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## REVIEW PAPER

# Pelargonium root (*Pelargonium sidoides* DC) extract in paediatric patients - food supplement or medicine?

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## Summary

*Pelargonium sidoides* DC is an interesting plant with various biological properties. Pharmaceutical companies and manufacturers of food supplements are particularly interested in its beneficial effects in upper respiratory tract infections. The search for new therapeutic options is especially important at a time when antibiotics are prescribed too often. However, due to proven clinical effects of extracts from *Pelargonium sidoides*, their use in diet supplements, especially intended for infants and small children, is highly disputable. The paper presents reports on the use of *Pelargonium sidoides* extracts in paediatrics and also tries to answer the question whether the pelargonium extract should be qualified as food supplement or medicine.

Key words: *Pelargonium sidoides* DC, root extract, clinical studies, children, food

Słowa kluczowe: *Pelargonium sidoides* DC, ekstrakt z korzenia, badania kliniczne, dzieci, żywność

## INTRODUCTION

*Pelargonium sidoides* DC belongs to traditional medicinal plants and is well known in South Africa. This plant grows in many countries. Most of botanical material is collected from wild places, hard-to-reach areas, but herbal material for pharmaceutical companies and other producers of plant preparations is also obtained from cultivated regions. African Zulu people use *P. sidoides* for thousand years as a medicinal herb with a wide range of biological activity.

Chemical composition of the plant is variable. Main, well characterized during phytochemical analyses constituents of *P. sidoides* root are prodelphinidins and methoxycoumarins. *P. sidoides* contains also phenolic acids, flavonoids, tannins and coumarins – especially coumarin glycosides or coumarin sulfates [1]. Among flavonoids, especially quercetin, orientin, vitexin and their derivatives can be distinguished. The most popular tannins present in plant preparations are catechins, galliccatechins or proanthocyanidins. The biological components located

in this plant are important for the pharmacological action of the plant and their preparations. Extracts from *P. sidoides* roots are especially important from the point of view of beneficial effects on the human. Probably, still not all active substances and/or their biological activity have been discovered. Therefore, extensive phytochemical analyses should be carried out in this area as well as wide research concerning potential biological activity of pelargonium root preparations.

Potential mechanism of action of this plant is interesting. A lot of studies have found *Pelargonium sidoides* activity as stimulant of immunological system. The immunomodulatory activity manifests itself primarily by the release of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and nitric oxides and also the stimulation of interferon- $\beta$  or natural killer activity. It can also act as phagocytosis factor. *In vitro* studies confirmed cytoprotective effect of pelargonium preparations against virus-induced cell destruction.

Many research papers suggest that therapeutic indications for the use of plant are as follow: symptoms of upper respiratory tract infections including common cold, such as blocked or runny nose, sore throat and cough [2-9]. Root extracts of *P. sidoides* and their representative constituents exhibit also moderate antibacterial and significant immunomodulatory capabilities. Preparations from *P. sidoides* root are often regarded as natural option for treating infections of the respiratory system (mainly common colds, cough, fever, rhinitis), especially by indigenous people of Africa [10-12].

Data present in the literature concerning the efficacy and safety of extract from *P. sidoides* root in treatment and for the prevention of respiratory tract infections in children have been here reviewed. On the other hand, the therapeutic activity of the plant supported by scientific data and relevant monographs calls into question the possibility of its use as a component of food supplements. In some European countries food supplements with pelargonium extracts are approved for children. In Germany licensed medicinal product exists and was officially registered [10]. It is well known that extract from the roots of *P. sidoides* [1:8-10, extraction solvent - ethanol 11% (w/w)] has been approved in cases of acute respiratory tract infections in Europe, Asia, Australia, and also in America [13]. Actually, on the Polish market there are also many products which contain extract from pelargonium root. They are usually multi-ingredient preparations in the status of food supplement. However, the question arises about the desirability of supplementing a plant preparation

with proven pharmacological effects, especially in children. A medicinal product with pelargonium root extract is also available on the Polish market. It is a traditional herbal medicinal product designed for adults and children from 6 years of age for the symptomatic treatment of the common cold.

There is no legal act prohibiting the use of this plant in food supplements. Due to the confirmed therapeutic effect, the authors of the study discuss the legitimacy of using pelargonium in food supplements that are food and should not demonstrate therapeutic activity.

## SCIENTIFIC MONOGRAPHS DESCRIBING PELARGONIUM ROOT

Pelargonium root has a European Scientific Cooperative on Phytotherapy monograph [1] and also European Union herbal monograph published by European Medicinal Agency, EMA [14]. Therapeutic indications of pelargonium radix indicated in these monographs are symptoms of upper respiratory tract infections. According to ESCOP these include cough, runny nose and sore throat [1]. The definition of the herbal material used in the monograph includes dried, cut or underground parts of the plant. EMA regards pelargonium radix as traditional herbal medicinal product for the symptomatic treatment of common cold.

According to EMA monograph the use of *P. sidoides* in children under 6 years of age has not been established due to lack of adequate data [14]. Interestingly, ESCOP does not recommend using pelargonium root in children under 2 years of age. In older children allows the use of ethanol extract [1:8-11, 12% (v/v)] in an amount depending on the age of the child [1]. Moreover, its safety during pregnancy and in breastfeeding women has not been established. This is completely understandable due to the lack of relevant scientific research in this area. Therefore, independently using pelargonium preparations during pregnancy and lactation is very risky. However, if a pregnant woman wants to use a product containing *P. sidoides*, medical advice is recommended.

## CLINICAL TRIALS CONDUCTED IN A GROUP OF CHILDREN OF DIFFERENT AGES

Different types of upper respiratory tract infections are very common childhood diseases. Their very often requires antibiotic or steroid treatment,

especially if allergy also occurs in the same time and additionally affects the worsening of the patient's condition. Therefore, alternative and effective treatment methods that can be used in children are still sought. These especially include the search for plant materials with beneficial effects in this area.

A lot of clinical trials demonstrated the efficacy of extract from pelargonium root in children and adolescents with acute bronchitis or having problems with other different respiratory infections. Unfortunately, the studies differed in the number of children included in the analysis and their age. Most often, children were divided into different age groups, which make it difficult to compare results in a particular age group.

In most trials *Pelargonium sidoides* extract (EPs® 7630) named Umckaloabo (it is ethanolic root extract, 1:9–11) has been used. The extract was administered in the form of tablets or liquid.

Most studies describing effectiveness of pelargonium preparations for respiratory tract infections in children (suffering from bronchitis, asthma, viral infections, tonsillitis, tonsillopharyngitis or other different or nonspecific upper tract infections) were randomized, double-blind and placebo-controlled [2, 4, 7, 9, 15]. Doses of extract EPs® 7630 used were as follow: 20 drops for 6 days [2], 60 or 90 mg daily [7], 30, 60 or 90 mg in tablet form a day [9], 60 drops daily for 6 days [15]. Multicenter studies were performed also very often [3, 8, 16] or only single pilot studies were described also in the literature [17]. Other scientific results indicate that pelargonium extract is an effective and safe preparation in the event of acute bronchitis in children [18]. Moreover, results of many trials confirm the beneficial effect of the tested extract on the condition of young patients and shortening the duration of the disease [2, 9, 17, 19, 20] or significantly relieved the severity of the symptoms as compared to control patients [2, 3, 13]. There are also reports documented that pelargonium preparations prevent asthma attacks during viral infections [21]. Several studies have indicated a specific dose of the extract that has been shown to be effective in clinical trials. Kamin *et al.* confirmed effectiveness of 60 mg and 90 mg EPs 7630 extract from the roots of *P. sidoides* (1:8–10), dried, extraction solvent: ethanol 11% (*w/w*) [7]. Matthys *et al.* regarded as useful 20 mg of the same extract in form of tablets, three times a day [9]. The efficacy of pelargonium ethanolic root extract (1:9–11) has been also confirmed in many clinical works [10].

It should be noted that in the scientific literature (clinical studies in children) it is difficult to find a

representative group of children <1 year old who have used pelargonium extract and confirm its safety. This is probably influenced by the fact that in most studies, children were divided into age ranges set by a particular researcher, without specifying the number of patients of each age. However, there has been a scientific report that specifically indicates the age of the children who can use this preparation. The aforementioned extract was used in children from the age of 1 year and is considered well tolerated [13].

## ADVERSE EFFECTS OBSERVED

It is likely that confirmation of adverse effects after consuming a given herbal material may affect the classification of the entire product. For pelargonium root extract several side effects were observed (both adults and children). Mild gastrointestinal complaints (diarrhoea, epigastric discomfort, nausea or vomiting, dysphagia), mild nasal and gingival bleeding and allergic reactions after applying the preparations from the plant have been reported (similar in adults and children). However, these ailments were rare [14]. The monograph does not specify the age of the patients [14]. In clinical trials with 7200 adults and children mild adverse reactions occurred in less than 15% of patients [10]. EPs 7630 extract was regarded as safe and well-tolerated treatment for acute bronchitis in both adults, children and also infants [3]. Other spontaneous ailments after taking pelargonium root extracts included also allergic skin reaction problems [1]. Possible hepatotoxicity and single hepatitis cases were reported in association with the administration of the medicinal product [22–24]. A few reports concerning some cases of hepatotoxicity in connection with the use of *P. sidoides* preparations have been analyzed by the Drug Commission of the German Medical Association (DCGMA). After careful analysis of the cases, it was found that the preparations from the plant are not a significant hepatotoxic factor [25]. A few cases of hypersensitivity reactions have been noted by WHO Programme [10]. According to Tabali *et al.* the complementary and alternative medicine drug (CAM) with the highest frequency of adverse drug reactions (ADRs) was *P. sidoides* root [26]. Their number was found by Tabali *et al.* at 0.21% (4 of 1,940 prescriptions). It was not a large number of adverse events reported and they were not really serious [26]. However, it can be seen that most scientific publications documented good safety results and lack of serious

adverse events in children after taking pelargonium root extracts [7, 9, 15, 19].

## CONCLUSIONS

*P. sidoides* DC activity in upper respiratory tract infections in children was confirmed in many well documented clinical trials listed in this paper. Dried and unpeeled parts of *P. sidoides* DC or *Pelargonium reniforme* CURT. are regarded as herbal substance found in relevant monographs [1]. The material complies with the monograph of the European Pharmacopoeia (pelargonium root). For the herbal substance or herbal preparations defined in this way, the dosage and therapeutic indications are specified in the monograph. According to beneficial therapeutic indications presented in EMA monograph, pelargonium root is a traditional herbal medicinal product for the symptomatic treatment of common cold [14]. Due to the benefits of the plant presented in scientific literature both drug and food supplement manufacturers are interested in this plant. An increasing number of products containing this ingredient are still being marketed. However, considering the above information concerning well confirmed clinical activity of *P. sidoides* root extract in upper respiratory tract infections, it is disputable to place this plant in products with the status of a food supplement. According to definition of food supplements, as it was defined in European law, they are concentrated source of different substances showing physiological or nutritional effect. They must of course supplement the diet of healthy people [27]. These products should not have activity reserved for medicinal products. Therefore, the food supplement should not have any therapeutic effect. Because of this, use of food supplements that include plants, their particular parts or preparations with proven pharmacological effects in children is risky, especially when they are served without consulting a doctor. Such herbal substances should not be listed as an ingredient of products belonging to the food category. According to the definition defined in the Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements, a food supplement is a foodstuff designed to supplement the consumer's daily diet [28]. It is difficult to imagine supplementing the diet with a product with documented therapeutic activity. In the light of the above information, pelargonium root preparation should not be used in children without

the knowledge of the attending physician, especially if they are already taking previously prescribed medicines. It is also difficult to predict whether or not any interactions will occur between these preparations. If yes, they can be dangerous to the child's health.

*Ethical approval: The conducted research is not related to either human or animal use.*

*Conflict of interest: Authors declare no conflict of interest.*

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