



### FAST TRACK

**The herbal cold remedy study did not specify whether the placebo had the same alcohol content as the treatment**

## Coumarins in herbal cold remedy are safe

Regarding your review<sup>1</sup> of the Lizogub study on *Pelargonium sidoides*:<sup>2</sup>

1. The product used in the study is sold in the United States. In fact, the introduction to the Lizogub study states: "An alternative treatment for the common cold is a liquid herbal drug preparation from the roots of *Pelargonium sidoides* (Willmar Schwabe Pharmaceuticals, Karlsruhe, Germany), the active ingredient in Umcka ColdCare and Zucol in the United States. Zucol is a rapid melt delivery form sold in the mass market by a subsidiary of Nature's Way known as Abkit."

2. Regarding the statement in the safety section, about plant coumarins and potential interactions with warfarin and aspirin, I offer a synopsis of a pharmacology study<sup>3</sup> completed in Germany: At oral doses of 10, 75, and 500 mg/kg per day for 2 weeks, the liquid herbal drug preparation 7630 did not influence the thromboplastin time (TPT), the partial TPT (PTPT), or thrombin time (TT) in rats. If the animals were given preparation 7630 (500 mg/kg PO) and warfarin (0.05 mg/kg PO) concomitantly for 2 weeks, there was no evidence of a statistically significant change in the anticoagulant effect of warfarin. Furthermore, pretreatment of rats with preparation 7630 (500 mg/kg PO) for 2 weeks had no effect on the pharmacokinetics of a single dose application of warfarin (0.2 mg/kg PO). This study demonstrates that subacute administration of preparation 7630 over a wide dose range has no effect on TPT, PTPT, and TT in the rat. Similarly, the anticoagulant effect of warfarin is not affected by concomitant application of preparation 7630, and pretreatment with

preparation 7630 produces no change in the pharmacokinetics of warfarin. Moreover, as the coumarins identified do not possess structural characteristics required for anticoagulant activity, it appears unlikely that an increased tendency to hemorrhage will occur in patients treated with preparation 7630.

In short, the plant coumarins in *Pelargonium sidoides* are structurally dissimilar to agents that would affect coagulation and are unlikely to cause any interaction with these drugs.

**Donald Brown, ND, VP**, Scientific and Educational Affairs, Nature's Way Products, Springville, UT

### References

1. Patrick G, Hickner J. This obscure herb works for the common cold. *J Fam Pract.* 2008;57:157-161.
2. 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.
3. Koch E, Biber A. Treatment of rats with the *Pelargonium sidoides* extract EPs 7630 has no effect on blood coagulation parameters or on the pharmacokinetics of warfarin. *Phytomedicine.* 2007;14(suppl 6):40-45.

## Herb study is not a practice changer

I looked up the original article on the *Pelargonium sidoides* and I had 2 concerns:

1. The study didn't specify if the placebo had the same alcohol content as the treatment. If not, then the results may have been entirely from the alcohol and not the *Pelargonium sidoides*. This potential study limitation should have been mentioned explicitly.

2. A difference in symptoms was noted at 5 days and was minimal at 10 days. Because the treatment was contin-

ued for 10 days, the difference at 5 days could have simply been a masking of the symptoms and not really any improvement in the disease process itself. Comparison with a common antihistamine or analgesic, or stopping the *Pelargonium* at 5 days, might have revealed if the herb really shortened the disease course.

So, I'm not sure this study shows as much as *The Journal of Family Practice* article indicates. I find any practice recommendation very concerning when this type of article is published without adequate analysis and comment by the reviewer.

David L. Weldy, MD, PhD, Department of Family Medicine, University of Toledo Medical Center

### **Drs. Patrick and Hickner respond**

## **Alcohol in cold remedy an unlikely factor**

We thank Dr. Brown for providing useful information on the composition of the products made by Nature's Way, noting that Umcka ColdCare "original" formula, an alcohol-based extract, is identical to the preparation used in the study. In addition, the excerpt from the study of the pharmacology of *Pelargonium sidoides*, which he summarizes, appears to further allay concerns that there might be adverse effects from the coumarin compounds in terms of increase in coagulation parameters or interaction with warfarin.

Dr. Weldy expresses concern that without knowing the composition of the placebo preparation, there may be other factors at play, especially the possibility that alcohol may be responsible for the outcomes rather than the *Pelargonium*.

We believe that it is highly unlikely that alcohol in the preparation is solely responsible for the superiority of the intervention over placebo. We noted that the placebo preparation was matched for color, smell, taste, and viscosity. It is true that no information was given as to the chemical composition of the placebo preparation, especially in terms of alcohol content. However, the dose is 30

drops (1.5 mL), which contains 12% alcohol by volume according to the manufacturer's web site. This translates to approximately 0.18 mL alcohol in each dose (3.6 drops)—a very small amount. We agree, however, that it would be important for the authors to make explicit the similarities and differences between the 2 preparations.

Dr. Weldy notes that there appears to be minimal difference between intervention and placebo at 10 days, which he interprets as indicating that the intervention only masks symptoms at 5 days and has no overall impact on shortening duration of symptoms. The primary and secondary objectives of the study were focused on symptom severity, which we view to be an important patient-oriented outcome, especially because patients purchase medicines for symptom relief. At 5 days, this difference is impressive, and at 10 days, the intervention remains superior, although the difference in scores is certainly narrower.

Further, according to the study results: "On day 10, the rate of patients with clinical cure was significantly higher in the treatment group (Cold Intensity Score [CIS]=0 points: 63.5%; CIS ≤1 symptom: 78.8%) than in the placebo group (CIS=0 points: 11.8%; CIS ≤1 symptom: 31.4%;  $P<.0001$  each)."

More than double the number of participants receiving the study preparation experienced complete or nearly complete symptom relief at day 10 than participants receiving placebo. We agree with Dr. Weldy in his assessment that it would be interesting to compare *Pelargonium sidoides* with "usual care," ie, supportive treatment, with other over-the-counter remedies in common use by our patients.

Articles considered for Priority Updates from the Research Literature undergo rigorous, systematic review according to the SIGN criteria. Further information on this process is available at [www.jfponline.com/purls](http://www.jfponline.com/purls).

Gail Patrick, MD, MPP, and John Hickner, MD, MSc Department of Family Medicine, University of Chicago

### **FAST TRACK**

**The difference in symptom severity is impressive—an important patient-oriented outcome**