Does Butterbur Prevent Migraines?
Darrell Hulisz, PharmD  |  February 02, 2015

Question

Is butterbur effective for preventing migraine headaches?

Response from Darrell Hulisz, PharmD

Associate Professor, Case Western Reserve University School of Medicine; Clinical Specialist in Family Medicine, University Hospitals, Case Medical Center, Cleveland, Ohio; Associate Clinical Professor of Pharmacy Practice, Ohio Northern University, Raabe College of Pharmacy, Ada, Ohio

The perennial shrub formally known as Petasites hybridus and commonly referred to as "butterbur" has been used for over 2000 years as an antispasmodic and analgesic natural remedy.\(^1\)-\(^3\) An extract of butterbur root (petasin) is thought to possess anti-inflammatory and vasoactive properties, which has led researchers to investigate its efficacy for migraine prophylaxis.\(^1\)-\(^7\)

Migraine sufferers can have disabling headaches that interfere with daily activities and adversely affect quality of life. Thus, preventive therapy is often used for patients with attacks that are frequent or last multiple days, are refractory to acute treatment, or are severe and disabling. Many patients with migraine use over-the-counter agents and dietary supplements for migraine prophylaxis despite a lack of well-controlled studies supporting their efficacy.\(^3\)

Butterbur extract (petasin) is the only natural supplement listed as having Level A evidence by the American Headache Society and American Academy of Neurology in their 2012 migraine prophylaxis guidelines.\(^4\) According to their evidence-based report, butterbur is "established as effective and should be offered for migraine prevention."\(^4\)

The exact mechanism of action of butterbur is unknown. Petasins appear to have calcium-channel–blocking effects that may contribute to the mechanism of action of butterbur root.\(^1\) On the basis of laboratory studies, butterbur also has anti-inflammatory and vasostrictive effects on the cerebral arteries via inhibition of the lipoxygenase pathway and leukotriene synthesis.\(^1,2\)

Grossmann and Schmidramsl\(^5\) published an early trial on butterbur for migraine prophylaxis. They conducted a randomized, double-blind, placebo-controlled study involving a 4-week run-in phase with no trial medication. To be eligible for study enrollment, patients needed to have three or more attacks per month within the past 3 months and a minimum of two attacks during the run-in phase.

The primary outcome was the frequency of migraine attacks per 4 weeks. Trial participants were randomly assigned to take two 25-mg capsules of Petasites hybridus extract twice a day or placebo.\(^5\)

Of the 60 participants enrolled, 58 completed the 12-week study. The frequency of attacks in the treatment group decreased by a maximum of 60% and was statistically significant at \(P < .05\). The frequency of monthly attacks decreased from a baseline of 3.3 ± 1.5 attacks to 1.8 ± 0.8 attacks after 4 weeks, 1.3 ± 0.9 attacks after 8 weeks, and 1.7 ± 0.9 attacks after 12 weeks. This was statistically significant vs placebo.

Five patients taking Petasites hybridus did not report a single migraine attack during the 8 weeks of treatment. In contrast, all patients in the placebo group reported at least one migraine during the treatment phase. No serious adverse effects were noted.
Given these results, the researchers concluded that *Petasites hybridus* extract may be an effective prophylactic treatment for migraine.[5]

Of note, the original statistical analyses were found to be flawed; subsequently, the study data were reanalyzed by a third-party biometrics institute after publication of the study.[6] Reanalysis showed a 45% reduction in migraine frequency vs the 60% originally reported—an outcome that was still statistically significant.

Lipton and colleagues[3] performed a randomized, three-arm, parallel-group, placebo-controlled trial that compared *Petasites hybridus* extract 50 mg twice a day and 75 mg twice a day vs placebo. For study enrollment, participants needed to have two to six attacks per month during the 3 months before the trial and a minimum of two attacks during the 4-week baseline period. The primary outcome measure was decrease in migraine frequency per month, calculated as percentage change from baseline over a 4-month treatment period.

A total of 245 participants were enrolled, with 202 completing the study. The migraine frequency reduction from baseline was as follows: 48% for *Petasites* extract 75 mg twice daily ($P = .0012$ vs placebo), 36% for *Petasites* extract 50 mg twice daily ($P = .127$ vs placebo), and 26% for placebo. The investigators concluded that *Petasites* extract 75 mg twice daily was more effective than placebo and is a well-tolerated preventive therapy for migraine. No serious adverse effects were noted in this trial.

Pothmann and Danesch[7] reported on 108 children aged 6-17 years in a multicenter, prospective, open-label study. Participants had had migraines for at least 1 year. They were treated with 50-150 mg of butterbur root extract, depending on their age, for 4 months.

This study did not have a placebo arm, but 77% of patients reported a reduction in the frequency of migraine attacks of at least 50%. Overall migraine attack frequency was reduced by 63%. After 4 months of treatment with the extract, 91% of patients felt substantially or at least slightly improved.

Mild gastrointestinal side effects, mainly belching, were the most common adverse effect, but no patients withdrew from study owing to side effects. Because of the open nature of this study, results should be interpreted with caution.

Several investigators have expressed concerns that unprocessed, or unpurified, butterbur may contain pyrrolizidine alkaloids, which are known to be hepatotoxic, mutagenic, and carcinogenic.[1,2,8,9] Butterbur is a botanical product that is marketed as a food supplement in the United States. Therefore, it is not subject to the same standards of purity and potency testing as proprietary prescription drugs.

As with other botanicals, assuring a consistent quality, along with the complex and variable chemistry of these products, is a challenge to clinicians and consumers as well as the supplement industry. There is a potential risk for botanical misidentification or adulteration. The purity and potency of botanicals is influenced by the soil conditions of the plant, time of harvest, plant processing and extraction methods, and storage conditions. Analytic techniques used to identify active and toxic constituents are often not standardized.[9] This presents a challenge, because the safety of butterbur products can only be assured by removing the toxic pyrrolizidine alkaloids to avoid hepatotoxicity.

Of note, most of the published studies of butterbur extract used a single commercial product, known as Petadolex®. This product had been considered to be free of pyrrolizidine alkaloids. However, a 2012 blog post in the lay press reported that the manufacturer of Petadolex® has altered its purification process and did not repeat all of the required safety studies.[10] In contrast, the manufacturer stands by its claim that the product is free of detectable pyrrolizidine alkaloids.[11]

To summarize, limited published data indicate that butterbur root extract, specifically from the *Petasites hybridus* plant, is efficacious in the prophylactic treatment of migraine. Overall, the sample sizes studied were small, and treatment duration was limited. Butterbur should not be used during pregnancy or lactation, in young children, or in people with severe kidney or liver disease until further safety testing has been conducted.
The question of which butterbur products are genuinely free of pyrrolizidine alkaloids remains an unresolved concern. Thus, further studies are needed before these products can be safely endorsed or recommended.

Acknowledgement: The author wishes to thank Stacy Henthorne for providing technical assistance.

References


