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# Cough phytotherapy in children

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*Cough is one of the most widespread causes of outpatient pediatrician's visits. There has been a notable increase in the use of phytogenic drugs recently, including treatment of respiratory infections in children. The article examines physiological and pathological effects of cough. Issues of phytotherapy efficiency and safety are covered. Data on the use of phytogenic drugs in the treatment of respiratory diseases are presented.*
***Key words:*** *cough, dry cough, productive cough, phytotherapy, children.*

Cough is one of the most frequent clinical situations that doctors encounter. Urgency of the cough issue is confirmed by a sufficiently high publishing activity about this topic: thus, search query "cough" in the English text database of medical and biological data "Pubmed" returned 37,526 results, search query "cough, children" – 9,730 results. Cough often causes deep worry in patients and in parents of coughing children. Cough is the main reason of 5-15% of all outpatient visits to pediatricians [1]. The rate of reference to doctors on the premises of cough is rather high even in adults – 3.6% (29.5mn out of 829.3mn visits) [2].
Cough is an important physiological protective reflex, which ensures removal of excessive secretion and foreign bodies from the respiratory tract. It is also widely known that cough is one of the major infection spread factors [3].
Cough and its complications may significantly influence life quality of patients and their milieu [4, 5].
3 consecutive phases are distinguished in the mechanics of cough:

- Phase 1 – inspiration – deep breath, which completes with glottis closure;
- Phase 2 – compression – contraction of thoracic and abdominal muscles in the setting of a fixed diaphragm;
- Phase 3 – expiration – once the glottis opens there is a high-velocity expiratory flow with secretion from the respiratory tract and/or foreign bodies.

Cough may be accompanied by a considerable increase in the vagus nerve tone. Cough generates sharp increase in the intrathoracic pressure – up to 300mm Hg – and develops high velocity of the expiratory flow – up to 500 miles/hour (85% of the speed of sound). Blood pressure may considerably increase in the expiratory phase of cough (systolic – up to 140mm Hg). Thus, besides positive physiological effects, cough may cause various complications, which affect almost all human body organs and systems.
Thus, cardiovascular complications include arterial hypotension, brady- and tachiarrythmia, loss of consciousness, rupture of subconjunctival, nasal and anal vessels.
General cough complications include such symptoms as hyperhidrosis, anorexia and weakness.
Digestive system complications include gastroesophageal reflux episodes, gastrorrhagia in patients with gastrostomy, rupture of hepatic cysts, herniation and splenic rupture.

Enuresis and urethral inversion of the bladder are the possible urinary system complications at cough.
Response of the musculoskeletal system to cough may vary from asymptomatic increase in the blood serum level of creatine phosphokinase to such extremely rare situations as rupture of rectus abdominis muscles, diaphragm and rib fractures.
Neurological cough complications include headache, vertigo, syncopal conditions, stroke caused by dissection of vertebral arteries, acute cervical radiculopathy, malfunction of ventriculoarterial shunts and nasal cerebrospinal fluid outflow.
Respiratory cough complications include asthma exacerbation, laryngeal trauma (laryngeal edema and hoarseness), tracheal or bronchial trauma, pulmonary interstitial emphysema with a potential risk of pneumothorax and concurrent conditions; hydrothorax may occur in patients treated with peritoneal dialysis.
Dermal complications include hemorrhagic rashes and burst of postoperative wounds.
Refractory persistent cough significantly affects psychological condition of patients: it forces them to change their lifestyle and may cause an obsessive fear of a severe disease in sensitive patients [6].
Cough most often develops in the setting of acute respiratory infections, especially in children [7]. Diagnostic search for an etiological cause of cough sometimes presents a problem. A large number of conditions have been recognized as possible causative factors of cough; in a range of cases, cough may be the only vivid symptom of a serious disease requiring immediate medical intervention.
Drugs used at cough are widely presented in the pharmaceutical market. Three main groups are distinguished on the basis of pharmacological qualities of these drugs: central and peripheral antitussive drugs, expectorant drugs and mucolytic drugs.
The use of antitussive drugs is restricted, especially in pediatric practice, to a small number of conditions with persistent cough or apparent cough tenderness: pertussis, dry pleurisy and chest injuries.
It is not advisable to combine antitussive drugs with expectorant and mucolytic action spectrum due to the risk of respiratory tract congestion with secretion and the difficulty of its evacuation due to cough suppression.
Thus, cough is most often treated with mucolytic and expectorant drugs. The history of use of synthetic drugs extends for decades; many of them have been studied sufficiently well and used widely (ambroxol, acetylcysteine, carbocisteine drugs). At the same time, interest to phytogenic drugs remains keen. The history of use of phytogenic drugs extends for centuries. Many centuries of empirical selection of plants distinguished them into therapeutic groups for the treatment of different diseases.
In a range of countries (e.g., in China) traditional medicine techniques, including herbal medicine, remain a priority. However, adherence to phytotherapy remains in European countries as well. Thus, the study in Germany [8] revealed a rise in the use of phytogenic drugs. The study involved the analysis of 413 questionnaires given to the parents who sought outpatient help with their children’s cough from pediatricians. Average age of the patients was 6.7±4.7 years. 85.5% of all the polled parents gave their children one or more phytogenic drugs. Interestingly, there was a statistically significant prevalence of financially affluent women with higher education living in big cities among those parents who applied phytotherapy to their children.
Adherence to alternative therapy, including herbal medicine, has been observed among patients with chronic obstructive pulmonary disease [9].
A review dedicated to side effects of medicinal plants has been published recently [10]; it involved the analysis of studies with minimum methodological error. Severe side reactions were observed only at the use of 4 out of the 50 studied phytogenic drugs. Moderate undesirable effects were observed at the use of 15 drugs; most drugs (31) had only mild side effects. In the group of studied plants, minimal side effects were observed in such plants as thyme, lavender, St. John's wort, calendula, echinacea, ginkgo biloba, valerian, salvia and melissa. One of the features

of herbal medicine is the possibility of using a combination of plants, the correct selection of which potentiates their desirable effects and levels their side effects [11].

Wide use of phytotherapy all over the world dictates the need in accurate standardization of the crude drug quality. Plant cultivation environment, proper and timely collection and preparation for processing are important factors of cumulation and preservation of the active components. Drugs made of raw materials collected in the environmentally neglected areas without observing sanitary standards and dried improperly may not only be void of any therapeutic effect, but also inflict harm to the body [12].

The existing data on phytotherapy are insufficient. With this issue in mind, the World Health Organization (WHO) launched the Traditional Medicine Program (WHO-TRM) in the framework of the global strategy "Health for all". Major work on this program started in 1978. A group of researchers from different countries collected an extensive material on the issues of use of medicinal plants. The WHO has so far issued a range of recommendations concerning the herbal raw material quality, methods of quality control and production of drugs [13-15]. Several collections of monographs on the most widely used medicinal plants were published in 1999-2010 under the aegis of the WHO [16]; they contain information on the requirements to the herbal raw material quality and sections dedicated to the therapeutic use, pharmacological qualities and safety of medicinal plants.

It is exceptionally important to determine the type of cough (dry or productive) when treating cough in the setting of an acute respiratory infection; this creates an opportunity for the differentiated prescription of drugs made of different medicinal plants.

One of the phytogenic drugs widely used for cough treatment is Herbion (KRKA, Slovenia). The drug is represented in the pharmaceutical market by 2 types of syrup: plantain syrup (for dry cough) and cowslip syrup (for productive cough).

Constituent components of the plantain syrup are selected for dry cough treatment. Active components of this drug are: aqueous extract of *Plantaginis lanceolatae herba*, aqueous extract of *Malva sylvestris* flowers and ascorbic acid. Syrup adjuvants are sucrose, methyl parahydroxybenzoate and orange oil.

Plantaginis lanceolatae herba has an expectorant, bacteriostatic and anti-inflammatory action spectrum; it also has antiviral activity due to the interferon genesis stimulation and cellular immunity modulation. As dry cough is usually observed in the first days of respiratory viral infections, this quality of plantain is especially relevant. Plantain potentiates glandular secretion of the respiratory tract's epithelium; this facilitates the mucus removal from bronchi and modifies dry troublesome cough, which appears on the early stages of respiratory infection, to productive cough. Moreover, the plant's active components stimulate regeneration processes in skin and mucous tunics and are conductive to the mucociliary clearance recovery.

Malva sylvestris flowers contain a large number of mucins, which envelop the gastrointestinal tract's mucous tunic and have an anti-inflammatory action. Active components of this plant are conductive to the reduction in the intensity of dry cough. The syrup also contains vitamin C, which increases resistance to infections and stimulates regeneration processes. Orange oil ensures good taste of the drug.

Cowslip syrup's active components are: extract of primula veris roots, extract of common thyme and levomenthol. Adjuvants are sucrose and methyl parahydroxybenzoate.

Primula veris roots have long been used in traditional medicine as an expectorant. This effect is caused by triterpene glycosides – primula veroside and prim veroside – contained in the plant. Primula veris also has spasmolytic action, stimulates secretion of gastric juice. All parts of the plant, including the roots (the drug's components), contain significant amounts of vitamin C.

Creeping thyme contains up to 2.5% of essential oil, thymol and carvacrol – up to 64%; moreover, the plant contains flavonoids. Thyme has expectorant effect and bronchial mucus secretion stimulatory action. It also has an established spasmolytic effect caused by noncompetitive non-specific response suppression of substances conductive to the smooth muscle tissue spasm (acetylcholine, histamine, L-noradrenaline etc.). Thyme essential oil and

thymol have antibacterial and antifungal qualities. Such causative agents as *Staphylococcus aureus, Streptococcus pneumoniae, Moraxella catarrhalis, Klebsiella pneumoniae, Escherichia coli, Salmonella typhimurium* and many other bacteria are susceptible to the active components of thyme. Antifungal effect of thyme manifests itself with regard to many fungi, including *Aspergillus, Saprolegnia, Zygorhynchus* and *Cryptococcus*. Thymol's antibacterial effect is 25 times as high as phenol's; however, thymol is far less toxic. Levomenthol's (from Latin *Mentha* - mint) action provides local anesthetic, analgesic and anti-inflammatory effects. Moreover, levomenthol has an *in vitro* bactericidal and antifungal effect due to coagulation of microbial cell proteins [11, 17, 18].

Syrup containing thyme, primula veris and levomenthol is indicated for treatment of productive cough with difficulty of sputum discharge.

Both types of syrup may be used in children of 2 years of age and older. The drugs are to be taken with a sufficient amount of warm tea or water.

Thus, accurately selected syrup components based on natural plant extracts are efficient at dry (Herbion plantain syrup) and productive cough (Herbion cowslip syrup). Good compatibility with other drugs, including antibiotics, allows using syrups not only for monotherapy, but also for combination therapy of cough (if necessary) in patients of 2 years of age and older.

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