

Complementary, Holistic, and Integrative Medicine: Butterbur

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Introduction

Petasites hybridus, a perennial shrub that grows in Europe, Asia, and North America, is commonly referred to as butterbur because the leaves of the plant have been used to wrap butter during warm seasons. (1)(2). Historically, butterbur has been used for a wide range of conditions, such as “urinary tract spasms,” back pain, asthma, and topical wound healing. (3)(4) Generally, bitter-tasting compounds extracted from the root of the butterbur plant, known as petasins, are the active ingredient. (4)

Definition and Description

Butterbur is a member of the *Asteraceae/Compositae* family and has been used medicinally for more than 2,000 years. (2) Recent research has evaluated butterbur to prevent asthma attacks, allergic rhinitis, and migraine headaches due to its anti-inflammatory and antispasmodic effects. (3)(5)(6)(7)(8)(9)(10)(11)(12)(13)

Evidence of Efficacy in Pediatrics

Evidence for the use of butterbur in children is promising, although preliminary. Data are based primarily on open-label, cohort-controlled trials in adults and children and randomized, controlled trials (RCTs) in adults.

Asthma

A prospective nonrandomized, open trial evaluated the effects of butterbur treatment in adults (n=64) and children (n=16) ages 6 to 17 years who had mild-to-moderate asthma. (14) Over an 8-week period, adults received 50 g of butterbur extract three times daily; children received 50 to 150 mg per day, depending on age. All patients were permitted to continue all other asthma medications. By the end of the study, the number and duration of asthma attacks had decreased by 48% and 75% respectively; FEV₁ improved by 70.6% and peak flow by 83.9%. After 16 weeks of follow-up, 42.9% of the patients had reduced their dose of inhaled steroid and 48.3% had reduced their use of short-acting beta-agonists.

Four of 80 patients dropped out of the study, but none of the terminations was due to adverse events caused by the extract. Generally, butterbur was well tolerated, with seven patients reporting a total of 11 adverse events. Pediatric patients experienced abdominal pain, flatulence, sneezing, allergic conjunctivitis, allergic rhinitis, and halitosis. Although the results are promising, methodologic limitations such as lack of blinding and control group leave this study susceptible to bias. Because the pediatric sample was small, these findings should be considered preliminary and in need of confirmation by larger, more rigorous studies.

Allergic Rhinitis

Although no pediatric studies were identified, several adult RCTs have evaluated the use of butterbur to prevent allergic rhinitis (Table), with mixed results.

Migraine Headaches

The efficacy of butterbur root for preventing migraines in adult populations is supported by evidence from randomized, placebo-controlled trials. (7)(17)(18) Similar data in pediatric populations are sparse.

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Table. Clinical Studies of Butterbur and Allergic Rhinitis in Adults

Investigator	Year	Study Type	Number of Adults	Intervention	Results
Kaufeler (5)	2006	Open postmarketing surveillance study	580	Commercially available butterbur leaf extract standardized to 8 mg petasins; average, two tablets daily	90% of patients reported improved symptoms of seasonal allergic rhinitis
Gray (13)	2004	Double-blind, placebo-controlled crossover study	30	Butterbur 50 mg twice daily	Insignificant results for subjective outcomes of intermittent allergic rhinitis
Lee (12)	2004	Double-blind crossover study versus fexofenadine and placebo	16	Butterbur 50 mg twice daily	Butterbur equally effective as fexofenadine compared with placebo
Lee (15)	2003	Double-blind, placebo-controlled crossover study	20	Butterbur 50 mg twice daily	Butterbur protected against adenosine monophosphate-induced nasal responsiveness in patients who had grass-sensitive seasonal allergic rhinitis
Thomet (16)	2002	Open clinical trial	6	Commercially available butterbur leaf extract standardized to 8 mg petasins; six tablets daily	Butterbur was tolerated and relieved symptoms in seasonal or perennial allergic rhinitis patients

One open-label study evaluated the effectiveness of a commercially available butterbur root extract for preventing migraine headaches in 108 children ages 6 to 17 years old who had a history of migraines, as diagnosed according to the International Headache Society (IHS) classification. (19) Dosing was stratified by age, with 6- to 9-year-olds receiving 50 mg daily and 10- to 17-year-olds receiving 100 mg daily, given twice daily for a 4-month period. Nonresponse was defined according to IHS guidelines for clinical trial evaluation of headaches. (20) Those who did not respond by 3 months were given a 50% higher dose for an additional 2 months. At the end of the study, 77.2% of the patients were considered responders, and monthly migraine attacks were reduced 63.2%. The duration of attacks was reduced by approximately 3 hours. Regarding the severity of migraine attacks, 81.6% of patients reported significant improvement and none reported worsening of migraine; two, however, terminated treatment early due to lack of efficacious results.

Investigators reported that 98.2% of patients had excellent tolerance, and 91.8% of patients reported feeling

well or better than before the treatment. Eight patients reported adverse events, none of which was serious, including mild belching, moderate nausea, and moderate abdominal pain (which was rated as “probably” related to the treatment). Methodologic limitations of this study included lack of blinding, lack of a control group, and limited follow-up. Accordingly, definite conclusions about efficacy cannot be drawn, and additional controlled studies must be conducted.

Evidence of Safety

In adults, the most commonly reported adverse event is eructation (belching), which occurs in approximately 20% of patients and rarely is accompanied by nausea and stomach pain. (3)(19) A postmarketing surveillance study analyzing butterbur treatment for seasonal allergic rhinitis found that adverse events were largely gastrointestinal, occurring at a rate of approximately 3.8%. (5)

In pediatric studies involving doses ranging from 50 mg to 150 mg daily, butterbur generally was well tolerated. The most common adverse effect reported was mild eructation; less common adverse effects included

nausea and abdominal pain, flatulence, sneezing, allergic conjunctivitis, halitosis, fatigue, and headache. (3)(6)(14)(19) Most of these events were mild and transient. (6)(14)(19)

The use of raw, unprocessed butterbur extracts containing pyrrolizidine alkaloid compounds should be avoided due to the potential for causing liver damage or cancer. (3)(10)(21)(22) These compounds have the potential for hepatotoxicity and carcinogenicity, and commercially available butterbur extracts are required to contain lower-than-detectable amounts (<0.08 ppm). (2) Four case reports of reversible cholestatic hepatitis have been linked to the long-term use of butterbur, but it is unknown which compounds are the cause. (21) Butterbur should be used only in commercial preparations in which the label clearly states that the extract is free of pyrrolizidine alkaloids.

No cases of allergic reactions have been reported, but they are possible because butterbur is a member of the *Asteraceae* family. (1) Additional research is warranted to determine the long-term safety of butterbur extract in pediatrics.

Pregnancy and Lactation

Evidence is insufficient to support the use of butterbur in women who are pregnant or lactating. Hepatotoxic pyrrolizidine alkaloids found in unprocessed butterbur have been reported to be excreted in human milk. (4) Butterbur currently is contraindicated in pregnancy and lactation. (10)

Drug Interactions

No clinical case reports have noted specific drug interactions with butterbur in adult or pediatric populations. In theory, however, it is recommended that other anticholinergic agents, such as diphenhydramine, dimenhydrinate, scopolamine, amitriptyline, and atropine, be avoided while using butterbur. (1)

Because pyrrolizidine alkaloids are metabolized by the CYP3A4 enzyme system in the liver, CYP3A4 inducers may increase their conversion to toxic metabolites. (4) Although commercially available butterbur should not contain pyrrolizidine alkaloids, caution may be warranted with the concomitant use of CYP3A4 inducers, such as carbamazepine, phenobarbital, phenytoin, and rifampin. (4)

Pharmacologic Action

Petasins are believed to play an important role in the biologic activity of butterbur. (14)(23) They have been found to inhibit the in vitro synthesis of leukotrienes in

human eosinophils, neutrophils, and macrophages. Petasins also may decrease mast cell production of leukotrienes and histamine release, although this hypothesis has not been proven. (9) Petasins also decrease the intracellular concentration of calcium, as well as inhibiting its mobilization. (9)(21) Butterbur's biologic effects on both leukotriene production and intracellular calcium corroborate its anti-inflammatory, antihistamine, and antispasmodic effects.

Administration/Dosage Forms

Studies conducted in children have found very good tolerance of butterbur with doses ranging from 50 mg to 150 mg per day, divided into two or three doses, for up to 16 weeks. (14)(19)

Commercially available extracts of butterbur used in clinical trials are standardized to contain 15% petasins or approximately 7.5 to 8.0 mg of petasin/isopetasin per 50-mg capsule. (1)(3) This concentration, however, may vary, depending on the preparation.

Raw herbs, herb capsules, and extracts that contain unprocessed butterbur should be avoided due to the possibility of such preparations containing hepatotoxic and carcinogenic pyrrolizidine alkaloids. (1)

Summary

Data about the use of butterbur in pediatrics are limited, but promising. Although preliminary data support the efficacy and tolerability of standardized, unsaturated pyrrolizidine alkaloid-free products in adults and children for the treatment of asthma and migraine prevention, additional research with better designed studies is warranted.

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