation or influence opioid-responsive sensory fibers located close to gustatory nerves. Recent reviews propose that some interaction between gustatory and cough pathways that modulates the activity of the nucleus of *tractus solitarius* at the level of the brainstem is possible (52, 53).

Honey should not be given to children younger than 12 months of age, as it might contain dormant endospores of *Clostridium botulinum*, raising some concerns about infant botulism (54). It also contains a high amount of invert sugar, one of the constituents of food related to tooth decay in small children (50).

Conclusions

The use of HMPs has a great practical value, as they are the drugs of choice in the self-treatment of uncomplicated respiratory infections in children. However, a lack of adequate safety data for use in self-medication of URIs is one of the most frequent reasons why a number of available and well-known HMPs cannot be recommended for self-treatment in children. Therefore, more high-quality, large randomised controlled trials, evaluating not only the effectiveness and safety of HMPs, but measuring other important secondary outcomes relevant to caregivers, the parents, such as the cost of the intervention and quality of life of the children, are urgently needed.

References

1. Meneghetti A. Upper Respiratory Tract Infections [Internet]. Medscape Reference: Drugs, Diseases & Procedures [updated 2020 Sep 11; cited 2022 Apr 27]. Available from: http://emedicine.medscape.com/article/302460-overview.
2. Peroš-Golubičić T, Tekavec-Trkanjec J. Upper respiratory tract infections. In: Blasi F, Dimipoulos G, editors. Textbook of Respiratory and Critical Care Infections. New Delhi: Jaypee Brothers; 2015; p. 16-29.
3. Škodrić-Trifunović V, Pilipović N, Stefanović B. Lečenje vanbolničkih pneumonija primenom savremenih terapijskih vodiča [Treatment of community-acquired pneumonia using the modern therapeutical guides]. Vojnosanit Pregl. 2006;63(11):967–70. (in Serbian).
4. Simoes EAF, Cherian T, Chow J, Shahid-Salles SA, Laxminarayan R, John TJ. Acute Respiratory Infections in Children. [Internet]. In: Jamison DT, Breman JG, Measham AR, et al., editors. Disease Control Priorities in Developing Countries. 2nd edition. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2006 [cited 2022 Apr 27]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK11786/.
5. Tesini BL. Common Cold - MSD Manual Professional Edition [Internet]. MSD Manual Professional Edition [updated 2022 Apr; cited 2022 Apr 27]. Available from: https://www.msdmanuals.com/professional/infectious-diseases/respiratory-viruses/common-cold.
6. Savić MM. Farmakoterapija prehlade i gripa [Pharmacotherapy of the common cold and influenza]. Arh Farm. 2011;61:152–64. (in Serbian).
7. Horvat O, Mijatović V, Milijasević B, Tomas A, Kusturica MP, Tomić Z, et al. Are There Striking Differences in Outpatient Use of Antibiotics Between South Backa District, Serbia, and Some Scandinavian Countries? Front Public Health. 2018;6:91.
8. Paut Kusturica M, Tomić Z, Bukumirić Z, Horvat O, Pavlović N, Mikov M, et al. Antibiotics in Serbian households: a source of potential health and environmental threats? Cent Eur J Public Health. 2015;23(2):114–18.
9. Horvat O, Mihajlović Ukropina M, Mijatović V, Sabo A. Susceptibility of common bacterial respiratory pathogens to antimicrobial agents in outpatients from South Backa District. Med Pregl. 2014; LXVII(3-4):71–7.
10. Petrović S, Maksimović Z. Biljni lekovi za respiratorna oboljenja kod dece [Herbal medicines for respiratory ailments in paediatric practice]. Arh farm. 2005;55:410–19. (in Serbian)
11. Miljković B, Vezmar Kovačević S, Vučićević K, Jovanović M, Kovačević M, Ćulafić M. Smernice za farmaceute u primarnoj zdravstvenoj zaštiti [Guidelines for pharmacists in primary health care]. [Internet]. Belgrade: University of Belgrade - Faculty of Pharmacy and Pharmaceutical Association of Serbia; 2021 [cited 2022 Apr 27]. (in Serbian). Available from: https://www.farmkom.rs/smernice.php.
12. Savić M, Milinković M. Infekcije gornjih respiratornih puteva i alergijski rinitis [Infections of upper respiratory tract and allergic rhinitis]. In: Ugrešić N, Stepanović-Petrović R, Savić M, editors. Pharmacotherapy for pharmacists, First edition. Belgrade: University of Belgrade - Faculty of Pharmacy; 2011; p. 187-209. (in Serbian).
13. European Medicinal Agency. EMA/HMPC/325716/2017. Final: European Union herbal monograph on *Hedera helix* L., *folium*. London, 2017 Nov 21.

14. European Medicinal Agency. EMA/HMPC/104095/2012. Final: Community herbal monograph on *Primula veris* L. and/or *Primula elatior* (L.) Hill, *radix*. London, 2012 Sep 19.
15. European Medicinal Agency. EMA/HMPC/342332/2013. Final: Community herbal monograph on *Thymus vulgaris* L. and *Thymus zygis* L., *herba*. London, 2013 Nov 12.
16. European Medicinal Agency. EMA/HMPC/59032/2017. European Union herbal monograph on *Thymus vulgaris* L., *Thymus zygis* L., *aetheroleum*. Final – Revision 1. Amsterdam, 2020 Jul 8.
17. European Medicines Agency. EMA/HMPC/892618/2011. Final: Community herbal monograph on *Eucalyptus globulus* Labill., *folium*. London, 2013 Apr 15.
18. European Medicines Agency. EMA/HMPC/307781/2012. Final: Community herbal monograph on *Eucalyptus globulus* Labill., *Eucalyptus polybractea* R.T. Baker and/or *Eucalyptus smithii* R.T. Baker, *aetheroleum*. London, 2014 Mar 25.
19. European Medicines Agency. EMA/HMPC/436679/2015. Final: European Union herbal monograph on *Althaea officinalis* L., *radix*. London, 2016 Jul 12.
20. European Medicines Agency. EMA/HMPC/749510/2016. Final: European Union herbal monograph on *Malva sylvestris* L. and/or *Malva neglecta* Wallr., *folium*. London, 2018 Nov 20.
21. European Medicines Agency. EMA/HMPC/749511/2016. Final: European Union herbal monograph on *Malva sylvestris* L., *flos*. London, 2018 Nov 20.
22. European Medicines Agency. EMA/HMPC/437858/2010 Corr. Final: Community herbal monograph on *Plantago lanceolata* L., *folium*. London, 2014 Jan 28.
23. European Medicines Agency. EMA/HMPC/678891/2013. Final: European Union herbal monograph on *Cetraria islandica* (L.) Acharius s.l., *thallus*. London, 2014 Nov 24.
24. European Medicinal Agency. EMA/HMPC/325715/2017. Final: Assessment report on *Hedera helix* L., folium. London, 2017 Nov 21.
25. Kraft K. Verträglichkeit von Efeublättertrockenextrakt im Kindesalter. Zeitschr Phytother. 2004;25:179-181.
26. European Medicines Agency. Doc. Ref.: EMA/HMPC/84990/2015 Corr.; Final: European Union herbal monograph on *Thymus vulgaris* L. or *Thymus zygis* L., *herba* and *Primula veris* L. or *Primula elatior* (L.) Hill, *radix*. London, 2016 Apr 5.
27. European Medicines Agency. Doc. Ref.: EMA/HMPC/85124/2015; Final: Assessment report on *Thymus vulgaris* L. or *Thymus zygis* L., *herba* and *Primula veris* L. or *Primula elatior* (L.) Hill, *radix*. London, 2016 Apr 5.
28. ESCOP Monograph 2nd Ed. *Thymi herba*. ESCOP (ESCOP 2003).
29. European Medicinal Agency. EMA/HMPC/52980/2017 Final – Revision 1: Assessment report on *Thymus vulgaris* L., *Thymus zygis* L., aetheroleum. Amsterdam, 2020 Jul 8.
30. European Medicinal Agency. EMA/HMPC/892615/2011. Assessment report on *Eucalyptus globulus* Labill., folium. London, 2013 Apr 15.
31. Chandorkar N, Tambe S, Amin P, Madankar C. A systematic and comprehensive review on current understanding of the pharmacological actions, molecular mechanisms, and clinical implications of the genus Eucalyptus. Phytomedicine Plus. 2021;1(4):100089.
32. Schmidgall J, Schnetz E, Hensel A. Evidence for bio adhesive effects of polysaccharides and polysaccharide-containing herbs in an *ex vivo* bioadhesion assay on buccal membranes. Planta Medica. 2000;66:48-53.

33. European Medicinal Agency. EMA/HMPC/436680/2015. Final: Assessment report on *Althaea officinalis* L., radix. London, 2016 Jul 12.
34. Fasse M, Zieseniss E, Bässler D. Dry irritating cough in children – a post-marketing surveillance involving marshmallow syrup. Praktische Pädiatrie. 2005;11:3-8.
35. Bässler D. Retrospective observational study of the application of Phytohustil® syrup for children up to 12 years of age [unpublished study]. Steigerwald Arzneimittelwerk GmbH; 2005.
36. European Medicines Agency. EMA/HMPC/437859/2010. Final: Assessment report on *Plantago lanceolata* L., folium. London, 2011 Nov 22.
37. European Medicines Agency. EMA/HMPC/437858/2010 Corr. Final: Community herbal monograph on *Plantago lanceolata* L., folium. London, 2014 Jan 28.
38. Hecker M, Völp A. Verträglichkeit von Isländisch-Moos-Pastillen bei Erkrankungen der oberen Atemwege-multizentrische Anwendungsbeobachtung mit 3143 Kindern. Forsch Komp Klas Nat. 2004;11(2):76-82.
39. European Medicinal Agency. EMA/HMPC/36866/2014. Assessment report on *Cetraria islandica* (L.) Acharius s.l., thallus. London, 2014 Nov 24.
40. European Medicines Agency. EMA/HMPC/280193/2013. Final: European Union herbal monograph on *Sisymbrium officinale* (L.) Scop., herba. London, 2014 Sep 30.
41. European Medicines Agency. EMA/HMPC/444244/2015. Final: European Union herbal monograph on *Pelargonium sidoides* DC and/or *Pelargonium reniforme* Curt., radix. London, 2018 Jun 5.
42. European Medicinal Agency. EMA/HMPC/166517/2015. Final: European Union herbal monograph on *Origanum majorana* L., herba. London, 2016 Sep 20.
43. Kamin W, Maydannik VG, Malek FA, Kieser M. Efficacy and tolerability of EPs 7630 in patients (aged 6-18 years old) with acute bronchitis. A randomized, double-blind, placebo-controlled clinical dose-finding study. Acta Paediatr. 2010a;99:537-43.
44. Kamin W, Maydannik VG, Malek FA, Kieser M. Efficacy and tolerability of EPs 7630 in children and adolescents with acute bronchitis: a randomized, double-blind, placebo-controlled multi-center trial with a herbal drug preparation from Pelargonium sidoides roots. J Clin Pharm Ther. 2010b;48:184-191
45. Blochin B, Haidvogl M, Heger M. Umckaloabo im Vergleich zu Acetylcystein bei Kindern mit acuter Bronchitis: prospective, randomisierte, kontrollierte, offene Studie zur Wirksamkeit und Vertraglichkeit. Der Kassenarzt. 1999;49:46-50
46. European Medicinal Agency. EMA/HMPC/444251/2015. Assessment report on *Pelargonium sidoides* DC and/or *Pelargonium reniforme* Curt., radix. London, 2018 Jun 5.
47. European Medicinal Agency. EMA/HMPC/522410/2013. Final – Revision 1: European Union herbal monograph on *Mentha x piperita* L., aetheroleum. Amsterdam, 2020 Jan 15.
48. European Medicinal Agency. EMA/HMPC/55843/2011. Final: European Union herbal monograph on *Matricaria recutita* L., flos. London, 2015 Jul 7.
49. European Medicinal Agency. EMA/HMPC/337066/2011. Final: Community herbal monograph on *Tilia cordata* Miller, *Tilia platyphyllos* Scop., *Tilia x vulgaris* Heyne or their mixtures, flos. London, 2012 May 22.

50. National Institute for Health and Care Excellence [Internet]. Public Health England. Cough (acute): antimicrobial prescribing. NICE guideline; 2019 Feb 7 [cited 2022 Apr 27]. Available from: https://www.nice.org.uk/guidance/ng120.
51. Oduwole O, Udoh EE, Oyo-Ita A, Meremikwu MM. Honey for acute cough in children. Cochrane Database Syst Rev. 2018;4(4):CD007094.
52. Eccles R. Mechanisms of the placebo effect of sweet cough syrups. Respir Physiol Neurobiol. 2006;152(3):340-48.
53. Eccles R. The Powerful Placebo Effect in Cough: Relevance to Treatment and Clinical Trials. Lung. 2020;198(1):13-21.
54. Goldman RD. Honey for treatment of cough in children. Can Fam Physician. 2014;60(12):1107-10.

Fitoterapija akutnih infekcija gornjih respiratornih puteva kod dece

Tatjana Kundaković[1], Zoran Maksimović[1,*]

[1]Univerzitet u Beogradu – Farmaceutski fakultet, Katedra za farmakognoziju, Vojvode Stepe 450, 11221 Beograd, Srbija

*Autor za korespondenciju:Zoran Maksimović, e-mail: zmaksim1@pharmacy.bg.ac.rs

Kratak sadržaj

Akutne infekcije gornjeg respiratornog trakta (IGRT) su najrasprostranjenije infekcije u populaciji, a posebno kod dece. Najčešće su virusnog porekla i spontano se povlače nakon približno nedelju dana. Bakterijske IGRT su ređe i uglavnom je reč o superinfekcijama akutnih virusnih infekcija. Terapija IGRT je simptomatska i usmerena ka ublažavanju kašlja, održavanju prohodnosti disajnih puteva i sprečavanju progresije oboljenja. Ukoliko nisu prisutni razlozi za upućivanje lekaru, roditelji treba da primenjuju opšte mere i pokušaju da ublaže simptome kašlja, bola u grlu i nazalne simptome primenom biljnih lekovitih proizvoda. Kod produktivnog kašlja, koriste se biljni ekspektoransi kao što su, na primer, ekstrakti *Hederae helicis folium*, u cilju olakšanja eliminacije mukusa. S druge strane, demulcentna sredstva (*Althaeae radix, Plantaginis lanceolatae folium*) ublažavaju suv kašalj smanjenjem lokalne iritacije. Med značajno smanjuje učestalost i težinu epizoda akutnog kašlja. Nazalni simptomi i bol u grlu se mogu ublažiti primenom biljnih lekovitih proizvoda na bazi ekstrakata *Sisymbrii officinalis herba*, *Pelargonii radix* i *Origani majoranae herba*. Ukoliko tokom nedelju dana primene ne dođe do poboljšanja stanja, potrebno je potražiti savet lekara.

Ključne reči: fitoterapija, biljni lekoviti proizvodi, akutne infekcije gornjih respiratornih puteva, deca