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Review Paper

A Review on Bromelain from Pineapple Peel

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ABSTRACT

Bromelain is a Proteolytic enzyme complex predominantly derived from the pineapple plant (Ananas comosus), with a long history of traditional use and growing scientific interest due to its diverse biological activities. Historically employed by indigenous populations of Central and South America for medicinal purposes, bromelain has since been extensively investigated for its biochemical, pharmacological, and therapeutic properties. The enzyme exhibits broad proteolytic activity over a wide pH range and demonstrates moderate thermal stability, supporting its suitability for medical and industrial applications. This review summarizes current knowledge on the physicochemical properties of bromelain, its extraction and purification techniques, and its evaluation through enzymatic, biochemical, and biological assays. Particular emphasis is placed on its therapeutic potential, including anti-inflammatory, immunomodulatory, cardioprotective, fibrinolytic, and anticancer activities, as evidenced by in vitro, in vivo, and clinical studies. Additionally, the review discusses the role of bromelain in surgical recovery and its applications in food processing, pharmaceuticals, cosmetics, and textile industries. Advances in extraction methods such as ultrafiltration, aqueous two-phase extraction, and reverse micellar systems are also highlighted. Overall, this review aims to provide a comprehensive overview of bromelain's multifaceted biological functions and commercial relevance, offering valuable insights for future research and industrial development.

INTRODUCTION

The origins of Bromelain can be traced to ancient South American civilizations, where the pineapple plant (*Ananas comosus*) naturally grows. Indigenous communities in Central and South America, especially in areas such as the Amazon rainforest and the Caribbean, traditionally used different parts of the pineapple for medicinal purposes, including aiding digestion, reducing inflammation, and promoting wound healing. Scientific interest in Bromelain emerged in the late nineteenth century, when researchers began

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investigating the therapeutic potential of enzymes derived from pineapple.[1-6]

The therapeutic potential of Bromelain arises from its biochemical and pharmacological characteristics. Crude Bromelain primarily contains a Proteolytic Glycoprotein enzyme, along with insoluble components such as minerals, pigments, protease inhibitors, organic acids, and organic solvents.[7-8]

The pineapple stem contains a high concentration of Bromelain, and its extraction is encouraged because the stem is a waste byproduct and therefore more economical than the fruit.[9].

Numerous benefits have been attributed to Bromelain, including the reversible inhibition of platelet aggregation, relief of sinusitis, recovery from surgical trauma, treatment of Thrombo phlebitis, pyelonephritis, angina pectoris, and bronchitis, as well as improved absorption of medications, especially antibiotics.[10-13]

Research indicates that this enzyme exhibits anti-inflammatory, cardio protective, immunomodulatory, antioxidant, and anticancer activities. Beyond its clinical uses, Bromelain is also employed in numerous sectors of the food and related industries, including beverage production, meat processing, textiles, and cosmetics. The breadth of these potential applications highlights its therapeutic significance, derived from its biochemical and pharmacological properties, and has led to a marked rise in scientific, pharmaceutical, and industrial interest in this compound.[14-15]

This review seeks to comprehensively analyze the multifaceted biological properties of bromelain and its effects on human health, drawing on contemporary research findings. It also explores existing and potential commercial applications of the enzyme within the medical and food sectors, as well as future prospects. Our objective is to provide meaningful and informative insights to assist other researchers engaged in Bromelain -related studies.[16]

PROPERTIES OF BROMELIAN

The enzymatic activity of bromelain has a broad range and remains effective between pH 5.5 and 8.0. Various protein fractions were isolated using different biochemical techniques, including sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS -PAGE), isoelectric focusing (IEF), and multicathodal PAGE.[17-18]

STRUCTURE AND BIOCHEMISTRY OF BROMELIAN

Bromelain is a proteolytic enzyme belonging to the class of cysteine proteases, characterized by the presence of a cysteine thiol group at its active site that is essential for catalytic activity. Crude bromelain is a complex mixture containing several cysteine endopeptidases, including fruit bromelain from pineapple fruit and stem-derived enzymes such as ananain, stem bromelain, and comosain, along with other constituents such as phosphatases, peroxidases, carbohydrates, ribonucleases, protease inhibitors, cellulases, glycoproteins, and organically bound calcium. Its functional activity depends on a sulfhydryl moiety. Stem bromelain possesses a relatively stable secondary structure and exhibits enzymatic activity over a pH range of 7 to 10; however, it undergoes irreversible inactivation at pH values above 10. At an extreme alkaline pH of 14, stem bromelain adopts a characteristic heat-induced gelatinous mass–like conformation. Moreover, bromelain demonstrates long-term stability when stored at temperatures below 20 °C.[19]

BIOGENESIS OF BROMELAIN

All parts of the pineapple plant, including the stem, core, peel, crown, and leaves, can be processed to isolate bromelain, although the concentration and composition of the enzyme vary among these tissues. The pineapple stem and fruit are the richest sources of bromelain, yielding substantially higher enzyme titres than the core, peel, and leaves. Notably, the stem and crown together constitute nearly 50% (w/w) of total pineapple processing waste, which makes bromelain recovery from pineapple by-products both economically viable and environmentally sustainable. Consequently, pineapple stem bromelain is the most commercially important form and is also considered therapeutically superior, as it exhibits greater proteolytic activity than fruit-derived bromelain.[19]

IMMOBULIZATION OF BROMELIAN

A major limitation in the therapeutic use of enzymes such as bromelain is the gradual loss of enzymatic activity during processing and storage. Enzyme immobilization has emerged as an effective strategy to enhance stability and maintain functional efficiency. For successful immobilization, the nature of interactions between the enzyme and the carrier must be carefully understood and precisely controlled. Several immobilization approaches have been explored for bromelain, including entrapment within hydrogels, adsorption onto chitosan-based matrices, covalent binding, and encapsulation into nanoparticles. Ataide et al. demonstrated that nanoencapsulation enables sustained release of bromelain, leading to time-dependent antiproliferative and antioxidant effects. Furthermore, bromelain nanoencapsulated in chitosan provided physical protection, promoted wound contraction, and ensured controlled release, making it particularly suitable for topical formulations requiring modified drug delivery. The selection of an appropriate carrier and immobilization technique can minimize carrier-induced alterations in bromelain's structural and functional characteristics, enhance its stability and activity across a broad pH range and elevated temperatures, and improve its anti-inflammatory and antimicrobial efficacy.[19]

MEDICAL BENEFITS

Evidence from clinical studies suggests that bromelain has potential therapeutic effects in a range of disorders.

1. Effects of Bromelain on Cardiovascular and Circulation

Bromelain has been reported to reduce the occurrence and intensity of angina pectoris and transient ischemic attacks (TIAs). It is considered beneficial in both the prevention and management of thrombophlebitis. In addition, it may contribute to the degradation of cholesterol plaques and demonstrates strong fibrinolytic properties. When combined with other nutrients, bromelain has also been shown to help protect skeletal muscle from ischemia–reperfusion injury.[20] Bromelain has shown effectiveness in managing cardiovascular diseases because it inhibits blood platelet aggregation, which helps reduce the likelihood of arterial thrombosis and embolism.[21]

2. Effect of Bromelain on Immunogenicity.

Bromelain has been suggested as a supportive therapy for managing chronic inflammatory, cancerous, and autoimmune conditions.[22] Bromelain is capable of interfering with the Raf-1/ERK-2 signaling pathways by suppressing T-cell signal transduction.[23]Exposure of cells to bromelain lowers the CD4(+) T-cell activation and diminishes CD25 expression.[24] In vitro studies have demonstrated that bromelain can regulate surface adhesion molecules on T cells, macrophages, and natural killer cells, while also stimulating peripheral blood mononuclear cells (PBMCs) to secrete IL-1β, IL-6, and tumor necrosis factor-α (TNF-α).[25,26]

3. Effect of Bromelain on Blood Coagulation and Fibrinolysis.

Bromelain affects blood coagulation by enhancing serum fibrinolytic activity and suppressing the formation of fibrin, a key protein in clot development.[27]At higher concentrations, bromelain significantly prolongs both prothrombin time (PT) and activated partial thromboplastin time (APTT).[28] Evidence from in vitro and in vivo investigations indicates that bromelain enhances fibrinolysis by stimulating plasminogen activation to plasmin, leading to the breakdown of fibrin.[29,30]

4. Effect of Bromelain on Cancer Cells

Studies suggest that bromelain exerts anticancer effects by influencing pathways that sustain malignancy and by acting on cancer cells, their microenvironment, and immune, inflammatory, and hemostatic processes.[31]Research on the anticancer potential of bromelain has largely involved in vitro and in vivo models using mouse and human cancerous and non-cancerous cells exposed to bromelain preparations. Beez et al. demonstrated that bromelain administration to chemically induced mouse skin papillomas significantly reduced tumor development and volume while inducing apoptotic cell death.[32]The potential application of a bromelain–acetylcysteine combination in cancer treatment has been the focus of recent discussion.[33]

5. Role of Bromelain in Surgery.

Administration of bromelain before a surgery can reduce the average number of days for complete disappearance of pain and postsurgery inflammation[34,35]. Trials indicate that bromelain might be effective in reducing swelling, bruising, and pain in
women having episiotomy.[36]

EXTRACTION METHODS OF BROMELAIN.

Bromelain is commercially obtained from pineapple via multiple processing steps, including extraction, purification, drying, and final powder formulation. Among these stages, isolation and purification are the most costly and labor-intensive, often requiring expensive materials and prolonged processing times.[37] In this regard, contemporary techniques—including precipitation, membrane-based filtration, reverse micellar systems, aqueous two-phase extraction, and chromatographic methods—have demonstrated significant potential.[38]

1. Ultrafiltration

Ultrafiltration is an attractive technique for protein separation and concentration and has been extensively applied at both laboratory and industrial scales.[39]The molecular weight limit of ultrafiltration membranes generally falls between 3 and 100 kDa.[40]The protein-rich raffinate is retained on the membrane side and recycled until the desired concentration is achieved. Purification of bromelain typically requires a transmembrane pressure of 0.5-4 bar, operating temperatures between 10 and 30 °C, and a pH range of 4-8.5, without the use of corrosive agents or harsh chemicals. However, complex carbohydrates present in pineapple extracts, particularly polysaccharides, can adversely affect membrane performance by forming aggregates with proteins under varying physicochemical conditions, leading to pronounced membrane fouling and a substantial reduction in permeate flux.[41]

2. Aqueous two-phase extraction (ATPE)

Aqueous two-phase extraction involves the formation of two immiscible aqueous phases generated by mixing a polymer with salts or by combining two incompatible polymers within the same solution.[42] Liquid–liquid extraction has attracted considerable attention as an alternative to more costly separation techniques, as it can simplify the overall process by replacing expensive methods or reducing the number of required processing steps.[43] It enables efficient fractionation of protein-rich mixtures by eliminating unwanted components such as polysaccharides, pigments, and interfering proteins that can diminish enzymatic activity.Under optimal conditions, the target protein preferentially partitions into the upper phase, which is characterized by lower density and polarity, while most contaminant proteins migrate to the denser, more polar, and hydrophilic phase and can be removed by centrifugation. Protein distribution between the two phases is governed by several parameters, including ionic strength, pH, temperature, polymer molecular weight, and the nature of the salt used. The high enzyme recovery typically observed in ATPE is attributed to the presence of polyethylene glycol (PEG), which induces conformational changes in the enzyme's active sites. However, increasing the molecular weight of PEG results in reduced partitioning of bromelain into the top phase.[44]

3. Reverse Micellar Extraction (RME)

Reverse micelles are nanosized, thermodynamically stable surfactant aggregates composed of an organic continuous phase that encapsulates a small aqueous core . In this system, the target protein is selectively entrapped within the micellar core, while most impurities remain in the surrounding organic phase. The transfer of proteins into and out of the micelles can be regulated by modifying parameters such as pH, ionic strength of the aqueous phase, and surfactant concentration. For bromelain, optimal forward extraction efficiency, purification factor, and specific activity have been reported at pH 7.0–8.0. Forward extraction using the anionic surfactant AOT was conducted by mixing equal volumes (10 mL each) of the organic phase (solvent/surfactant) and the aqueous phase (enzyme extract with salt). In the cationic CTAB/isooctane system, the organic phase contained a co-solvent mixture of hexanol (5%, v/v) and butanol (15%, v/v). Back extraction was performed with 0.5 M potassium bromide. After thorough mixing for 1 h, the phases were separated by centrifugation at 4000 g for 15 min, and the recovered aqueous phases from both extraction steps were analyzed for bromelain activity and total protein content.[45]

EVALUATION

1. **Enzymatic and Biochemical Evaluation of Bromelain**

Bromelain consists of a group of sulfur-containing proteolytic enzymes primarily obtained from the pineapple plant (*Ananas comosus*). Its protease activity is typically assessed through substrate degradation methods such as casein, gelatin, or azocasein assays, along with standardized measurements of enzymatic units including GDU and CDU. The enzyme functions effectively over a broad pH range, approximately 5.5 to 8.0, and exhibits reasonable stability at elevated temperatures, making it suitable for various pharmaceutical and industrial uses.[46]

2. Anti-Inflammatory and Analgesic Evaluation

Experimental studies conducted in cell cultures and animal models indicate that bromelain regulates key inflammatory mediators, including prostaglandins, bradykinin, and various cytokines. Through its effects on immune cell movement and enhancement of fibrinolytic processes, bromelain helps to lessen tissue swelling, pain, and inflammatory responses.[47]

3. Anticancer Activity Evaluation

The anticancer properties of bromelain have been investigated using various cancer cell lines and experimental animal models. Findings from these studies indicate that bromelain can slow tumor progression, trigger programmed cell death, and interfere with signaling pathways associated with metastasis, including NF-κB, MAPK, and Akt.[48]

4. Immunomodulatory Evaluation

Bromelain influences immune responses by suppressing the activation of CD4⁺ T lymphocytes and modifying the expression of cell surface adhesion molecules. These immunomodulatory actions play an important role in its anti-inflammatory activity and support its therapeutic potential in disorders involving immune dysfunction.[49]

5. Clinical Evaluation and Therapeutic Use

Clinical investigations have assessed the effectiveness of bromelain in conditions such as postsurgical inflammation, sinus disorders, osteoarthritis, thrombophlebitis, and wound repair. The outcomes of these studies suggest that bromelain helps decrease swelling, accelerates healing, and alleviates pain while being generally well tolerated with few adverse effects.[50]

6. Industrial and Pharmaceutical Evaluation

Owing to its effective protein-degrading capability and biodegradable nature, bromelain has been investigated for use in a wide range of industries, including food processing for meat tenderization and protein hydrolysis, pharmaceutical products to enhance drug uptake, as well as cosmetic and textile manufacturing.[50]

CONCLUSION

Bromelain, a proteolytic enzyme complex derived mainly from *Ananas comosus*, represents a biologically active compound with substantial therapeutic and industrial relevance. Extensive research has demonstrated that bromelain possesses a broad spectrum of pharmacological properties, including anti-inflammatory, immunomodulatory, cardioprotective, fibrinolytic, antioxidant, and anticancer activities. Evidence from in vitro, in vivo, and clinical studies supports its effectiveness in managing inflammatory conditions, cardiovascular disorders, immune-related diseases, surgical trauma, and certain malignancies, while maintaining a favorable safety profile.

The enzyme's wide pH tolerance, moderate thermal stability, and strong proteolytic efficiency further enhance its applicability across multiple domains. Advances in extraction and purification strategies—such as ultrafiltration, aqueous two-phase extraction, and reverse micellar systems—have significantly improved bromelain recovery and activity, offering cost-effective and scalable alternatives for industrial production. Utilization of pineapple stem waste as a primary source also promotes sustainability and economic feasibility.

Beyond its medical value, bromelain continues to gain importance in food processing, pharmaceuticals, cosmetics, and textile industries due to its biodegradability and functional versatility. Despite promising outcomes, further well-designed clinical trials and mechanistic studies are needed to optimize dosage, delivery systems, and long-term safety. Overall, bromelain remains a multifunctional enzyme with considerable potential for future therapeutic development and commercial exploitation, warranting continued scientific and industrial exploration.

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