

This obscure herb works for the common cold

Practice changer

Offer patients *Pelargonium sidoides* (30 drops 3 times a day) to reduce the severity and duration of common cold symptoms and to get patients back to work sooner.¹

Strength of recommendation

B: A single well-designed randomized controlled trial

Lizogub VG, Riley DS, Heger M. Efficacy of a *Pelargonium sidoides* preparation in patients with the common cold: A randomized, double blind, placebo-controlled clinical trial. *Explore (NY)* 2007; 3:573-584.

ILLUSTRATIVE CASE

A 39-year-old, otherwise healthy woman presents to your clinic with a sore throat, nasal congestion, and dry cough she's had since yesterday. She wants an antibiotic, but your evaluation reveals an uncomplicated viral upper respiratory infection—a common cold. You would like to provide her with an alternative treatment, but you are aware of the lack of evidence for clear benefit of zinc lozenges, echinacea, and vitamin C. Is there any other medication that might benefit this patient?

Yes. *Pelargonium sidoides*, a species of South African geranium used for centuries in Zulu medicine,² shows promise as an herbal remedy for respiratory infections. Two randomized trials show that

extracts of *P sidoides* improve symptoms of acute bronchitis which, like the common cold, is usually caused by a virus.³⁻⁵

There is a plausible biological mechanism of action. *In vitro* studies show that *Pelargonium* extract induces the interferon system and up-regulates cytokines important in protecting host cells from viral infection.⁶

BACKGROUND

■ \$17 billion dollar cold

Our patients want more relief from cold symptoms and are clearly willing to pay for it. Americans spend approximately \$2.9 billion annually on over-the-counter (OTC) cold preparations and \$1.1 billion on unnecessary antibiotics.⁷ The term “common cold” refers to a collection of symptoms, including sore throat, rhinorrhea, nasal congestion, cough, low-grade fever, and malaise, usually self-limited and lasting 10 to 14 days, caused by a number of viruses, most commonly by a rhinovirus.⁸ According to the 2005 National Ambulatory Medical Care Survey, the common cold is the third most common diagnosis in physicians' offices behind only hypertension and well-infant/child visits.⁹ A 2001 US telephone survey determined that approximately 500 million episodes of non-influenza viral infection occur annually, resulting in direct costs of \$17 billion for physician services and medications and approximately 200 million missed days of work.⁷

CONTINUED

Gail Patrick, MD, MPP
Department of Family Medicine,
The University of Chicago

John Hickner, MD, MSc
Pritzker School of Medicine,
The University of Chicago

PURLs EDITOR

Bernard Ewigman, MD, MSPH
Department of Family Medicine,
The University of Chicago

FAST TRACK

A plausible biological mechanism is induction of the interferon system and up-regulation of cytokines important in protecting host cells from viral infection

PURLs methodology

This study was selected and evaluated using FPIN's Priority Updates from the Research Literature (PURL) Surveillance System methodology. The criteria and findings leading to the selection of this study as a PURL can be accessed at www.jfponline.com/purls.

CLINICAL CONTEXT

■ Evidence proves most cold remedies don't work

Although colds are common and result in annoying symptoms and missed work, much of the money spent on remedies is wasted. A truly effective treatment would be valuable to our patients.

Despite brisk sales, evidence for the efficacy of various cold remedies is inconclusive and contradictory. We found 6 Cochrane reviews of cold treatments, including antitussives, antihistamines, decongestants, vitamin C, echinacea, and zinc lozenges. With the exception of pseudoephedrine for nasal symptoms, the evidence that any product improves symptoms or decreases the duration of the cold is not encouraging.

Cough medications. The 2004 Cochrane Review of OTC medications for cough¹⁰ found no consistent evidence that any of them work. Codeine was no more effective than placebo for reducing cough symptoms. Three efficacy studies of dextromethorphan for cough showed either no difference or small but possibly clinically insignificant improvement in cough over placebo. One study of guaifenesin showed benefit over placebo in reducing cough frequency; another one showed no benefit over placebo.

Vitamin C, echinacea. Three Cochrane reviews found no conclusive evidence of benefit over placebo for either vitamin C¹¹ or echinacea¹² in treating the common cold.

Zinc. A new panel has been convened by the Cochrane group to reassess the effectiveness of zinc, but a 1999 Cochrane review¹³ found no benefit for zinc over placebo.

Antihistamines are not effective for relieving cold symptoms.¹⁴

Pseudoephedrine is the only medication with good-quality evidence for effectiveness, but only for reducing nasal symptoms.¹⁵ The authors concluded that patients may be encouraged to continue pseudoephedrine for up to 5 days if found to be effective with the first dose. Nasal

congestion and discharge, however, are only 2 of the many irritating symptoms of a cold.

STUDY SUMMARY

■ Duration and severity of symptoms are reduced

This was a multicenter, prospective, double-blind, placebo-controlled randomized trial to evaluate the effectiveness of a liquid herbal preparation from the roots of *Pelargonium sidoides* for decreasing the duration and severity of symptoms of the common cold.

Patient characteristics. Patients were recruited from 8 outpatient departments in Ukraine between December 2003 and May 2004. Two hundred and seven (207) patients were eligible. The number of ineligible and excluded patients was not stated. These 207 patients were randomized into 1 of 4 groups:

- 52 received 30 drops 3 times daily vs 51 patients who received placebo
- 52 patients received 60 drops 3 times daily vs 52 patients who received a higher-dose placebo.

The report gives the outcomes of the low-dose arm only. Two-thirds of the participants were women; all were Caucasian. Patients in the treatment and placebo groups were similar in terms of recurrent disease, prior use of medication for the common cold, smoking, and alcohol and caffeine consumption. All had a negative Group A beta-hemolytic strep test.

Inclusion criteria. Patients included men and women 18 to 55 years of age; able to provide written informed consent; with 2 major cold symptoms (nasal discharge, sore throat) and at least 1 minor cold symptom (nasal congestion, sneezing, scratchy throat, hoarseness, cough, headaches, muscle aches, or fever) or presence of 1 major cold symptom and at least 3 minor cold symptoms; duration of symptoms 24 to 48 hours.

Exclusion criteria were any acute ear, nose, throat and respiratory tract disease other than the common cold;

FAST TRACK

This study evaluated a liquid preparation of *Pelargonium sidoides* vs placebo for cold symptoms

You can be a "REALITY CHECKER"

If you are in full-time clinical practice, a medical director of a practice, or otherwise directly involved in decision-making about adopting new practices, join our team of "reality checkers." Just email me at be.editor@gmail.com



Bernard Ewigman, MD, MSPH

positive rapid strep test; 6 or more episodes of recurrent tonsillitis, sinusitis, or otitis within the past 12 months or any chronic ear, nose, throat or respiratory tract disease; treatment with antibiotics, glucocorticoids, or antihistamine drugs during the 4 weeks prior to enrollment in the trial; treatment with cold medications that might impair the trial results (eg, decongestants, local anesthetics); and use of cough or pain relief medications, or any other treatment for the common cold within 7 days prior to enrollment in the trial.

Treatment regimen. Patients were assigned to take 30 drops of either the study herbal preparation or 30 drops of placebo 3 times daily, at least 30 minutes before or after a meal, from day 1 continuing to day 10. The investigational drug and placebo were supplied by Dr. Willmar Schwabe GmbH & Co. (Karlsruhe, Germany). The investigational medication is a preparation of the roots of *P. sidoides*, extraction solution: ethanol 11% (1:8-10) (wt/wt). The placebo was matched for color, smell, taste, and viscosity. Paracetamol (acetaminophen) tablets were allowed for all patients for fever greater than 39°C.

Primary endpoint. Severity of cold symptoms was evaluated using the Cold Intensity Score (CIS), a validated scale derived from the sum of scores for 10 cold-related symptoms (nasal drainage, sore throat, nasal congestion, sneezing, scratchy throat, hoarseness, cough, headaches, muscle aches, and fever) on a scale of 0 to 4, where 0 = not present and 4 = very severe, to a maximum of 40 points. At baseline, the mean total CIS was comparable in both treatment and placebo groups (17.8 ± 4.0 vs 16.9 ± 3.4). From baseline to day 5, the mean total CIS decreased by 10.4 ± 3.0 in the treatment group vs 5.6 ± 4.3 in the placebo group ($P < .0001$).

Secondary endpoints. The number of patients achieving clinical cure (defined by CIS ≤ 1) by day 10 was significantly higher in the treatment group (78.8% vs

31.4%, $P < .0001$). The mean duration of days absent from work was significantly lower in the treatment group (6.9 ± 1.8 vs 8.2 ± 2.1 , $P < .0003$), as was number of days with less than 100% usual activity level (7.1 ± 1.5 vs 8.7 ± 1.3 , $P < .0001$). Data for both the primary and secondary endpoints were evaluated according to an intention-to-treat analysis. Both the intervention and placebo sides each had 4 patients that became ineligible after initial randomization. No patients were lost to follow-up.

Safety and tolerability. Patients in the low-dose arm experienced 3 nonserious adverse events, and 1 experienced mild epistaxis. Two additional patients (1 in the treatment and 1 in the placebo group) experienced moderate to severe tracheitis, not attributable to the study medication. Tolerability was rated slightly better in the treatment than placebo group on day 5. Forty-nine of 52 patients (94%) in the treatment group rated the preparation as good or very good tolerability vs 42 of 51 patients (82%) in the placebo group.

WHAT'S NEW?

■ A first

This is the first study that demonstrates the efficacy and safety of *P. sidoides* in the treatment of the common cold. More importantly, this degree of improvement in cold symptoms is dramatically better than other common OTC treatments, including vitamin C, echinacea, and zinc preparations.

CAVEATS

■ How is this different from other cold remedies?

Patients are already spending a lot on cold remedies; this study suggests money would be better spent on having a ready supply of *Pelargonium* in the medicine cabinet, and it appears to be safe.

Other initially promising complementary and alternative therapies, such as zinc, echinacea, and vitamin C, have not been shown to be effective with more vigorous evaluation. We recognize that

FAST TRACK

To get the benefits, treatment must start early. Patients could be advised to buy the medication, to have on hand

FAST TRACK

This degree of improvement in cold symptoms is far better than other OTC treatments

this is only 1 clinical trial, and the results may not be replicated in future trials. However, we are impressed by the effect size—twice the size as that seen for placebo, with a reduction in half of total cold symptom severity over 5 days and a reduction of missed time from work by more than a full day on average over placebo.

In vitro studies suggest a physiologic mechanism that is consistent with the study outcomes.

Similar findings are reported for symptom reduction in acute bronchitis.

Safety

There were no significant adverse events in this study, which is consistent with the findings of the studies of acute bronchitis.¹²⁻¹⁴ *P sidoides* has been widely used in Germany since the 1980s, with an annual sale value in 2002 of \$55 million or 4.1 million packages.

The Uppsala Monitoring Centre, in conjunction with the World Health Organization international pharmacovigilance program, received 34 case reports between 2002 and 2006 of allergic reactions to ethanolic herbal extract of *Pelargonium* root, 2 of which involved life-threatening circulatory collapse requiring emergency medical attention. Given the extremely rare occurrence of these events we believe the minimal risk is acceptable. The others involved rash and pruritus.

Also of note: contact dermatitis to *Pelargonium* houseplants has been reported. As a result, product information will be added to product packaging, warning of common reactions of gastrointestinal complaints (gastric pain, heartburn, nausea, and diarrhea) as well as the potential for serious allergic reaction. In addition, since some of the active compounds are plant coumarins, there is a theoretical risk of interaction with warfarin and aspirin but no serious bleeding events have been reported.¹⁶

It is also recommended that individuals with renal or hepatic disease or wom-

en who are pregnant or breastfeeding avoid use of this preparation, as safety studies have not been performed.

Other study design issues

A few other issues struck us as important when assessing the validity of this study. For example, 1 of the authors appears to be an employee of the pharmaceutical company that manufactures the preparation, raising the conflict of interest issue.

We were also curious about why the results of the high-dose arm were not reported in this manuscript. Could there have been a higher rate of adverse events in the high-dose arm? Knowing how many patients were ineligible or excluded, and the efficacy or safety in the high-dose arm would give us more confidence in the findings, but we decided that these were not necessarily fatal flaws.

Bottom line

Despite the above caveats, this was a well-designed randomized controlled trial that suggests that *P sidoides* is impressively efficacious in decreasing the duration and severity of the common cold. In the final analysis, we think that these findings justify recommending this to our patients.

CHALLENGES TO IMPLEMENTATION**■ 2-day window**

The medication was started within 48 hours of the onset of symptoms. We generally see patients seeking treatment for the common cold well after the first 2 days. The efficacy of *Pelargonium* is no doubt less when started later in the course of the illness. Colds resolve spontaneously, so to get the benefit of this treatment, it likely must be started early.

Our conclusion is that patients could be advised to purchase the medication to have on hand at home at the start of the cold season.

Availability of the drug

P sidoides is available in the US under the brand name Umcka Coldcare.

The preparation used in the study is marketed in Europe by ISO-Arzneimittel¹⁷ under the name Umckaloabo, which is a combination of the Zulu words for lung symptoms and breast pain.¹⁸

Our Internet search on the term “*Pelargonium sidoides*” failed to yield a distributor of the German preparation used in the study that would be available in the United States. However, a different manufacturer, Nature’s Way, distributes a number of similar preparations containing extract of the root of *P sidoides* under the name Umcka Coldcare. Umcka Coldcare appears to be readily available for purchase, both on-line and through local health food stores, for less than \$20 per 4-oz (120-mL) bottle. A different retailer, African Red Tea, offers syrup, 1:10 ethanolic extract for \$29.95 for 100-mL bottle.¹⁹ Like the German preparation, these formulations are delivered by dropper. ■

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FAST TRACK

There were no significant adverse events, consistent with studies of acute bronchitis