

Properties and Therapeutic Application of Bromelain

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Abstract: Bromelain belongs to a group of proteindigesting enzymes commercially obtained from pineapple fruits or stems. Fruit bromelain and root bromelain are prepared in different ways and have different enzymes. "Bromelase" usually means "root bromelain". Bromelain also has some anticancer properties and promotes apoptosis. This article reviews the key properties and clinical uses of bromelain along with effective formulas. Pineapple has been used as a part of folk medicine since ancient times and is also included in many herbal preparations. Bromelain is a complex mixture of proteases extracted from the fruits or stems of bromeliad plants.

The potential of using herbal products to prevent and treat diseases has long been recognized. Pineapple, commonly known as pineapple, produces a group of enzymes called bromelain, which has a sulfhydryl moiety. It has been shown that the antiinflammatory effect of bromelain is effective in the treatment of diseases such as osteoarthritis, rheumatoid arthritis and asthma, and the antiinflammatory effect of bromelain is by inducing apoptosis, inhibiting angiogenesis and improving the immune system activity prevent disease..

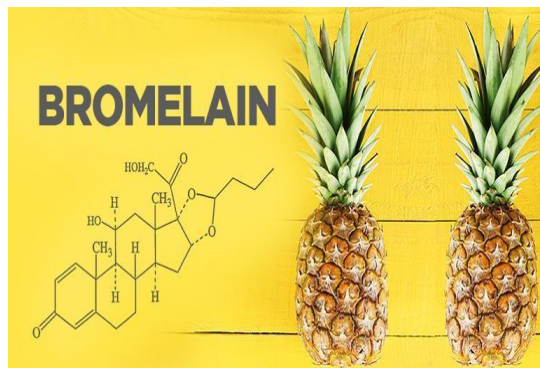
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I. INTRODUCTION

Bromeliad is the common name for Ananas comosus (synonyms: A. sativus, Ananassa sativa, Bromelia ananas, B. comosa). Bromeliads are important members of the bromeliad family and are grown in many tropical and subtropical countries, including the Philippines, Thailand, Indonesia, Malaysia, Kenya, India and China. It has been used as a medicinal plant in many cultures.

The high level of bromelain in pineapple stems requires the removal of bromelain because unlike the pineapple fruit, which is generally used as food, the stems are disposable and therefore inexpensive. Bromelain is believed to have many medical benefits, including reversing the inhibition of platelet aggregation, treating sinusitis, surgery, thrombophlebitis, pyelonephritis, angina, bronchitis, and improving drug absorption, especially antibiotics.

Bromelain causes fibrinogen to produce products at least similar to those produced by plasmin. Experiments in mice have shown that antibiotics such as sodium bicarbonate preserve the proteolytic activity of bromelain in the intestine. Bromelain is considered a dietary supplement and is available free to the public at health food stores and pharmacies in the United States and Europe. Current evidence suggests that bromelain may be a promising candidate for the development of future oral therapies for cancer patients.



In the sixteenth and seventeenth centuries, the pineapple plant entered the AsiaPacific region and became the first commercial crop. Bromelain is a complex mixture of natural proteolytic enzymes from pineapple (Pineapple Cossus) that has significant healing properties. There is also interest in bromelain, which has been used in folk medicine for many years in the treatment of various health problems. The potential therapeutic value of bromelain is attributed to its biochemical and pharmacological properties; The essence of crude bromelain is a proteolytic enzyme called glycoprotein, in addition to insoluble substances such as minerals, color pigments, protease inhibitors, organic acids and organic solvents.

Biochemical properties

The crude aqueous extract obtained from the stems and fruits of pineapple is called bromelain. It is a mixture of different thiol endopeptidases and other products such as phosphatases, glucosidases, peroxidases, cellulases, glycoproteins, carbohydrates and various protease inhibitors.

Today, bromelain is produced from cold pineapple juice by centrifugation, ultrafiltration, and freeze-drying. This process produces a yellow powder whose enzymatic activity is determined by different substrates such as casein (FIP units), gelatin (gelatin digestion units) or chromogenic tripeptides.

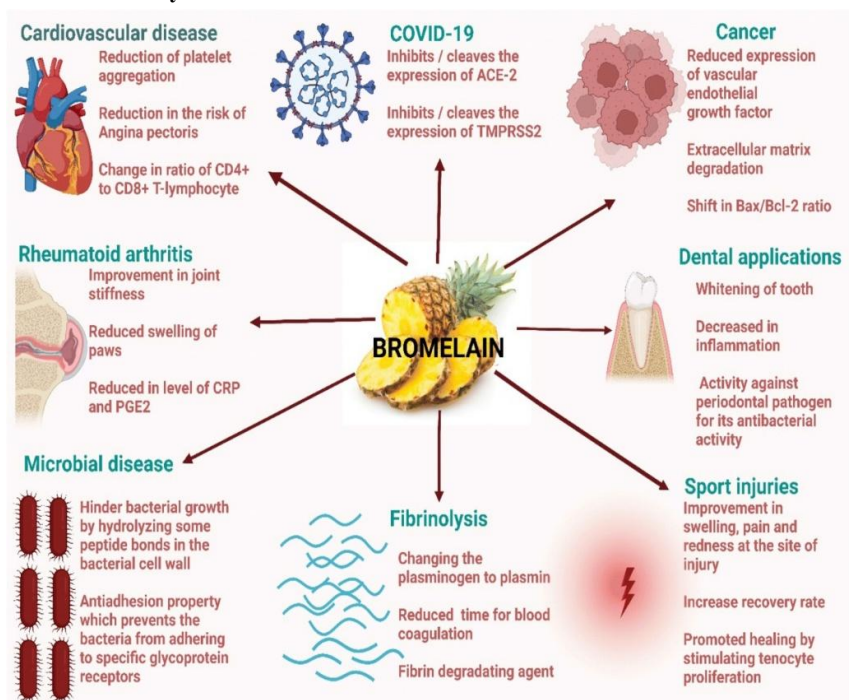
Absorption and Bioavailability

The body can absorb too much bromelain; About 12 grams of bromelain per day will not cause serious side effects. Bromelain is absorbed from the intestine in an inactive form; Approximately 40% of registered bromelain is absorbed from the intestine as a low molecular weight form. Bromelain has been shown to retain its proteolytic activity in plasma and also interact with two antibodies in plasma, α 2macroglobulin and α 1antichymotrypsin. A recent study showed that bromelain in juice stabilized at 3.66 mg/mL 4 hours after vaccination, and bromelain in blood remained at 2.44 mg/mL after 4 hours of reaction.

Medical uses

Studies show that bromelain may help treat many conditions.

Cardiovascular and Circulatory Effects of Bromelain



Bromelain may prevent or reduce the severity of angina and ischemic attacks (TIA). It is used in the prevention and treatment of thrombophlebitis. It also destroys cholesterol plaques and increases fibrinolytic activity. Combination of bromelain and other nutrients against skeletal muscle ischemia/reperfusion injury.

Cardiovascular disease (CVD) includes coronary arteries and heart disease, heart disease (heart attack), cerebrovascular disease (stroke), high blood pressure (hypertension), peripheral artery disease, rheumatic disease, heart failure study, and congenital sexual heart disease. Stroke and heart disease are the leading causes of death; Approximately 65% of people with diabetes die from stroke or heart disease. Bromelain is useful in the treatment of heart disease as it is an inhibitor of platelet aggregation, thus reducing the risk of arterial thrombosis and embolism.

Bromelain Diminishes Osteoarthritis

Osteoarthritis is the foremost common shape of joint pain in Western nations; in USA predominance of osteoarthritis ranges from 3.2 to 33% subordinate on the joint. A combination of bromelain, trypsin, and rutin was compared to diclofenac in 103 patients with osteoarthritis of the knee. After six weeks, both medications brought about in significant and comparable diminishment within the torment and inflammation. Bromelain may be a nourishment supplement that will give an elective treatment to nonsteroidal anti-inflammatory sedate (NSAIDs). It plays an imperative part within the pathogenesis of joint pain.

Effect of bromelain on immunogenicity

Bromelain has been suggested as adjunctive therapy in the treatment of inflammatory, malignant and autoimmune diseases. In vitro experiments have shown that bromelain can regulate adhesion molecules of T cells, macrophages, and natural killer cells and stimulate peripheral blood mononuclear cells (PBMC) to secrete IL-1 β , IL-6, and tumor necrosis factor α (TNF α).

Effect of bromelain on coagulation and fibrinolysis

Bromelain affects coagulation by increasing the fibrinolytic ability of the blood and inhibiting the synthesis of fibrin (a protein involved in clotting). In rats, bromelain reduces blood levels of fibrinogen in a dose-dependent manner. When bromelain concentration is higher, prothrombin time (PT) and activated partial thromboplastin time (APTT) are prolonged. In vitro and in vivo studies have shown that bromelain is a potent fibrinolytic because it promotes the conversion of plasminogen to plasmin and increases fibrinolysis by breaking down fibrin.

Effects of Bromelain on Diarrhea

There is evidence that bromelain can prevent some of the effects of certain enteric bacteria (such as *Vibrio cholerae* and *Escherichia coli*) whose enterotoxin can cause diarrhea in animals. Bromelain appears to exert this effect by interfering with intestinal secretory signaling pathways such as adenosine 3':5'-cyclic monophosphatase, guanosine 3':5'-cyclic monophosphatase, and calcium-dependent signaling cascades. Other studies have suggested a different course of action. Bromelain supplementation, active in *E. coli* bacteria, acts as an antiadhesion agent by proteolytically altering the receptor binding site to prevent the bacteria from binding to any glycoprotein receptors in the intestinal mucosa.

4.6. Effects of Bromelain on Cancer

Recent studies have shown that bromelain can alter important pathways that promote malignant tumors. It is assumed that the anti-inflammatory effect of bromelain results from its direct effect on cancer cells and their microenvironment, as well as from the regulation of the immune, inflammatory and hemostatic systems.

Bromelain has been shown to increase the expression of p53 and Bax, which are well known to induce apoptosis in mouse skin. Bromelain also reduces the activity of cell survival regulators such as Akt and Erk, thereby promoting apoptosis in tumors. Different studies have demonstrated the role of NF- κ B, Cox-2, and PGE2 as cancer promoters. There is evidence that NF- κ B signaling and overexpression play an important role in many types of cancer.

Effects on cell growth and survival. In normal cell growth and development are well controlled, disorders in the cell cycle cause cell growth to be wasted and turn into cancer cells. There are many mechanisms in the cell that protect its DNA from damage caused by toxicity and genomic instability.

Apoptotic processes are essential for the development and maintenance of homeostasis of biological systems. Failure of the normal apoptotic process leads to cellular transformation and gives rise to cancer cells. The process of apoptosis is characterized by cell shrinkage, chromatin condensation, DNA fragmentation and activation of cysteine special proteases called caspases.

The role of bromelain in surgery

Giving bromelain before surgery can reduce postoperative pain and the days between pain. Trials show that bromelain may be effective in reducing swelling, stiffness, and pain in women undergoing episiotomy. Today, bromelain is used to treat inflammation and sports injuries.

Studies have shown that these fibrinolytic products cause the absorption of edema from the bloodstream. These products reduce swelling, bruising, pain and post-treatment time after injury or surgery. There is evidence that bromelain reduces edema through fibrin degradation.

Role of Bromelain in Debridement of Burns

Removal of damaged tissue from wounds or second/third burns is called debridement. Bromelain used in cream form (3-5% bromelain in the lipid matrix) may be beneficial in necrotic tissue and accelerate healing. Bromelain contains the enzyme escharase, which is responsible for this effect. Escharase is a non-proteolytic enzyme and does not have hydrolase activity on native proteins or various glycosaminoglycan substrates. Their activities vary greatly depending on the plan.

Bromelain be useful in the management of CoVID-19?

There are currently no approved medications to treat CoVID19. Antibiotics, antivirals, and herbal combinations have been tested in the hope of slowing the spread of the disease. All of these medications are only part of the treatment for CoVID19. Treatment initially focuses on treating CoVID19 associated pneumonia, one of the most serious complications of the disease. It was later determined that multiorgan failure often results from a cytokine storm that causes inflammation and elicits systemic coagulopathy. To prevent CoVID19, it is necessary to develop new drugs that inhibit viral replication and reduce the development of the SARS-CoV-2 pathophysiological response in the body.

Bromelain has been shown to be an effective antiinflammatory and neuroprotective agent. People with coronavirus ID19 report headaches, fever, fatigue, and malaise. Bromelain provides a wide window for treating neurological symptoms by inhibiting prostaglandins (especially PGE2) and bradykinin, which is known for headaches and fever. Bromelain reduces oxidative stress in the body by inhibiting cellular peroxidation, nitric oxide synthesis and antioxidant enzymes. Therefore, the biological activity of bromelain may slow the spread of CoVID19. Because limited studies report its antiinflammatory properties, it may be more effective when used with one or two anti-inflammatory drugs.

Antimicrobial activity

Bromelain supplementation protects animals against diarrhea caused by Escherichia coli and Vibrio cholerae bacterial enterotoxin. Bromelain acts as an antiadhesion agent by modulating receptor binding sites and affecting intestinal secretory signaling pathways. These two concepts illustrate the benefits of bromelain against certain infections, as well as its ability to inhibit some effects of specific enteric bacteria and its effectiveness in relieving antibiotic pain. In vitro evidence also shows that bromelain has antihelminthic activity against intestinal nematodes, Trichuris muris and Spiralis polygyrus.

Bromelain toxicity-

The toxicity of bromelain to mice, rats and rabbits is very low, with an LD50 (lethal dose) of more than 10 g/kg. Six months later, toxicity tests were performed on dogs whose bromelain levels were increased to 750 mg/kg per day, and the results showed no toxicity.

No carcinogenic or teratogenic effects were seen when administered to rats at a daily dose of 1500 mg/kg and there were no changes in diet, cardiovascular, developmental, spleen, renal or hematology parameters.

II. CONCLUSION

Bromelain has many medical benefits, but its mechanism of action is unclear. The fact is that it has been proven that bromelain is well absorbed by the human body after oral administration and does not cause serious side effects even with longterm use. All the evidence reviewed in this article shows that bromelain can be used as a longterm health benefit to prevent cancer, diabetes, and many heart diseases.

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