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Bromelain

INTRODUCTION

Bromelain, derived from pineapple stems, has a long history as a digestive aid. More recently, it has been shown to have multiple applications primarily related to its systemic anti-inflammatory effects. Its physiological effects are attributed to its proteolytic activity, as its capacity to catabolize proteins not only assists with digestion, but also appears to modulate the activity of a wide spectrum of proteins. Both in vivo and in vitro data suggest it has anti-edematous, anti-inflammatory, antithrombotic, and fibrinolytic activity.[1,2]

WHAT IS BROMELAIN?

Bromelain is a general term for a combination of multiple proteolytic enzymes classified as cysteine or thiol proteinases, which refers to the presence of cysteine residues and disulfide bonds essential to its catalytic activity.[3] Bromelain is also classified as an endopeptidase; that is, it targets the interior of proteins rather than the ends.

Though nearly all bromelain is derived from the stem of the pineapple (where it is most abundant), variations of bromelain are derived from the pineapple fruit as well as from the palm tree. Stem bromelain is comprised of at least six different types of enzymes with optimal proteolytic activity near pH 7, with a range of pH 7–10.[3,4]

MECHANISM OF ACTION

Most of bromelain's physiological effects are attributed to its proteolytic activity, which itself is recognized to represent a cumulative action of the various proteases in the enzyme. Additionally, some evidence suggests that there may be non-proteolytic components of bromelain partly responsible for its effects.[1]

As a digestive aid, bromelain assists with protein catabolism over a fairly wide pH range. It has also been shown to stimulate pancreatic enzyme production and improve epithelial integrity in experimental models. This potentially occurs by both increasing the bioavailability of free amino acids subsequent to protein digestion, and by modulating microbiota populations, specifically increasing the abundance of *Akkermansia muciniphila*.[3,5]

In addition to its function as a digestive enzyme, bromelain has been shown to be absorbed in the digestive tract and retain its enzymatic activity in the blood, thereby providing more systemic effects.[6] Its half-life in the blood is in the range of 6–9 hours. It is primarily stabilized by binding to alpha 2-macroglobulin and alpha 1-antichymotrypsin.[6]

Bromelain has been shown to inhibit several inflammatory signals, such as tumour necrosis factor (TNF) and nuclear factor-kappa B (NF-kappaB).[7–9] For example, in vitro studies using biopsied colonic tissue from patients with inflammatory bowel disease found that bromelain reduced the expression of several proinflammatory cytokines and chemokines, including TNF, interferon-gamma, and granulocyte colony-stimulating factor.[7] In vitro models have also shown that bromelain inhibits cyclooxygenase-2 expression and inactivates NF-kappaB.[8] In addition, bromelain has demonstrated antioxidant and fibrinolytic properties, along with modulating numerous signalling pathways in experimental models, including those related to autophagy.[3,9,10]

Perhaps the best clinical data demonstrating bromelain's anti-inflammatory effects are related to musculoskeletal health. In an open-label trial, bromelain supplementation was shown to reduce acute knee pain as well as stiffness and function with a dose-dependent effect.[11] In another 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.[12] More rapid recovery and reduction of pain and swelling following multiple types of minor trauma have been reported with bromelain as well.[2,13]

ASSESSMENT

Bromelain has a long history of safe use, without adverse effects, in preclinical and clinical studies.[3] Safety is not well-established during pregnancy/lactation, and it should be used with caution in individuals with a pineapple allergy.[14] Theoretical interactions with anticoagulant medications exist, though none have been substantiated.[15] Bromelain has been reported to increase the concentration of several antibiotics, potentially increasing their effectiveness.[13]

Use with caution in individuals who are pregnant or breast-feeding, are taking anticoagulant agents, anti-inflammatory agents, or antibiotics, have gastrointestinal lesions/ulcers, or are having surgery.

GENERAL RECOMMENDATIONS AND DOSING

As a digestive aid, take 1 capsule per day with food; for systemic effects, take on an empty stomach (1.5 hours before or after a meal).

SUMMARY

Bromelain has a well-established role as a digestive enzyme. It is now also recognized to be absorbed intact and retain its proteolytic activity in the blood, allowing for more systemic effects. Many experimental models have shown that its proteolytic activity influences multiple signalling pathways, many related to the expression of inflammatory compounds. Clinical data for bromelain also demonstrate improvements in pain, stiffness, and function for osteoarthritis of the knee, as well as reductions in pain and inflammation for various minor traumas.

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