

Bromelain – 500 mg

Introduction

Bromelain, extracted from pineapple stems, is a combination of multiple proteolytic enzymes. Initially identified in 1876 and extracted from pineapple stems in 1957, bromelain has a long history of use as a digestive aid, acting over a wide pH range to catabolize dietary protein.¹

Additionally, bromelain is well-absorbed and has been clearly shown to retain its enzymatic activity in the blood, with an estimated half-life of 6–9 hours.² Although most of its physiological effects have been attributed to its proteolytic activity, bromelain is also thought to possess a variety of other active enzymatic components, including phosphatases, glucosidase, cellulases, peroxidases, and glycoproteins, which may contribute to its effects.³ While its most clinically established indications are for pain and inflammation, such as osteoarthritis, it has also demonstrated fibrinolytic and antioxidant properties, and appears to modulate many inflammatory and metabolic signalling pathways.^{1,4}

About Bromelain

The proteolytic enzyme activity of bromelain has been classified as a cysteine proteinase, as it has active sulfhydryl groups. It has also been specifically classified as an endopeptidase, hydrolyzing amino acid bonds from the interior of a protein rather than the terminal ends.¹ In addition to actively degrading dietary proteins, experimental models have shown that it stimulates pancreatic enzyme production and improves epithelial integrity. These effects may be because of an increase in the bioavailability of free amino acids subsequent to protein digestion, or possibly by modulation of microbiota populations, specifically by increasing the abundance of *Akkermansia muciniphila*.^{1,5} There is also some evidence from a murine study that bromelain retains its proteolytic activity throughout the digestive tract, and may reduce gastrointestinal inflammation.⁶ This is exemplified by an in vitro reduction of the expression of several proinflammatory cytokines and chemokines found to be elevated in the colonic biopsies of patients with inflammatory bowel disease, including tumour necrosis factor (TNF), interferon-gamma, and granulocyte colony-stimulating factor.⁷

Bromelain's systemic effects are likely a result of the stabilization of its enzymatic activity in the blood, achieved by binding to alpha 2-macroglobulin and alpha 1-antichymotrypsin.² Bromelain's ability to reduce inflammation and pain may in part be because of an inhibition of several inflammatory mediators. In vitro, bromelain has been shown to inhibit cyclooxygenase-2 (COX-2) and inactivate NF-kappaB, and inhibit lipopolysaccharide (LPS) induced inflammatory mediators, including both COX-2 and inducible nitric oxide synthetase (iNOS).^{8,9} Many other effects of bromelain have been observed in experimental models, including fibrinolytic, anti-edematous, and immunomodulatory effects, as well as an upregulation of autophagy.^{4,10,11}

Most of the clinical evidence for bromelain relates to its musculoskeletal effects, specifically reductions in pain and swelling. An open-label trial (in a dose-dependent manner) showed that bromelain reduced acute knee pain as well as stiffness and function.¹² In a controlled clinical trial of mild/moderate knee osteoarthritis, bromelain had similar efficacy to standard therapy at four weeks. By 16 weeks, improvements in total WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) scores, including subscales for pain, stiffness, and function, were observed with bromelain supplementation. Comparison to standard treatment was not possible at 16 weeks because of the large number of adverse effects in the standard therapy group.¹³ More rapid recovery and reduction of pain and swelling following multiple types of minor trauma, including that induced by acute exercise, have been reported with bromelain as well, with uncontrolled trials also suggesting a possible benefit for sinusitis.^{3,14–16}

General Recommendations & Dosing

Clinical dosing for bromelain was 500 mg per day in the controlled trial for knee osteoarthritis, though doses as high as 12 g per day have been used with an excellent safety profile.^{1,13}

When used as a digestive aid, it is recommended to take one capsule per day with food. For systemic effects, bromelain should be taken on an empty stomach (1.5 hours before or after a meal). Bromelain should be used with caution in individuals with a pineapple allergy.¹⁷ Use with caution in individuals who are pregnant or breastfeeding, are taking anticoagulant agents, anti-inflammatory agents, or antibiotics, have gastrointestinal lesions/ulcers, or are having surgery.

Indication	Dosage	Results
Mild-to-moderate knee osteoarthritis ¹³	500 mg per day	Improvements in total WOMAC scores, including subscales for pain, stiffness, and function
Acute (knee) pain ¹²	200–400 mg per day	Improvements in all WOMAC symptom scores, including stiffness and function, with greater effect at 400 mg vs. 200 mg
Intense exercise (competitive cyclists) ¹⁵	1000 mg per day	Lower fatigue, trend toward testosterone stabilization
Acute sinusitis (children) ¹⁶	500 F.I.P. per day (F.I.P. = Fédération Internationale Pharmaceutique), roughly equivalent to 56–95 mg bromelain per day	Faster recovery, shorter mean duration than standard therapy

Drug Interactions

Bromelain has been reported to increase the concentration of several antibiotics, potentially increasing their effectiveness.³ Theoretical interactions with anticoagulant and anti-inflammatory medications exist, though none have been substantiated.¹⁸

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