

HERBS/ TEAS & HOMEOPATHY

Natural Supplements for Migraine Prevention: Butterbur and Feverfew

James P. Meschino, DC, MS

Migraine headaches afflict one in 19 adults, of which 75 percent are women. Migraines also occur in an estimated 3 percent to 7 percent of children. Overall, one in four households has a resident who is a migraine sufferer. Migraines are most often described as one-sided, severe, pulsating headache pain that lasts from four to 72 hours. Other symptoms that often occur during a migraine attack include nausea, vomiting and extreme sensitivity to light and noise.

Unfortunately, many drugs used to prevent and treat migraines can produce significant side effects, addiction and dependency. As a result, many migraine sufferers seek help from more natural, nontoxic solutions, such as chiropractic care, acupuncture, dietary modifications and nutritional supplements. In recent years, human clinical trials have shown that supplementation with specific dosages of the herbs butterbur and feverfew can reduce the frequency of migraine attacks by at least 50 percent in migraine sufferers.

Butterbur

Butterbur is an herb that contains active constituents (petasin and isopetasin) that block key steps in the production of migraine headaches. These active constituents inhibit the synthesis of inflammatory chemicals such as leukotrienes and prostaglandin E2, which can trigger migraines. Petasin and isopetasin have an antispasmodic effect on vascular walls and appear to have an affinity for cerebral blood vessels. Butterbur extract also appears to act as a natural beta blocker, stabilizing normal flow of blood to the brain. This action helps control blood pressure and prevents spasm of blood vessels, which are also key processes in preventing the onset and progression of migraines.

In a double-blind study published in *Neurology*, researchers gave 202 migraine sufferers butterbur extract or a placebo for a three-month period. After 12 weeks, the butterbur-supplemented group reported approximately 50 percent fewer migraines than usual. In a 12-week, double-blind study published in *Headache*, 58 migraine sufferers were given butterbur extract or a placebo twice daily. The butterbur group had 50 percent fewer migraines than usual, while the placebo group's migraines declined by only 10 percent.²



Butterbur supplementation also was shown to lower the incidence of migraines in children and adolescents by 77 percent, according to a four-month trial published in *Headache*.³ The effective daily dosage for adults is reported to be 75 mg (standardized to minimum 15 percent sesquiterpenes as petasines), twice per day. A single dosage of 75 mg per day can be used for children six years and older, as well as teenagers.

Feverfew

Feverfew, a member of the sunflower family, has been used for centuries in European folk medicine as a remedy for headaches and other conditions. The migraine-relieving activity of feverfew is believed to be due to parthenolide, an active compound that helps relieve smooth muscle spasms. In particular, it helps prevent the constriction of blood vessels in the brain (one of the leading causes of migraine headaches). Like butterbur, parthenolide also inhibits the production of prostaglandin hormones that cause inflammation of blood vessels. Feverfew inhibits excessive aggregating of platelets, which also normalizes blood flow - an effect credited for reducing migraine frequency and severity.

Recent clinical studies published in *Clinical Drug Investigations* and *Headache* showed that supplements containing a standardized extract of feverfew reduced migraine attacks by 50 percent in chronic migraine sufferers. ⁴⁻⁵ To be most effective, feverfew should be standardized to contain the maximum amount of parthenolide, which has been shown to account for the herb's anti-inflammatory and other medicinal properties. As such, I recommend supplementation with feverfew at 325 mg (standardized grade of parthenolide concentration of 0.7 percent), twice daily,

which is the highest yield presently available in the marketplace.

As an aside, the parthenolide fraction of feverfew has also been explored for its anti-cancer properties due to its ability to reduce nuclear factor kappa beta, an important transcription factor in the proliferation of many cancer cells. Parthenolide also demonstrates other impressive anti-cancer properties such as inducing programmed cell death of cancer cells via up-regulation of tumor necrosis factor stimulation.

A Combination Approach

In conjunction with chiropractic adjustments, soft-tissue techniques, acupuncture, stress-reduction programs, the removal of foods from the diet that act as triggers, and other treatments shown to be useful in migraine control, the addition of a twice-daily supplement containing the effective doses of butterbur and feverfew should also be included in an evidence-based approach to treating migraines. In the early stages of a migraine attack, the patient can try taking three to four capsules as a single dose in an attempt to abort the migraine. If this effort fails to halt the migraine, other standard pharmaceutical drugs designed for migraine control can be used as a rescue medication.

Here is an example of a combination supplement containing butterbur and feverfew, which contains optimal amounts of their medicinal ingredients. One capsule contains: butterbur root 75 mg (standardized to minimum 15 percent sesquiterpenes as petasines; feverfew 325 mg (standardized grade of parthenolide concentration of 0.7 percent). Adults: take one capsule twice per day for migraine prevention. At the first sign of a migraine, consider taking three to four capsules as a single dose to help abort or minimize the attack. Children ages 10 and up should take one capsule per day for migraine prevention.

Cautionary Notes

To derive the best possible prophylactic effect for migraine patients, it is best to recommend a supplement that contains both butterbur and feverfew, at the dosages and standardized grades proven to reduce the frequency and severity of migraine attacks. It is important to make sure that the butterbur extract does not contain pyrrolizidine alkaloids, which are toxic to the liver and may cause other serious problems.

Provided the pyrrolizidine alkaloid compounds have been removed from butterbur, the only reported side effects involve burping or mild gastrointestinal discomfort in rare cases. Butterbur does not have any reported drug-nutrient interactions and has an excellent safety profile to date.

Feverfew also has an impressive safety record. It may inhibit the activity of platelets; thus, individuals taking blood-thinning medications (such as aspirin and warfarin) should have their INR monitored during the early stages of supplementation to ensure that platelet clotting behavior remains within the desired range. Some infrequent side effects of feverfew include abdominal pain, indigestion, flatulence, diarrhea, nausea, vomiting and nervousness. Individuals with allergies to chamomile, ragweed, or yarrow are likely to be allergic to feverfew. Pregnant and nursing women, as well as children under age 6, should not take a supplement containing feverfew and butterbur.

References

- 1. Lipton RB, Göbel, H,Einhäupl KM, et al. Petasites hybridus root (butterbur) is an effective preventive treatment for migraine. *Neurology*, 2004;63:2240-4.
- 2. Mauskop A, Grossman WM, Schmidramsl H. Petasites hybridus (Butterbur root) extract is effective in the prophylaxis of migraines: results of a randomized, double blind trial. *Headache*, 2000;40:420.

- 3. Pothmann R, Danesch U. Migraine prevention in children and adolescents: results of an open study with a special butterbur root extract. *Headache*, 2005;45:1-8.
- 4. Maizels M, Blumenfeld A, Burchette R. A combination of riboflavin, magnesium, and feverfew for migraine prophylaxis: a randomized trial. *Headache*, 2004;44(9):885-90.
- 5. Shrivastava R, Pechadre JC, John GW. Tanacetum parthenium and Salix alba (Mig-RL) combination in migraine prophylaxis: a prospective, open-label study. *Clin Drug Invest*, 2006;26(5):287-96.

Resources

- Lipton RB, Scher AI, Steiner TJ, et al. Patterns of health care utilization for migraine in England and in the United States. *Neurology*, 2003;60:441-88.
- Silberstein SD, Lipton RB, Dalessio DJ, eds. *Wolff's Headache and Other Head Pain, 7th Edition*. Oxford, UK: Oxford University Press, 2001.
- Murphy JJ, Heptinstall S, Mitchell JR. Randomised double-blind placebo controlled trial of feverfew in migraine prevention. *Lancet*, 1988;2:189-92.
- Johnson ES, Kadam NP, Hylands DM, Huylands PJ. Efficacy of feverfew as prophylactic treatment of migraine. *BMJ*, 1985;291:569-73.
- Peikert A, Wilimzig C, Kohne-Volland R. Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study. *Cephalalgia*, 1996;16:257-63.
- Schoenen J, Jacquy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis. A randomized controlled trial. *Neurology*, 1998;50:466-70.
- Grossman M, Schmidramsl H. An extract of Petasites hybridus is effective in the prophylaxis of migraine. *Int J Clin Pharmacol Ther*, 2000;38:430-35.
- Ziolo G, Samochewiec L. Study on clinical properties and mechanism of action of Petasites in bronchial asthma and chronic obstructive bronchitis. *Pharm Acta Helv*, 1998;72:359-80.
- Barsom S. Behandlung von koliken und spasmen in der urologie mit einem pflanzlichen spasmolytikum. *Erfahrungsheilkunde*, 1986;35:1-11.
- Gruia FS. Pflanzliche analgetika: therapie bei WS syndrom. Biol Med, 1987;3:454.
- Diener HC, Rahlfs VW, Danesch U. The first placebo-controlled trial of a special butterbur root extract for the prevention of migraine: reanalysis of efficacy criteria. *Eur Neurol*, 2004;51:89-97.
- Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia*, 1988;8(suppl 7):1-96.
- Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*, 2000;55:754-62.
- Gray RN, Goslin RE, McCrory DC, et al. Drug treatment for the prevention of migraine headache. Technical review 2.3, February 1999. Prepared for the Agency for Health Care Policy and Research under contract number 29009402025. Available from the National Technical Information Service; NTIS accession no. 127953.
- Mathew NT, Saper JR, Silberstein SD, et al. Migraine prophylaxis with divalproex. *Arch Neurol*, 1995;52:281-6.
- Mathew NT, Rapoport A, Saper J, et al. Efficacy of gabapentin in migraine prophylaxis. *Headache*, 2001;41:119-28.
- Storey JR, Calder CS, Hart DE, Potter DL. Topiramate in migraine prevention: a double-blind, placebo-controlled study. *Headache*, 2001;41:968-75.
- Thomet OA, Wiesmann UN, Blaser K, Simon HU. Differential inhibition of inflammatory effector functions by petasin, isopetasin and neopetasin in human eosinophils. *Clin Exp Allergy*, 2001;31:1310-20.

- Brune K, Bickel D, Peskar BA. Gastro-protective effects by extracts of Petasites hybridus: the role of inhibition of peptido-leukotriene synthesis. *Planta Med*, 1993;59:494-6.
- Scheidegger C, Dahinden C, Wiesmann U. Effects of extracts of individual components from Petasites on prostaglandin synthesis in cultured skin fibroblasts and on leucotriene synthesis in isolated human peripheral leucocytes. *Pharm Acta Helv*, 1998;72:359-80.
- Thomet OA, Wiesmann UN, Schapowal A, et al. Role of petasin in the potential antiinflammatory activity of a plant extract of Petasites hybridus. *Biochem Pharmacol*, 2001;61:1041-7.
- Sheftell F, Rapoport A, Weeks R, et al. Montelukast in the prophylaxis of migraine: a potential role for leukotriene modifiers. *Headache*, 2000;40:158-63.
- Pearlman EM, Fisher S. Preventive treatment for childhood and adolescent headache: role of once-daily montelukast sodium. *Cephalalgia*, 2001;21:461.
- Ko W, Lei C, Lin Y, Chen C. Mechanisms of relaxant action of S-petasine and S-Isopetasin, sesquiterpenes of Petasites formosanus, in isolated guinea pig trachea. *Planta Med*, 2001:67:224-9.
- Wang G-J, Shum AY-C, Lin Y-L, et al. Calcium channel blockade in vascular smooth muscle cells: major hypotensive mechanism of S-petasine, a hypotensive sesquiterpene from Petasites formosanus. *J Pharmacol Exp Ther*, 2001;297:240-6.
- Danesch U, Rittinghausen R. Safety of a patented special butterbur root extract for migraine prevention. *Headache*, 2003;43:76-8.
- Lipton RB, Göbel, H, Einhäupl KM, et al. Petasites hybridus root (butterbur) is an effective preventive treatment for migraine. *Neuorology*, 2004;63:2240-4.
- Pothmann R, Danesch U. Migraine prevention in children and adolescents: results of an open study with a special butterbur root extract. *Headache*, 2005;45:1-8.
- Mauskop A, Grossman WM, Schmidramsl H. Petasites hybridus (Butterbur root) extract is effective in the prophylaxis of migraines: results of a randomized, double blind trial. *Headache*, 2000;40:420.
- Barsby RW, Salan U, Knight DW, Hoult JR. Feverfew and vascular smooth muscle: extracts from fresh and dried plants show opposing pharmacological profiles, dependent upon sesquiterpene lactone content. *Planta Med*, 1993;59(1):20-5.
- Chen CF, Leung AY. Gene response of human monocytic cells for the detection of antimigraine activity of feverfew extracts. *Can J Physiol Pharmacol*, 2007;85(11):1108-15.
- Curry EA III, Murry DJ, Yoder C, et al., Phase I dose escalation trial of feverfew with standardized doses of parthenolide in patients with cancer. *Invest New Drugs*, 2004;22(3):299-305.
- De Weerdt CJ, Bootsma HPR, Hendriks H. Herbal medicines in migraine prevention. Randomized double-blind placebo controlled crossover trial of a feverfew preparation. *Phytomedicine*, 1996;3:225-30.
- Diener HC, Pfaffenrath V, Schnitker J, et al. Efficacy and safety of 6.25 mg t.i.d. feverfew CO2-extract (MIG-99) in migraine prevention: a randomized, double-blind, multicentre, placebo-controlled study. *Cephalalgia*, 2005;25(11):1031-41.
- Ernst E, Pittler MH. The efficacy and safety of feverfew (Tanacetum parthenium L.): an update of a systematic review. *Public Health Nutr*, 2000;3(4A):509-14.
- Evans RW, Taylor FR. "Natural" or alternative medications for migraine prevention. *Headache*, 2006;46(6):1012-8.
- Heck AM, DeWitt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. *Am J Health Syst Pharm*, 2000;57(13):1221-7.
- Henneicke-von Zepelin HH. Feverfew for migraine prophylaxis. *Headache*, 2006;46(3):531.
- Johnson ES, Kadam NP, Hylands DM, Hylands PJ. Efficacy of feverfew as prophylactic treatment of migraine. *BMJ*, 1985;291:569-73.
- Klepser TB, Klepser ME. Unsafe and potentially safe herbal therapies. *Am J Health Syst Pharm*, 1999;56(2):125-38; quiz 139-41.
- Maizels M, Blumenfeld A, Burchette R. A combination of riboflavin, magnesium, and feverfew

- for migraine prophylaxis: a randomized trial. *Headache*, 2004;44(9):885-90.
- Martin K, et al. Parthenolide-depleted feverfew (Tanacetum parthenium) protects skin from UV irradiation and external aggression. *Arch Dermatol Res*, 2008;300(2):69-80.
- Mauskop A. Alternative therapies in headache. Is there a role? [Review] *Med Clin North Am*, 2001;85(4):1077-84.
- Miller L. Herbal medicinals: selected clinical considerations focusing on known or potential drug-herb interactions. *Arch Intern Med*, 1998;158(20):2200-11.
- Murphy JJ, Heptinstall S, Mitchell JR. Randomised double-blind placebo-controlled trial of feverfew in migraine prevention. *Lancet*, 1988;2:189-92.
- Palevitch D, Earon G, Carasso R. Feverfew (Tanacetum parthenium) as a prophylactic treatment for migraine: a double-blind controlled study. *Phytotherapy Res*, 1997;11:508-11.
- Pattrick M, Heptinstall S, Doherty M. Feverfew in rheumatoid arthritis: a double-blind, placebo controlled study. *Ann Rheum Dis*, 1989;48:547-9.
- Pfaffenrath V, Diener HC, Fischer M, et al. The efficacy and safety of Tanacetum parthenium (feverfew) in migraine prophylaxis--a double-blind, multicentre, randomized placebocontrolled dose-response study. *Cephalalgia*, 2002;22(7):523-32.
- Pittler MH, Vogler BK, Ernst E. Feverfew for preventing migraine. [Review] *Cochrane Database Syst Rev*, 2000;(3).
- Shrivastava R, Pechadre JC, John GW. Tanacetum parthenium and Salix alba (Mig-RL) combination in migraine prophylaxis: a prospective, open-label study. *Clin Drug Invest*, 2006;26(5):287-96.
- Silberstein SD. Preventive treatment of headaches. Curr Opin Neurol, 2005;18(3):289-92.
- Sumner H, Salan U, Knight DW, Hoult JR. Inhibition of 5-lipoxygenase and cyclo-oxygenase in leukocytes by feverfew. Involvement of sesquiterpene lactones and other components. *Biochem Pharmacol*, 1992;43(11):2313-20.
- Vogler BK, Pittler MH, Ernst E. Feverfew as a preventive treatment for migraine: a systematic review. *Cephalalgia*, 1998;18(10):704-8.
- Won YK, Ong CN, Shi X, Shen HM. Chemopreventive activity of parthenolide against UVB-induced skin cancer and its mechanisms. *Carcinogenesis*, 2004;25(8):1449-58.
- Wu C, Chen F, Rushing JW, et al. Antiproliferative activities of parthenolide and golden feverfew extract against three human cancer cell lines. *J Med Food*, 2006;9(1):55-61.
- Yao M, Ritchie HE, Brown-Woodman PD. A reproductive screening test of feverfew: is a full reproductive study warranted? *Reprod Toxicol*, 2006;22(4):688-93.
- Zhang S, Lin ZN, Yang CF, et al. Suppressed NF-kappaB and sustained JNK activation contribute to the sensitization effect of parthenolide to TNF-alpha-induced apoptosis in human cancer cells. *Carcinogenesis*, 2004;25(11):2191-9.

SEPTEMBER 2010