AN OVERVIEW OF CLINICAL APPLICATIONS OF BROMELAIN
Tejashree Shanbhag1, Sukaina Abbas2, Amruta Kothare3*
Department of Life Sciences,
K.C. College, Churchgate, Mumbai 400 020, Maharashtra, INDIA

Abstract: Pineapple has been used as a traditional medicine by several cultures through time. Bromelain is a proteolytic mixture extracted from various parts of the pineapple. Its various properties such as their anticancer activity, antimicrobial activity, anti-inflammatory activity and antioxidant activity have been established and studied extensively. Bromelain has also been effective in burn injury treatment and debridement of the skin. This review aims to study the clinical properties and applications of Bromelain.
Keywords: Bromelain, Pineapple, antitumor, antioxidant, clinical applications.

I. Introduction
Bromelain is a protease derived from the stem and fruit of the pineapples (Ananas comosus). Stem bromelain (EC 3.4.22.32) along with Ananain (EC 3.4.22.31) and comosain have also been found to be the constituents in pineapple stems [1]. Different parts of the pineapple plant such as peel, core, crown and the leaves have been discovered to have similar proteases [2]. The pineapple plant entails different concentrations and proportions of Bromelain that exhibit different characteristics depending upon the part in which it is present. [3]. Proteases of the pineapple stem (EC 3.4.22.32) contain sulfhydryl groups crucial for its proteolytic activity [4]. Unlike other plant proteases, pineapple proteases aren’t present during the early stages of fruit development but their levels start to increase during maturity and remain high with a significantly small decrease in its activity [5]. Whilst proteases from fig and papaya, are found in early development of the fruit and significantly reduces upon maturation [4]. Various applications of bromelain have been studied since a long period of time, particularly management of tumor growth, coagulating blood, heightened activity with antibiotic action and its anti-inflammatory properties have been studied extensively. Bromelain has also been explored as a line of treatment for bronchitis, angina pectoris, sinusitis and cancer.
Thus, this review aims to map the applications of Bromelain that so far have been studied and established.

II. Antitumor and Anticancer activity
The migration and proliferation of glioma cells is reduced under the influence of bromelain. The other cells surrounding the area remain unaffected and viable by the treatment and can proliferate. P53 expression is increased and mitochondrial apoptotic pathway is activated due to expression of Bax under the influence of bromelain which led to selective induced apoptosis of the tumor cells [6]. In the treatment of hepatocellular carcinoma cells, Bromelain led to downregulation in the levels of COX-2 and VEGF (angiogenic biomarkers) which in turn led to reduction in tumor neo-capillary density when compared to untreated cells [7]. Cell growth in human gastric carcinoma Kato III decreased by 80% when exposed to either Bromelain singularly or when combined with other chemotherapeutic agents like cis platinum. [8]. It is found to cause apoptosis in breast cancer cells [9], [10].

III. Antimicrobial activity
A study done by Ozlen and Chatsworth state that proteolytic enzymes such as papain and Bromelain can be used to fix skin problems like wrinkles, acne and dry skin. Bromelain exhibited anti-helminthic effect against H. polygyrus by attacking the protective cuticle of the worm [11]. This mechanism of action suggested that resistance towards bromelain would be slow to develop. The purified cysteine protease was more effective than the crude protease [12]. Bromelain prevents diarrhea by protecting the intestine from the effects of bacterial enterotoxins produced by Escherichia coli and Vibrio cholerae. [13]. Bromelain showed antibacterial efficacy against periodontal pathogens, namely, S. mutans, A. actinomycetemcomitans, P. gingivalis [14]. A study done by Yong ker Loon established the efficacy of Pineapple extract against Staphylococcus aureus which is associated with a wide range of infections [15]. Bromelain partially purified from pineapple core was studied for its antimicrobial action against S. aureus, S. epidermidis and Propionibacterium acne and showed promising results [16]. Conversely, Bromelain proven to be an anti-fungal as it also stimulates the phagocytosis of Candida albicans [17].
IV. Antioxidant effect

Extracts of the pineapple were made in methanol; ethyl acetate and water and their antioxidant activity has been established [18]. Antioxidant properties of different varieties of pineapple have also been established. Different amounts of phenolic compounds were present in different varieties of pineapples. The highest antioxidant activity was exhibited by the Morris pineapple variety [19]. The total phenolic content and antioxidant activities of methanolic extract extracts of pineapple and superoxide anion scavenging activity has been established [20].

V. Anti-inflammatory

Inflammation is the body’s attempt of self-protection against external stimuli or foreign bodies, it includes distention of capillary and enhances their permeability which caused the tissue to inflate and appear inflamed. Bromelain has appeared to be an excellent candidate because of its analgesic and anti-inflammatory effects [22]. Four polyphenolic compounds isolated from pineapple, catechins, epicatechins, gallic acid and ferulic acid exhibited antioxidant capacities [23].

Figure 1: Effect of Bromelain on certain mediators of acute inflammation [21].

VI. Immunity

Bromelain has exhibited anti-inflammatory effects by regulation of cell surface molecules like CD 14, CD 44, CD 16, CD 21, Cd 128 which are involved with cellular adhesion and T cell management. It is also associated with hyaluron receptor CD44 associated with leukocyte migration and induction of proinflammatory mediators [24]. PGE2 inhibition has been observed under the influence of Bromelain, the action is very similar to one produced by NSAIDs [25].

VII. Debridement

The removal of infected or damaged tissue from a burn site on the skin, to promote the healing of the remaining tissues, is referred to as debridement. [26]. Stem Bromelain contains a non-proteolytic component that breaks the connection with healthy tissue and denatured tissue from burn. This component is known as “Escharase”. It is very specific and does not act upon healthy cells. Tissue can undergo successful debridement giving rise to a bed of tissue ready for grafting [27].

However, Bromelain was not very effective in debridement of eschar caused by frostbite wounds. It was concluded that the “patent vasculature, resulting tissue edema and a lack of coagulation of proteins found in the freeze injury are sufficient to inactiva te the bromelain enzyme before tissue digestion and dissection can be effected [28].

VIII. Other applications

Healing time after trauma surgical procedures have been greatly reduced by Bromelain. It has showed significant reduction of edema and pain as well as bruises. (MacKay et al, 2003). Bromelain has exhibited anti-fibrinolytic activity. Transient ischemic attacks have been minimized and prevented in invivo and invitro studies. Prolonged studies show that bromelain may also exert anti-hypertensive effects in certain species. (Taussig et al 1979, Giacca et all 1956).

In case of deficiency in pepsin and trypsin, Bromelain can be used as an adequate replacement due to its stability and activity in the stomach as well as the small intestine. It is active and stable over a wide pH range. When combined with oxbithe, pancreatin and bromelain, it lowered the stool fat excretion in patients with pancreatic steatorrrhea. There was also improvement in pain management and flatulence. (Balakrishnan et al, 1981)

IX. Discussion and Conclusion

Bromelain has been highly favored to be studied as an enzyme due to the various properties it exhibits in various fields. Bromelain induces apoptosis in cancerous cells; exhibits antimetastatic potential and causes reduction in tumor size making it an excellent candidate to explored in the line of the cancer treatment strategies. Due to its
effects and interaction with the immune system, Bromelain shows to be a very promising candidate in the treatment and mitigation of cancers and this line of treatment can be further explored for combination treatment and management of cancer. Bromelain reduces joint tenderness and stiffness alleviating the symptoms of arthritis. It lessens the severity of Transient Ischemic attacks. For enzymatic treatment of burn tissues, Bromelain is regarded as a potential candidate. Bromelain also effects the growth of certain pathogenic microorganisms which include periodontal pathogens as well as pathogens involved in cutaneous infections such as *P. gingivalis, S. epidermidis* and *Propionibacterium acnes*. Due to its low toxicity and side effects, it can also be explored as line of treatments or preventive measures for diseases such as Acne vulgaris, gingivitis etc. caused by these pathogens. Unlike most biological components, Bromelain does not have a loss in function during absorption by the body retaining its maximum activity. It also has very low toxicity of a LD50 of around 10g/kg when studied in mice and rabbit. [33]

Bromelain is a natural boon from nature that could if used properly maintain overall health and wellbeing of a person. The other benefits of utilization of Bromelain is that the enzyme is present in copious amounts in mature fruits unlike papaya and figs where the enzymes are present in earlier stages of fruit development. Bromelain is also present in various parts of the fruit that are not commonly consumed and usually discarded and various budget friendly and high yielding purification strategies have been developed for the extraction of the enzyme.

X. References


Acknowledgements

We thank K.C. College, Science Honors Program ‘JIGYAASA’, under which the above topic was considered for research work.