

Select Nutritional Components to Support Migraine Headaches

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A migraine headache is classified as one of the primary inherited headache disorders. It is estimated that thirty-six million Americans, or about 12% of the population, suffer from migraine headaches.¹ “Over excitability of specific areas of the brain”¹ is specifically noted in migraine headaches. Common migraine triggers include: specific foods and beverages, such as aged cheese, alcoholic beverages, food additives such as nitrates (in pepperoni, hot dogs, luncheon meats), and monosodium glutamate (MSG), commonly found in Chinese food. These triggers are thought to be responsible for up to 30% of migraines.² Other triggers include: excessive caffeine, menstrual period, excessive fatigue, missing meals, or changes in normal sleep patterns. The primary symptom is intense throbbing in an area of the head. Other common associated symptoms include: sensitivity to light, noise, odors, nausea and vomiting, stomach upset or abdominal pain, loss of appetite, fatigue, dizziness, and blurred vision.² Rare symptoms include fever and diarrhea.

According to the World Health Organization, migraine is one of the 20 most disabling medical illnesses. Although there is no cure for migraines, recognized treatment options are available. Nutritional supplementation can also be of benefit; as certain compounds have demonstrated benefits in mitigating vascular effects, thus aiding to control migraine headaches. These compounds will be discussed below.

Riboflavin referred to as vitamin B2. (vitamin G), is a water-soluble B-vitamin involved in the formation of flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN). Both FAD and FMN function in oxidation-reduction reactions, and act as coenzymes in the mitochondrial respiratory chain, as well as in numerous other pathways. There are also numerous other FAD and FMN-linked enzymes, including xanthine oxidase, cytochrome reductase, glutathione reductase, and lactate dehydrogenase, all of which play important roles in the body. Riboflavin also functions in the redox cycle of glutathione. Glutathione is a major antioxidant, and plays an important role as a participant in protecting organisms from reactive oxygen species, such as hydroperoxides.

Riboflavin deficiency may impair iron absorption, increase intestinal loss of iron, and/or impair iron utilization for the synthesis of hemoglobin.³ Riboflavin is also essential for metabolism regulation. In relation to headaches, Boehnke, C, et al. noted a significant reduction in the frequency of headaches with riboflavin intake. Prophylactic treatment with riboflavin (400mg/ day) was demonstrated to both reduce migraine attack frequency, and to attenuate the use of abortive antimigraine therapy.⁴

Butterbur (*Petasites hybridus*) is a perennial shrub that has lilac-pink flowers and can grow up to three feet high. It is found throughout Europe, as well as in parts of Asia and North America. The genus name, *Petasites*, is derived from the Greek word “petasos”, which is the felt hat worn by shepherds. Its botanical and common names are attributed to its broad leaves, up to three feet in diameter. Its common name is attributed to the large leaves being used to wrap butter during warm weather.⁵ Its habitat is typically wet, marshy ground, damp forests, or adjacent to rivers or streams.

Butterbur has been used for hundreds of years to treat aches and pains, including headache.⁶ There are numerous studies outlining the benefits of butterbur for migraine prophylaxis. In a study comparing Butterbur root extract and music therapy in pediatric migraines, both were demonstrated to cause greater headache reduction as compared to placebo. Butterbur root extract and music therapy might also be superior to placebo and may represent promising treatment approaches in the prophylaxis of pediatric migraine.⁷ In another study group daily consumption of *Petasites* extract at a dose of 75mg, bid was demonstrated to decrease the frequency of migraine attacks by 48%, compared to the placebo group ($p = 0.00102$).⁸ In a separate study migraine frequency improved in $\geq 50\%$ in 45% in the Butterbur group, while improvement in the placebo group was only 15%.⁹ Butterbur has also been demonstrated to reduce smooth muscle spasm. It is believed that Butterbur likely acts through calcium channel regulation and inhibition of peptide leukotriene biosynthesis, thus influencing the inflammatory cascade associated with migraine.¹⁰

Importantly, Butterbur from differing manufacturers varies in the quantity of the targeted active phytochemical group called petasins. A high quality Butterbur will possess distinguishable quantities of the six different petasins, including: 3-desoxy-neopetasol, isoperasin, neo-petasin, petasin,¹¹ neo-S-petasin and S-petasin. In examining different sources of Butterbur, a Chinese extract evaluated did not show the presence of sesquiterpenes, suggesting the absence of petasins. This demonstrates the importance of supplier evaluation, which allows product formulation with the raw materials possessing the most activity.

Contraindications:

- Butterbur is not recommended for those with dermatologic conditions, as butterbur may cause skin discoloration, pruritus, rash, and/or hot flushes.^{12,13}
- Butterbur is not recommended for those with gastrointestinal diseases, as discoloration of stools, dysphagia, vomiting, burping, upset stomach, pain, nausea, diarrhea, indigestion, bitter taste, flatulence, and constipation have been reported.^{12,13,14,15,16,17,18,19,20,21}
- Butterbur is not recommended in patients with somatoform disorders.^{13,20}
- Caution is advised when used in patients with certain musculoskeletal conditions, as arthralgia, limb pain, and other pain complaints have occurred in some patients treated with butterbur.²¹

- Butterbur is not recommended in patients with eye conditions, as according to secondary sources, butterbur may cause itchy eyes.²²
- Butterbur is not recommended in patients with respiratory conditions as butterbur may cause respiratory problems such as difficulty breathing and wheezing.^{12,13,20}
- Butterbur is not recommended in patients with hepatic disorders or those taking anticholinergic agents, as butterbur may increase liver enzyme levels, particularly when administered in high doses.^{12,21,23}

Feverfew (*Tanacetum parthenium*) Feverfew is a daisylike perennial, herbaceous herb. The name feverfew is derived from the Latin word febrifugia, meaning “fever reducer,” and was traditionally used as an antipyretic. It is noted to possess aperient (constipation relief), carminative, and bitter properties, and is also useful as an emmenagogue (stimulates blood flow in the pelvic area and uterus areas). It is also said to, “allay any distressing sensitiveness to pain.”²⁴ The 17th Century English herbalist Culpeper wrote of the effectiveness of this herb for headache and uterine disorders.²⁵

The active principles are noted to include one or more of the sesquiterpene lactones, including parthenolide, which is the main sesquiterpene lactone in feverfew.²⁶ Other potentially active constituents include flavonoid, glycosides and pinenes. Noted pharmacology properties include: anticancer, anti-inflammatory, cardiogenic, anti-spasmodic, an emmenagogue, as well as an enema for worms. Parthenolide comprises up to 85% of the total sesquiterpene content and is found primarily in the superficial leaf glands (0.2%-0.5%), but not in the stems.^{27,28,29}

Feverfew also possesses anti-inflammatory activity. Extracts of the above ground parts and leaf extracts have been noted to suppress prostaglandin production, with leaf extracts inhibiting to a lesser extent. It is assumed that the lipophilic compounds other than parthenolide may be associated with its anti-inflammatory activity, particularly with reducing human neutrophil oxidative burst activity, as indicated by some studies.^{30,31,32}

Contraindications:

- Feverfew is contraindicated in patients allergic to other members of the Asteraceae family, such as aster, chamomile, chrysanthemum, ragweed, sunflower, tansy, and yarrow. Due to its potential antiplatelet effects, it is not recommended for use in patients undergoing surgery. Patients with blood-clotting disorders should consult their health care provider prior to using products containing feverfew.
- Pregnant women should not use the plant because the leaves possess emmenagogue activity (ejection of the placenta and fetal membranes) and may induce abortion. It is also not recommended for breastfeeding mothers or for use in children younger than 2 years of age.

Coenzyme Q10 (emulsified). Migraine due to mitochondrial impairment has been theorized in certain individuals.^{34,35} As a component of the electron transport chain Coenzyme

Q10 (CoQ10) participates in aerobic cellular respiration, generating energy as ATP, and thus functions as a necessary component in cellular energy production. Ninety-five percent of the body’s energy is produced in this manner. In addition to CoQ10’s assistance in cellular energy production, it also functions as an antioxidant. Low levels of CoQ10 have been reported in numerous disease states as well as in the ageing.^{36,37,38,39} Several factors have an effect on the serum and/or tissue concentrations of CoQ10. These factors include genetic mutations, ageing, cancer, as well as therapy from certain drugs, most notably the statin medications used in the management of cholesterol.

CoQ10 has been proposed as a prophylaxis for migraines, especially in children and women of childbearing age.⁴⁰ Magnetic resonance spectroscopy (MRS) studies suggest an impaired energy metabolism in the brain and skeletal muscle of migraine patients.⁴¹ Since CoQ10 plays an essential role in the mitochondrial respiratory chain via its function as a redox carrier, permitting the “transfer of reducing equivalents from complex I and complex II to complex III”⁴², a deficiency in CoQ10 results in insufficient transfer of protons across the inner mitochondrial membrane.⁴³ This, in turn, affects the “generation of adenosine triphosphate and all adenosine triphosphate-dependent metabolic processes.”⁴³ Additionally, “a defect of reduced nicotinamide adenine dinucleotide (NADH) dehydrogenase, citrate synthase, and cytochrome-c-oxidase platelet activities in migraine patients” has also been noted.⁴⁴ According to Bianchi, A, et al., “if a decreased energy state characterizes the migraineur’s brain, compounds such as CoQ10, which improves mitochondrial function, could theoretically be used in migraine prophylaxis.”⁴⁵ In an open label investigation (non-blinded) Rozen TD, et al. demonstrated that CoQ10 at a dose of 150mg/day, was effective as a migraine preventive.⁴⁶ In addition, Barbiroli, B., et al. demonstrated improvements in both muscle and energy metabolism with CoQ10 administration in patients with “mitochondrial cytopathies”.⁴⁷

Polyphenolic-Like Compounds(derived from *Lensesculenta* extract) (**Phytolens**[®]). Migraine as well as headache duration has been correlated to oxidative/antioxidative parameters, thus, antioxidants are proposed as beneficial adjuncts in migraine physiology. Polyphenolic-like compounds (from Phytolens[®]) possess numerous antioxidant characteristics, including the ability to quench both organic free radicals, and superoxide anions. They have also been demonstrated to prevent the oxidation of ascorbic acid in solution, and prevent the autoxidation of linoleic acid *in vitro*, more effectively than BHT and alpha tocopherol. Specifically, these compounds were noted to “have beneficial effects on inflammation via the attenuation of peroxynitrite-induced apoptosis and macrophage-dependent immunity.”⁴⁸ Distinctively defined, these compounds are “a water-soluble extract of polyphenolic antioxidants from non-soy legumes.”⁴⁸

Polyphenols are noted as compounds that possess antioxidant properties both *in vivo* and *in vitro*.⁴⁹ They have also been associated with an inhibition of epidermal lipid peroxidation,

with the degree inhibition dependent upon the polymerization in polyphenol structure. Also noted was the greater degree of polymerization in the polyphenol structure, the greater inhibitory potential towards lipid peroxidation.⁵⁰

Procyanidins are known to possess many beneficial properties. Specifically, the procyanidins from grape seed “are known to exert anti-inflammatory, anti-arthritic and anti-allergic activities, prevent skin aging, scavenge oxygen free radicals and inhibit UV radiation-induced peroxidation activity.”⁵⁰

The combination of the above noted nutrients (MygranX™) were utilized as part of a small clinical evaluation to determine its effect on migraines in select patients.⁵¹ Preliminary data indicated that it reduced headache severity in four of the six patients, while five out of six patients reported reduction in frequency. Other noted experiences included an improvement in mental sharpness, and an increased interest in participation in outside activities. Side effects noted were mild, and included nausea and some gastrointestinal disturbances.

As a consequence of the many harmful oxidative reactions that take place in the body, as part of the metabolic and physiological processes that occur, the generation of reactive oxygen species, which include: superoxide radical anions, hydroxyl radicals, and hydrogen peroxides, results in oxidative reactions, and in turn oxidative stress. These oxidative reactions may be harmful to the body, thus, the need for antioxidant support. For that reason, “the hypothesis of oxidative stress in migraine is supported by various studies.”^{52,53,54,55} Nutritional compounds, specifically antioxidant compounds, may assist in mitigating the effects that stress may play in migraine pathology.

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