REVIE WARTICLE

Medicinal and nutritional characteristics of pineapple in human health: A review

Noel Lalhruaitluangi, Debashis Mandal*

Department of Horticulture, Aromatic and Medicinal Plants, Mizoram University, Aizawl-796004, Mizoram, India

ARTICLE INFO	ABSTRACT
Received : 27.02.2024 Accepted : 22.04.2024	Pineapple (<i>Ananas comosus</i>) is the third most important fruit in world production. The fruit is a source of balanced nutrients that provide the human body with valuable macro and micro-nutrients, including calcium, carbohydrates, vitamins, minerals, fiber, enzymes, and bioactive compounds that aid in the process of digestion and contribute to human health. Pineapple can be used as a supplementary nutritional fruit for good personal health. It possesses the biologically useful ingredient bromelain, which has demonstrated significant anti-inflammatory, antibiotic, anti-cancer, and anticoagulative properties. The multitude of potential uses of bromelain, combined with the effects of many other nutrients found in pineapple, allows us to appreciate not only its unquestionable taste but also the other benefits of this fruit. Antioxidants in pineapples help fight against free radicals, preventing cancers, heart diseases, and lowering cholesterol levels. Pineapple has abundant health benefits and also has the potential for breakthroughs in the food industry and agriculture sector. The present review will focus on the developments and future scopes of the medicinal and nutritional properties of pineapple.
a Creative Commons license: Attribution 4.0	Keywords: Antioxidant, bromelain, health, nutritional, pineapple
	Citation: Lalhruaitluangi, N. & Mandal, D. (2024). Medicinal and nutritional characteristics of pineapple in human health: A review. <i>Journal of Postharvest Technology</i> , 12 (2): 1-13.

INTRODUCTION

Pineapple (*Ananas Comosus*) is the most important and delicious fruit among other fruits cultivated worldwide, and India is one of the leading producers of pineapple (Salve and Ray, 2020). It is a wonderful tropical fruit having exceptional juiciness, vibrant tropical flavor, and immense health benefits. It is a non-climacteric fruit with high nutritional value that can be consumed in fresh or processed form such as canned fruit, juice, jam, jelly, fiber production, wine, etc. Pineapple itself is a nature's healing fruit that has many health benefits (Joy and Abraham et al., 2013). Pineapples have a unique flavor and taste and are rich in nutrients and antioxidants, which make them attractive to consumers due to their great health benefits. Pineapples are often introduced in the diet as a treatment or to prevent constipation because they increase bowel movement, improve intestinal health, and clean the kidneys. Pineapple is also recommended as a medical diet for certain diseased persons. The U.S. National Library of Medicine lists bromelain as a proteolytic digestive enzyme. When taken with meals, bromelain aids in the digestion of proteins, working to break proteins down into amino acids. Pineapple contains 81.2 to 86.2% moisture and 13-19% total solids, of which sucrose,

glucose, and fructose are the main components. Carbohydrates represent up to 85% of total solids, whereas fiber makes up 2-3%. Of the organic acids, citric acid is the most abundant in it. The pulp has a very low ash content, nitrogenous compounds, and lipids (0.1%). From 25-30% of nitrogenous compounds are true proteins. Out of this proportion, ca. 80% has proteolytic activity due to a protease known as Bromelain. Fresh pineapple contains minerals such as Calcium, Chlorine, Phosphorus, and Sodium (Farid and Shaheen, 2015). Pineapple fruits exhibit high moisture (81.2 to 86.2%), high sugars, soluble solids content, ascorbic acid, and low crude fiber. Thus, pineapple can be used as a supplementary nutritional fruit for good personal health. The pineapple fruits are normally consumed fresh or as fresh pineapple juice. Field ripe fruits are best for eating fresh, and it is only necessary to remove the crown, rind, eyes, and core. Pineapple may be consumed fresh, canned, juiced, and is found in a wide array of foodstuffs - dessert, fruit salad, jam, yogurt, ice cream, candy, and as a complement to meat dishes. In the current review, an attempt is made to collect the available information from existing literature related to nutritional and medicinal properties of pineapple to improve human health.

NUTRITIONAL VALUE OF PINEAPPLE

Pineapple (*Ananas comosus*) possesses a pleasant taste and aroma (Baruwa, 2013). The succulent fruit is perishable and seasonal, but it contains sugar, the protein-digesting enzyme bromelain, good amounts of citric and malic acids, as well as vitamins, which contribute to its flavor (Joy, 2010; Hemalatha and Anbuselvi, 2013). Pineapple, along with its sweet flavor, is very rich in essential nutrients, including potassium and calcium, vitamin C, copper, folate, glycans, fiber, and other crucial factors. All these substances make pineapple an excellent candidate as part of a balanced dietary weight-reduction plan. One of the most favorable aspects of its composition is that it contains a minimum amount of fat and sodium but contains high quantities of carbohydrates (Kumar, 2021). The substantial amylose content of pineapple stem starch (34.4 percent), which was approximately twice that of maize, more than double that of cassava starch (15.4 percent), and five times that of rice (6.5 percent), is responsible for certain technical characteristics such as high gelatinization temperature, enthalpy, and pasting temperature. As a result, the highest solubility percentage (more than 32 percent) is found in pineapple starch (Nakthong et al., 2017).

Pineapple peel contains insoluble fiber-rich fractions that have greater potential and uses in the production of low-calorie, high-fiber foods (Huang et al., 2011). Darshini et al. (2021) reported that the use of pineapple pomace powder for fiber enhancement is due to its improved versatility due to the presence of a balanced amount of soluble and insoluble dietary fiber, as well as the presence of bioactive compounds associated with them. Fiber makes up about 76 percent of pineapple by component (peel and pomace), with 99.2 percent being insoluble and 0.8 percent being soluble. In addition to being high in dietary fiber, pineapple pomace also contains calcium, phosphorus, and iron (Kumar, 2021). Dietary fiber plays an essential role in promoting several physiological and metabolic beneficial effects, particularly as a bulking agent, normalizing intestinal motility, preventing constipation, and decreasing the intestinal absorption of cholesterol and glucose (Hu and Zhao, 2018). They can be used as a food ingredient to increase the nutritional quality of foods (Devi et al., 2016). Pineapple peel and crown leaves have a high content of ferulic acid and are commonly available in the local agriculture industry (Tang and Hassan 2020).

Li et al. (2014) identified polyphenolic metabolites from pineapple peel (i.e., catechin, epicatechin, gallic acid, and ferulic acid) that contribute to the reduction of oxidative stress-related diseases. These metabolites can be integrated into the bioprocess to produce valuable by-products or food ingredients. Pineapple is a rich source of vitamins and minerals. Half a cup of pineapple juice provides up to 28 mg (50 percent) of an adult's daily recommended amount of vitamin C. Sugar content plays an important role in the flavor characteristics and commercial assessment of pineapple. Pineapple contains 81.2 to 86.2% moisture and 13-19% total solids, of which sucrose, glucose, and fructose are the main components. The peak in sucrose concentration is attained at the full yellow stage and then declines. Carbohydrates are the main source of energy in the human diet for performing various body functions as they control blood glucose and also promote proper functioning of the brain and gastrointestinal processes (Muir et al., 2009). Carbohydrates represent up to 85% of total solids, whereas fiber makes up 2-3%. Pineapples also contain manganese, which belongs to trace elements. One cup of pineapple juice supplies 1.3 mg of manganese, which covers

up to 73% of the daily requirement. It is a cofactor for a number of enzymes essential for energy production and antioxidant processes. The organic acid concentration in pineapple juice is in the range of 0.6-1.2%, depending on the variety of pineapple. Citric acid makes up 87% of total acid, and malic acid is another significant organic acid.

Pineapple juice contains ascorbic acid and is a good source of vitamin C. Ascorbic acid or vitamin C fights bacterial and viral infections, is an effective antioxidant, and helps the body absorb iron. Half a cup of pineapple juice provides 50 percent of an adult's daily recommended amount of vitamin C. Several essential minerals exist in pineapples, including manganese, a trace mineral instrumental in the formation of bone, as well as the creation and activation of certain enzymes. Pineapples also include copper, another trace mineral. It assists in the absorption of iron and regulates blood pressure and heart rate (Debnath, 2012).

MEDICINAL VALUE OF PINEAPPLE

Pineapples are a rich source of antioxidants that fight against free radicals and prevent cell damage. They help in preventing cancers, heart diseases, arthritis, and lowering cholesterol levels. Malic acid helps boost the body's immunity, firm and smooth the skin, and reduce the risk of metal intoxication. Furthermore, malic acid helps maintain oral health, hence preventing gingival diseases and dental plaque formation. Manganese in pineapples helps strengthen bones and connective tissues. It helps strengthen gums, keeping teeth healthy and strong (Debnath et al., 2012). Vitamin C found in pineapple juice also helps as a great remedy for oral health and can reduce the risk of gingivitis and periodontal disease. It also helps the body fight against bacteria and toxins that invade human gum tissues (Chapple et al., 2012) and helps repair damaged tissues and keep the lymphatic system working healthily. Pineapples are abundant in vitamin C, which boosts our immune system due to its strong antioxidant effect and helps cure cold and cough. Furthermore, it enhances iron absorption from the intestinal tract and prevents urinary infections during pregnancy (Hossain et al., 2015).

Pineapple is a good source of manganese, which is an essential cofactor in a number of enzymes important for energy production and antioxidant defense. This high level of manganese in pineapple benefits the skin, collagen, cartilage, and bone material. Studies have also indicated that pineapple juice is good for the health of the pharynx and larynx. A combination of glucosamine, chondroitin sulfate, and manganese may significantly improve the symptoms of mild to moderate osteoarthritis of the knee (Khalid et al., 2015). Higher amounts of potassium and lower amounts of sodium in pineapples help maintain normal blood pressure levels. They treat intestinal worms and relieve nausea. Pineapple leaves have been traditionally used in Chinese medicine as anti-dyspepsia and anti-diarrheal agents. Other properties such as anti-diabetic, anti-oxidative, and anti-dyslipidemic have also been reported, indicating its potential to serve as medicine. Roasted unripe fruit juice is used by different communities in Gohpur of Sonitpur district, Assam, India for strangury (Saikia, 2006). The Garo tribal community of Netrakona district in Bangladesh uses fruit juice for fever and leaf juice for helminthiasis and jaundice (Rahmatullah et al., 2009). The root and fruit are either eaten or applied topically as an anti-inflammatory and proteolytic agent. It is traditionally used as an anthelmintic agent in Tripura. A root decoction is used to treat diarrhea (Debnath et al., 2012). Phytochemical analysis of pineapple leaf extract revealed the presence of alkaloids, flavonoids, saponins, and tannins, all of which are said to be hypoglycemic and analgesic (Faisal et al., 2014). It is believed that pineapple leaf extract may be used as a cheaper alternative method for reducing glucose levels in diabetic patients.

MEDICINAL PROPERTIES OF BROMELAIN

Bromelain is known for its clinical applications, particularly the modulation of tumor growth, blood coagulation, improvement of antibiotic action, and anti-inflammatory properties of therapeutic value (Ali et al., 2015).

Effects of bromelain on blood coagulation and fibrinolysis

Hikisz and Slomczewska (2021) reported that studies on the anticoagulant properties of bromelain were carried out as early as the second half of the 19th century, almost 70 years ago. The ex vivo studies were performed on patients after myocardial infarction, stroke, or high aggregation value orally administered bromelain. It has been shown that bromelain causes a decrease in platelet aggregation, thus reducing the risk of arterial thrombosis and embolism. These results were confirmed in later numerous studies conducted both in vitro and in vivo, where bromelain was shown to cause platelet inhibition in a dose-dependent manner. Bromelain influences blood coagulation by increasing the serum fibrinolytic ability and by inhibiting the synthesis of fibrin, a protein involved in blood clotting. In vitro and in vivo studies have suggested that bromelain is an effective fibrinolytic agent as it stimulates the conversion of plasminogen to plasmin, resulting in increased fibrinolysis by degrading fibrin (Pavan et al., 2012). Bromelain restricts the production of fibrin by reducing some of the clot formation process intermediates (factor X and prothrombin) and accelerating fibrogenesis (Fan et al., 2018). It has also been reported that cytokines cause thrombosis by increasing platelet aggregation (Jose and Manuel, 2020). Bromelain inhibits platelet aggregation due to its suppression of proinflammatory cytokines (Errasti et al., 2013). It has been shown to prevent thrombosis by inhibiting platelet aggregation, primarily by increasing the plasmin concentration. Thrombosis and coagulation are important for ventilation, and during COVID infections, it causes respiratory problems in patients by reducing respiratory distress (Zalavadiya and Ganatra, 2022).

Effects of bromelain on osteoarthritis

The earliest reported studies investigating bromelain were a series of case reports on 28 patients with moderate or severe rheumatoid or osteoarthritis (Kwatra, 2019). Bromelain is a food supplement that could be used instead of non-steroidal antiinflammatory drugs (NSAIDs) (Brien et al., 2004). It plays a crucial role in the development of arthritis. Bromelain has analgesic properties, which are thought to come from its direct interaction with pain mediators like bradykinin (Zalavadiya and Ganatra, 2022), which promotes smooth muscle contraction and blood vessel dilation (Bryant et al., 2009). The low cost and wide availability of bromelain make it an excellent treatment for arthritis-related rheumatoid arthritis. Given that bromelain significantly decreased pain and stiffness in patients with osteoarthritis (Walker et al., 2002), it may be considered a risk-free alternative. Moreover, studies have shown that bromelain has a positive effect on arthritis (osteoarthritis and rheumatoid arthritis) (Pavan et al., 2012) and increases the treatment effectiveness of degenerative joint pain problems when used in combination with other nutraceuticals, such as turmeric (Conrozier et al., 2014). A clinical study found that bromelain was successful in patients with inflammation due to arthritis and resulted in a substantial or total decrease in swelling of the soft tissue (Grover and Samson, 2016). A combination of bromelain, trypsin, and rutin was compared to diclofenac in 103 patients with osteoarthritis of the knee. After six weeks, both treatments resulted in a significant and similar reduction in the pain and inflammation.

Antibiotic properties of bromelain

Due to its good proteolytic properties and very low systemic cytotoxicity, bromelain has found wide application in the treatment with antibiotics as a substance that increases their activity. It has been shown that antibiotic therapy combined with bromelain reveals increased effectiveness (in contrast to the antibiotic used alone) in many diseases, such as sinusitis, bronchitis, pneumonia, pyelonephritis, thrombophlebitis, perirectal and rectal abscesses, or cutaneous infections caused by Staphylococcus (Neubauer, 1961 and Ryan, 1967). Shahid et al. (2002) showed that a combination of bromelain, rutin, and trypsin, when used as adjunctive therapy in treating sepsis in children, caused the increased activity of antibiotics. The obtained results indicate that using bromelain, rutin, and trypsin combined with antibiotics is an effective adjunct treatment for early improvement in children and adolescents with sepsis.

In respiratory infections such as influenza virus, chronic bronchitis, staph infection, thrombophlebitis, cellulitis, pyelonephritis, and in perirectal and rectal ulcers, sinus infections, and bladder infections, the integration of bromelain and antibiotic treatment

has been shown to be more effective than antibiotics alone (Rathnavelu et al., 2016). Additionally, bromelain increased protein consumption in elderly patients with decreased protein absorption in conjunction with enzymes derived from Aspergillus niger fungus (Glade et al., 2001).

Effects of bromelain on surgery

Bromelain administration prior to surgery can reduce the average number of days for complete pain and post-surgery inflammation disappearance (Mynott et al., 1966 and Tassman et al., 1964). Bromelain appears to be effective in reducing swelling, bruising, and pain in women who have had an episiotomy (Tassman et al., 1964). Bromelain is now commonly used to treat acute inflammation and sports injuries (Zalavadiya and Ganatra, 2022; Brien et al., 2004).

Effects of bromelain on immunogenicity

Bromelain has been recommended as an adjuvant therapeutic approach in the treatment of chronic inflammatory, malignant, and autoimmune diseases (Barth et al., 2005). Moreover, there is evidence that oral therapy with bromelain produces certain analgesic and anti-inflammatory effects in patients with rheumatoid arthritis, which is one of the most common autoimmune diseases (Pavan et al., 2012). In vitro experiments have shown that bromelain has the ability to modulate surface adhesion molecules on T cells, macrophages, and natural killer cells and also induce the secretion of IL-1 β , IL-6, and tumor necrosis factor α (TNF α) by peripheral blood mononuclear cells (PBMCs) (Hale and Haynes, 1992; Lehmann et al., 1996; Desser et al., 1993; Desser et al., 1994; Eckert et al., 1999; Engwerda et al., 2001 a,b). Bromelain can block the Raf-1/extracellular-regulated-kinase-(ERK-) 2 pathways by inhibiting the T cell signal transduction (Mynott et al., 1999). Treatment of cells with bromelain decreases the activation of CD4(+) T cells and reduces the expression of CD25 (Secor et al., 2009). Moreover, there is evidence that oral therapy with bromelain produces certain analgesic and anti-inflammatory effects in patients with rheumatoid arthritis, which is one of the most common autoimmune diseases (Leipner et al., 2002).

Role of bromelain in debridement of burns

The removal of damaged tissue from wounds or second/third-degree burns is termed as debridement. Bromelain applied as a cream (35% bromelain in a lipid base) can be beneficial for debridement of necrotic tissue and acceleration of healing. Bromelain contains escharase, which is responsible for this effect. Escharase is nonproteolytic and has no hydrolytic enzyme activity against normal protein substrate or various glycosaminoglycan substrates. Its activity varies greatly with different preparations (Houck et al., 1983). Enzymatic debridement using bromelain is better than surgical debridement, as surgical incision is painful, non-selective, and exposes the patients to the risk of repeated anesthesia and significant bleeding (Hu et al., 2011; Miller et al., 1992; Sheridan et al., 1994; Salisbury et al., 1990). Pavan et al. (2012) reported that as bromelain facilitates the debridement mechanism and provides improved, faster healing and efficient re-epithelialization, bromelain has been suggested as a valid approach for treating postoperative wounds and relieving discomfort, swelling, and other side effects.

Effects of bromelain on cardiovascular disease

Modern medicine is constantly looking for new treatment strategies to reduce costs and cardiovascular complications, and more importantly, to slow the progression of CVDs (Keziah and Devi, 2018). High hopes are associated with natural compounds of plant origin, usually characterized by effective biological effects with very low systemic side effects, which are often smaller than those of synthetic drugs (Li et al., 2020; Vazhappilly et al., 2019). Systematic studies suggest that bromelain, due to its biological properties, is an attractive compound in treating several CVDs (Manzoor et al., 2016; Rathnavelu et al., 2016; Pavan et al., 2012). Due to its anticoagulant and fibrinolytic properties, bromelain is used for the prevention and treatment of thrombophlebitis (Hikisz and Slomczewska, 2021). Bromelain induces the disruption of thrombus, reduces platelet clumping and blood viscosity (Maurer, 2001). It also prevents or minimizes the severity of angina pectoris and transient ischemic attack (TIA) (Nieper, 1978).

In vivo studies showed that bromelain, due to its excellent fibrinolytic properties, caused the dissolution of atherosclerotic plaque with high efficiency, thereby reducing the risk of atherosclerotic disease. In addition, 73 patients with acute thrombophlebitis given bromelain in combination with painkillers experienced a significant decrease in inflammatory symptoms such as pain, swelling, and high temperature (Seligman, 1969). Bromelain inhibits attacks of angina, resulting in symptomatic relief in hypertension (Maurer, 2001) and can also prevent or minimize transient ischemic attack (TIA). It is useful in the prevention and treatment of thrombophlebitis. It may also break down cholesterol plaques and exert potent fibrinolytic activity. A combination of bromelain and other nutrients protects against ischemia/reperfusion injury in skeletal muscle (Neumayer et al., 2006). Bromelain has been effective in the treatment of CVDs as it is an inhibitor of blood platelet aggregation, thus minimizing the risk of arterial thrombosis and embolism (Heinicke et al., 1972). In recent research, bromelain was found to attenuate the development of allergic airway disease (AAD), while altering CD4+ to CD8+ T lymphocyte populations. From this reduction in AAD outcomes, it was suggested that bromelain may have similar effects in the treatment of human asthma and hypersensitivity disorders (Secor et al., 2005). According to several in vivo studies, bromelain increases the efficiency of the heart, improves arterial flow, decreases arterial dissections, and increases angiogenesis (Juhasz et al., 2008; Neumayer et al., 2006). Previous studies have shown that treatment with bromelain decreases apoptosis and endothelial cell damage in hepatic ischemia (Bahde et al., 2007; Bloomer, 2007) and has also been reported to protect against muscle tissue hepatic encephalopathy injury (Neumayer et al., 2006; Bloomer, 2007; Shibayama, 1986; Chobotova et al., 2010). It increases the permeability of the blood vessel wall that, as a consequence, improves the uptake of oxygen, nutrients, and blood fluidity (Shibayama, 1986; Eckert et al., 1999). When altering populations of CD4+ and CD8+ T lymphocytes, bromelain can lify the development of allergic airway disease (AAD). This progress in AAD suggests that the treatment of human asthma and hyperactivity disorders can be substantially affected by bromelain (Secor et al., 2005).

Anti-cancer properties of bromelain

Recent studies have shown that bromelain has the capacity to modify key pathways that support malignancy. Presumably, the anticancer activity of bromelain is due to its direct impact on cancer cells and their microenvironment, as well as the modulation of immune, inflammatory, and haemostatic systems (Chobotova et al., 2010). Bromelain has been shown to prevent nuclear factor B (NF-B) translocation by G2/M arrest and to contribute to cell death in human epidermoid cancer cells (Baez et al., 2007). The disruption of normal apoptotic functions influences cell transformation and aids in cancer cell development. Cell shrinkage, chromatin condensation, DNA fragmentation, and activation of caspases are involved in the apoptotic process (Ferris and Grandis, 2007). Mitochondrial (intrinsic) or death receptor pathways (extrinsic) typically initiate apoptosis. Bromelain selectively induces apoptosis in cancer cells by upregulating the expression of p53, and the mitochondrial apoptotic pathway is triggered by increased Bax expression and release of cytochrome c (Hussain and Harris, 2007). Bromelain was also shown to inhibit bacterial endotoxin (LPS)-induced NF-κB activity as well as the expression of PGE2 and Cox-2 in human monocytic leukemia and murine microglial cell lines (Bhui et al., 2009).

Bromelain was found to have effective anticancer activity against breast cancer cells - MCF7, MDA-MB231, and GI-101A. Bromelain not only inhibited tumor cell proliferation and colony formation but also influenced several critical biochemical processes, ultimately leading to their death by apoptosis/autophagy (Dhandayuthapanit et al., 2012; Raeisi et al., 2019; Bhui et al., 2010). Excellent information on the complexity of molecular activities of bromelain in modulating the expression of key genes, including proliferation, migration, and DNA integrity, was provided by the studies of Fouz et al. (2014). Undoubtedly, the primary mechanism of action of bromelain in breast cancer cells is the induction of apoptosis. Programmed cell death is carried out mainly through the mitochondrial route, with a bromelain-dependent increase in the activity of caspases 3 and 9. Analysis of gene expression showed that bromelain also increased the activity of proapoptotic proteins from the Bcl-2 family, with a simultaneous decrease in the expression of their anti-apoptotic partners. At the same time, in addition to inducing cancer cell death, enzymatic degradation of cell DNA and inhibition of their cell cycle in the G2/M phase were observed due to the activation of cell cycle inhibitors (Dhandayuthapanit et al., 2012; Raeisi et al., 2019; Bhui et al., 2011). It is worth noting that several reports indicate that bromelain is effective in inhibiting the development of other types of cancer - soft tissue sarcoma (Dong et al., 2019), lung (Bhatnagar et al., 2014), and oral cancer cells (Lee et al., 2019). An innovative application of bromelain in available chemotherapy was proposed by Mekkawy et al. (2020).

Bromelain as anti-inflammatory

Bromelain was prescribed as an adjunctive treatment strategy for chronic inflammatory, malignant, and autoimmune disorders and was reported to increase the treatment efficiency in the diseases (Pavan et al., 2012; Kargutkar and Brijesh, 2018). In the treatment of patients' respiratory problems and hyperactivity disorders, bromelain, as a protease itself, is thought to produce similar effects to those found with other proteases (Secor et al., 2005). Bromelain has been shown to produce both analgesic and anti-inflammatory effects in patients with rheumatoid arthritis when taken orally (Leipner et al., 2001). Bromelain also reduced the cell-damaging effect of advanced glycation products (AGEs) through the degradation of their proteolytic receptors and, consequently, regulated the inflammation. Regarding its analgesic properties, bromelain administration prior to surgery will also promote a more prompt dissipation of discomfort and pain in the post-operative period. These analgesic properties also mean that in women who underwent episiotomy, bromelain can be useful in reducing swelling, bleeding, and discomfort (Stopper et al., 2003; Lee et al., 2018).

Colonic inflammation

Bromelain can reduce the severity of colonic inflammation (Hale, 2004; Hale et al., 2005) and bromelain's anti-inflammatory function also results in proteolytic action by eradicating cell surface receptors that are implicated in leukocyte defects and activation (Hale et al., 2010). Bromelain also differs in the release of other chemokines, thus decreasing the incidence and frequency of persistent colitis. Bromelain is considered to be an innovative treatment for intestinal inflammatory disease (Onken et al., 2008). Patients with ulcerative colitis have also shown a significant symptomatic improvement following application of bromelain (Kane and Goldberg, 2000), and it has also been stated that the release of some chemokines has been impaired, thus reducing the incidence and severity of colitis (Manzoor et al., 2016).

Sinus inflammation

Bromelain has been documented to be beneficial in the treatment of sinusitis and can be used to manage the infection (Baez et al., 2007). Once more, the low cost of bromelain makes it an attractive alternative to established medicinal treatments. In children with serious sinus infections, treatment with bromelain has been reported to minimize the duration of symptoms and facilitate complete recovery compared with normal treatment regimens (Selzer et al., 1967). Patients with sinusitis have reported full relief from breathing problems and nasal mucosal infection (Ahle and Hamlet, 1987).

CONCLUSION

Pineapple has become one of the most profitable fruits in recent years owing to its unique taste and aroma, abundant volatile compounds, and nutritional values. The benefits of pineapple consumption are unquestionable as it is a highly nutritious fruit with numerous health benefits, a source of functional food ingredients which possess antimicrobial, antioxidant, and other therapeutic characteristics. Naturally, pineapples will not replace the foundations of healthy eating, but they certainly will supply a number of essential nutrients providing economic potential for farmers, entrepreneurs, and consumers. This review also suggests that bromelain, a proteolytic enzyme, is a promising candidate as an effective health supplement in treating cardiovascular diseases, blood coagulation and fibrinolysis, debridement of burns, other inflammation-related diseases, and many types of cancer. It has a wide range of therapeutic benefits resulting from biochemical and pharmacological properties, generating a substantial increase in interest among scientists and the pharmaceutical and food industries.

REFERENCES

- Ahle, N. W., & Hamlet, M. P. (1987). Enzymatic frostbite eschar debridement by bromelain. Annals of Emergency Medicine, 16, 1063–1065.
- Ali, A. A., Milala, M. A., & Gulani, I. A. (2015). Antimicrobial effects of crude bromelain extracted from pineapple fruit (Ananas comosus (Linn.) Merr.). Advances in Biochemistry, 3, 1-4.
- Baez, R., Lopes, M. T., Salas, C. E., & Hernandez, M. (2007). In vivo antitumoral activity of stem pineapple (Ananas comosus) bromelain. Planta Medica, 73, 1377-1383.
- Bahde, R., Palmes, D., Minin, E., Stratmann, U., Diller, R., Haier, J., & Spiegel, H. U. (2007). Bromelain ameliorates hepatic microcirculation after warm ischemia. Journal of Surgical Research, 139, 88–96.
- Barth, H., Guseo, A., & Klein, R. (2005). In vitro study on the immunological effect of bromelain and trypsin on mononuclear cells from humans. European Journal of Medical Research, 10, 325–331.
- Baruwa, O. I. (2013). Profitability and constraints of pineapple production in Osun State, Nigeria. Journal of Horticultural Research, 21, 59-64.
- Bhatnagar, P., Patnaik, S., Srivastava, A. K, Mudiam, M. K. R., Shukla, Y., Panda, A. K., Pant, A. B., Kumar, P., & Gupta, K. C. (2014). Anti-cancer activity of bromelain nanoparticles by oral administration. Journal of Biomedical Nanotechnology, 10, 3558–3575.
- Bhui, K., Prasad, S., George, J., & Shukla, Y. (2009). Bromelain inhibits COX-2 expression by blocking the activation of MAPK regulated NF-kappa B against skin tumor-initiation triggering mitochondrial death pathway. Cancer Letters, 282, 167–176.
- Bhui, K., Tyagi, S., Prakash, B., & Shukla, Y. (2010). Pineapple bromelain induces autophagy, facilitating apoptotic response in mammary carcinoma cells. BioFactors, 36, 474–482.
- Bhui, K., Tyagi, S., Srivastava, A. K., Singh, M., Roy, P., Singh, R., & Shukla, Y. (2011). Bromelain inhibits nuclear factor kappa-B translocation, driving human epidermoid carcinoma A431 and melanoma A375 cells through G2/M arrest to apoptosis. Molecular Carcinogenesis, 51, 231–243.
- Bloomer, R. J. (2007). The role of nutritional supplements in the prevention and treatment of resistance exercise-induced skeletal muscle injury. Sports Medicine, 37, 519–532.
- Brien, S., Lewith, G., Walker, A., Hicks, S. M., & Middleton, D. (2004). Bromelain as a treatment for osteoarthritis, a review of clinical studies. Evidence-Based Complementary and Alternative Medicine, 1, 251–257.
- Bryant, C. D., Chand, H. P., Zhang, J., Wiltshire, T., Tarantino, L. M., & Palmer, A. A. (2009). A major QTL on chromosome 11 influences psychostimulant and opoid sensitivity in mice. Genes Brain Behaviour, 8, 795-805.
- Chapple, I. L. C., Milward, M. R., Ling-Mountford, N., Weston, P., Carter, K., Askey, K.,... Dallal, G. E. (2012). Adjunctive daily supplementation with encapsulated fruit, vegetable and berry juice powder concentrates and clinical periodontal outcomes : A double-blind RCT. Journal of Clinical Periodontology, 39, 62–72. Chobotova, K., Vernallis, A. B., & Majid, F. A. (2010). Bromelain's activity and potential as an anti-cancer agent : Current evidence and perspectives. Cancer Letters, 290, 148–156.
- Conrozier, T., Mathieu, P., Bonjean, M., Marc, J.F., Renevier, J.L., & Balblanc, J.C. (2014). A complex of three natural antiinflammatory agents provides relief of osteoarthritis pain. Alternative Therapies in Health & Medicine, 20(1), 32.
- Darshini, Jr., Terdal, D., & Jagadesh, S.L. (2021). Utilization of pineapple pomace powder as a functional ingredient in bread. Journal of Pharmacognosy and Phytochemistry, 10, 322-327.

- Debnath, P., Dey, P., Chanda, A., & Bhakta, T. (2012). A survey on pineapple and its medicinal value. Scholars Academic Journal of Pharmacy, 1, 24-29.
- Desser, L., Rehberger, A., & Paukovits, W. (1994). Proteolytic enzymes and amylase induce cytokine production in human peripheral blood mononuclear cells in vitro. Cancer Biotherapy, 9, 253-263.
- Desser, L., Rehberger, A., Kokron, E., & Paukovits, W. (1993). Cytokine synthesis in human peripheral blood mononuclear cells after oral administration of polyenzyme preparations. Oncology, 50, 403-407.
- Devi, L. K., Karoulia, S., & Chaudhary, N. (2016). Preparation of high dietary fib er cookies from pineapple (Ananas comosus) pomace. International Journal of Science and Research, 5, 1368-1372.
- Dhandayuthapani, S., Perez, H. D., Paroulek, A., Chinnakkannu, P., Kandalam, U., Jaffe, M., & Rathinavelu, A. (2012). Bromelaininduced apoptosis in GI-101A breast cancer cells. Journal of Medicinal Food, 15, 344–349.
- Dong, L., Badar, S., Pillai, K., Akhter, J., Mekkawy, A. H., & Morris, D. L. (2019). Bromelain and N-acetylcysteine as therapeutic agents for soft tissue sarcoma. International Journal of Clinical and Experimental Medicine, 12(12), 13311-13324.
- Eckert, K., Grabowska, E., Stange, R., Schneider, U., Eschmann, K., & Maurer, H. R. (1999). Effects of oral bromelain administration on the impaired immune cytotoxicity of mononuclear cells from mammary tumor patients. Oncology Reports, 6, 1191-1199.
- Engwerda, C. R., Andrew, D., Ladhams, A., & Mynott, T. L. (2001). Bromelain modulates T cell and B cell immune responses in vitro and in vivo. Cellular Immunology, 210, 66-75.
- Engwerda, C. R., Andrew, D., Murphy, M., & Mynott, T. L. (2001a). Bromelain activates murine macrophages and natural killer cells in vitro. Cellular Immunology, 210, 5-10.
- Errasti, M. E., Caffini, N. O., Pelzer, L. E., & Rotelli, A. E. (2013). Anti-inflammatory activity of Bromelia hieronymi, comparison with bromelain. Planta Medica, 79, 207-213.
- Faisal, M. M., Hossa, F. M. M., Rahman, S., Bashar, A. B. M. A., Hossan, S., & Rahmatullah, M. (2014). Effect of methanolic extract of Ananas comosus leaves on glucose tolerance and acetic acid -induced pain in Swiss albino mice. World Journal of Pharmaceutical Research, 3, 24-34.
- Fan, P., Gao, Y., Zheng, M., Xu, T., Schoenhagen, P., & Jin, Z. (2018). Recent progress and market analysis of anticoagulant drugs. Journal of Thoracic Disease, 10(3), 2011-2025.
- Farid, M. H., & Shaheen, A. (2015). Nutritional value and medicinal benefits of pineapple. International Journal of Nutrition and Food Sciences, 4, 84-88.
- Ferris, R. L., & Grandis, J. R. (2007). NF-kB gene signatures and p53 mutations in head and neck squamous cell carcinoma. Clinical Cancer Research, 13, 5663–5664.
- Fouz, N., Amid, A., & Hashim, Y. Z. H. Y. (2014). Gene expression analysis in MCF-7 breast cancer cells treated with recombinant bromelain. Applied Biochemistry and Biotechnology, 173, 1618–1639.
- Glade, M. J., Kendra, D., & Kaminski, M. V., Jr. (2001). Improvement in protein utilization in nursing home patients on tube feeding supplemented with an enzyme product derived from Aspergillus niger and bromelain. Nutrition, 17, 348-350.
- Grover, A. K., & Samson, S. E. (2016). Benefits of antioxidant supplements for knee osteoarthritis: Rationale and reality. Nutrition Journal, 15. Doi: 10.1186/s12937-015-0115-z.
- Hale, L. P. (2004). Proteolytic activity and immunogenicity of oral bromelain within the gastrointestinal tract of mice. International Immunopharmacology, 4, 255–264.

- Hale, L. P., & Haynes, B. F. (1992). Bromelain treatment of human T cells removes CD44, CD45RA, E2/MIC2, CD6, CD7, CD8, and Leu 8/LAM1 surface molecules and markedly enhances CD2-mediated T cell activation. Journal of Immunology, 149, 3809-3816.
- Hale, L. P., Greer, P. K., Trinh, C. T., & James, C. L. (2005). Proteinase activity and stability of natural bromelain preparations. International Immunopharmacology, 5, 783–793.
- Hale, L. P., Chichlowski, M., Trinh, C. T., & Greer, P. K. (2010). Dietary supplementation with fresh pineapple juice decreases inflammation and colonic neoplasia in IL-10-deficient mice with colitis. Inflammatory Bowel Diseases, 16, 2012–2021.
- Heinicke, R. M., van der Wal, L., & Yokoyama, M. (1972). Effect of bromelain (Ananase) on human platelet aggregation. Experientia, 28, 844–845.
- Hemalatha, R., & Anbuselvi, S. (2013). Physicochemical constituents of pineapple pulp and waste. Journal of Chemistry and Pharmaceutical Research, 5, 1577-1584. Hikisz, P., & Slomczewska, J. B. (2021). Beneficial properties of bromelain. Nutrients, 13, 1-36.
- Hossain, M. F., Akhtar, S., & Anwar, M. (2015). Nutritional value and medicinal benefits of pineapple. International Journal of Nutrition and Food Sciences, 4, 84-88.
- Houck, J. C., Chang, C. M., & Klein, G. (1983). Isolation of an effective debriding agent from the stems of pineapple plants. International Journal of Tissue Reactions, 5, 125-134.
- Hu, H., & Zhao, Q. (2018). Optimization extraction and functional properties of soluble dietary fiber from pineapple pomace obtained by shear homogenization-assisted extraction. RSC Advances, 8, 41117-41130.
- Hu, W., Wang, A. M., Wu, S. Y., Zhang, B., Liu, S., Gou, Y. B., & Wang, J. M. (2011). Debriding effect of bromelain on firearm wounds in pigs. Journal of Trauma and Acute Care Surgery, 71, 966-972.
- Huang, Y. L., Chow, C. J., & Fang, Y. J. (2011). Preparation and physicochemical properties of fiber-rich fraction from pineapple peels as a potential ingredient. Journal of Food and Drug Analysis, 19, 318-323.
- Hussain, S. P., & Harris, C. C. (2007). Inflammation and cancer: an ancient link with novel potentials. International Journal of Cancer, 121, 2373-2380.
- Jose, R. J. and Manuel, A. 2020. Covid-19 cytokine storm, the interplay between inflammation and coagulation. The Lancet Respiratory Medicine, 8, 46-47.
- Joy, P. P. 2010. Benefits and uses of pineapple. Pineapple Research Station, Kerala Agricultur al University, Kerala, India.
- Joy, P.P. and Abraham, M. 2013. Fruits, benefits, processing, preservation and pineapple recipes. Technical bulletin. Pineapple Research Station, Kerala Agricultural University, Kerala, India.
- Juhasz, B., Thirunavukkarasu, M., Pant, R., Zhan, L., Penumathsa, S. V., Secor, E. R., Srivastava, S. et al. 2008. Bromelain induces cardioprotection against ischemia-reperfusion injury through Akt/FOXO pathway in rat myocardium. American Journal of Physiology: Heart and Circulatory Physiology, 294, H1365-H1370.
- Kane, S. and Goldberg, M. J. 2000. Use of bromelain for mild ulcerative colitis. Annals of Internal Medicine, 132, 680.
- Kargutkar, S. and Brijesh, S. 2018. Anti-inflammatory evaluation and characterization of leaf extract of Ananas comosus. Inflammopharmacology, 26, 469–477.
- Keziah, S. M. and Devi, C. S. 2018. Focalization of thrombosis and therapeutic perspectives, A memoir. Oriental Pharmacy and Experimental Medicine, 18, 281–298.
- Khalid, N., Suleria, H. A. R. and Ahmed, I. 2015. Pineapple juice. In Handbook of Functional Beverages and Human Health (pp. 489-400). CRC Press, Boca Raton, United States.

Kumar, A. 2021. Utilization of bioactive components present in pineapple waste. The Pharma Innovation Journal, 10, 954-961.

- Kwatra, B. 2019. A review on potential properties and therapeutic applications of bromelain. World Journal of Pharmacy and Pharmaceutical Sciences, 8, 488-500.
- Lee, J. H., Lee, J. B., Lee, J. T., Park, H. R. and Kim, J. B. 2018. Medicinal effects of bromelain (Ananas comosus) targeting oral environment as an anti oxidant and anti-inflammatory agent. Journal of Food and Nutrition Research, 6, 773–784.
- Lee, J. H., Lee, J. T., Park, H. R., and Kim, J. B. 2019. The potential use of bromelain as a natural oral medicine having anticarcinogenic activities. Food Science & Nutrition, 7, 1656–1667.
- Lehmann, P. V. (1996). Immunomodulation by proteolytic enzymes. Nephrology Dialysis Transplantation, 11, 953-955.
- Leipner, J., Iten, F., & Saller, R. (2001). Therapy with proteolytic enzymes in rheumatic disorders. BioDrugs, 15, 779–789.
- Li, H., Sureda, A., Devkota, H. P., Pittala, V., Barreca, D., Silva, A. S., Tewari, D., Xu, S., & Nabavi, S. M. (2020). Curcumin, the golden spice in treating cardiovascular diseases. Biotechnology Advances Journal, 38, 107343.
- Li, T., Shen, P., Liu, W., Liu, C., Liang, R., Yan, N., & Chen, J. (2014). Major polyphenolics in pineapple peels and their antioxidant interactions. International Journal of Food Prop, 17, 1805-1817.
- Manzoor, Z., Nawaz, A., Mukhtar, H., & Haq, I. (2016). Bromelain, Methods of extraction, purification and therapeutic applications. Brazilian Archives of Biology and Technology, 59. https://doi.org/10.1590/1678-4324-2016150010
- Maurer, H. R. (2001). Bromelain, Biochemistry, pharmacology and medical use. Experientia, 58, 1234–1245.
- Mekkawy, M. H., Fahmy, H. A., Nada, A. S., & Ali, O. S. (2020). Study of the radiosensitizing and radioprotective efficacy of bromelain (a pineapple extract), In vitro and in vivo. Integrative Cancer Therapy, 19, 1534735420950468.
- Miller, J. G., Carruthers, H. R., & Burd, D. A. R. (1992). An algorithmic approach to the management of cutaneous burns. Burns, 18, 200-211.
- Muir, J.G., Rose, R., Rosella, O., Liels, K., Barrett, J.S., Shepherd, S.J., & Gibson, P.R. (2009). Measurement of Short-Chain Carbohydrates in Common Australian Vegetables and Fruits by High-Performance Liquid Chromatography (HPLC). Journal of Agricultural and Food Chemistry, 57, 554–565. https://doi.org/10.1021/jf802700e.
- Mynott T. L., Luke, R. K. J., & Chandler, D. S. (1966). Oral administration of protease inhibits enterotoxigenic Escherichia coli receptor activity in piglet small intestine. Gut, 38, 28-32.
- Mynott, T. L., Ladhams, A., Scarmato, P., & Engwerda, C. R. (1999). Bromelain, from pineapple stems, proteolytically blocks activation of extracellular regulated kinase-2 in T cells. Journal of Immunology, 163, 2568–2575.
- Nakthong, N., Wongsagonsup, R., & Amornsakchai, T. (2017). Characteristics and potential utilizations of starch from pineapple stem waste. Industrial Crops and Products, 105, 74–82.
- Neubauer, R. A. (1961). A plant protease for potentiation of and possible replacement of antibiotics. Experimental Medicine and Surgery, 19, 143-160.
- Neumayer, C., Fügl, A., Nanobashvili, J., Blumer, R., Punz, A., Gruber, H., Polterauer, P., & Huk, I. (2006). Combined enzymatic and antioxidative treatment reduces ischemia-reperfusion injury in rabbit skeletal muscle. Journal of Surgical Research, 133, 150–158.
- Nieper, H. A. (1978). Effect of bromelain on coronary heart disease and angina pectoris. Acta Medica Empirica, 5, 274-278. Onken, J. E., Greer, P. K., Calingaert, B., and Hale, L. P. (2008). Bromelain treatment decreases secretion of pro-inflammatory cytokines and chemokines by colon biopsies in vitro. Clinical Immunology, 126, 345–352.

- Pavan, R., Jain, S., Shraddha, and Kumar, A. (2012). Properties and therapeutic application of bromelain : A review. Biotechnology Research International, 1-6. https://doi.org/10.1155/2012/976203
- Perwez Hussain, S., and Harris, C. C. (2007). Inflammation and cancer : An ancient link with novel potentials. International Journal of Cancer, 121(10), 2373–2380.
- Raeisi, F., Raeisi, E., Heidarian, E., Shahbazi-Gahroui, D., and Lemoigne, Y. (2019). Bromelain inhibitory effect on colony formation : An in vitro study on human AGS, PC3, and MCF7 cancer cells. Journal of Medical Signals and Sensors, 9(4), 267–273.
- Rahmatullah, M., Mukti, I. J., Haque, A. K. M. F., Mollik, M. A. H., Parvin, K., Jahan, R., Chowdhury, M. H., and Rahman, T. (2009). An ethno botanical survey and pharmacological evaluation of medicinal plants used by the Garo tribal community living in Netrakona district, Bangladesh. Advances in Natural and Applied Sciences, 3(3), 402-18.
- Rathnavelu, V., Alitheen, N. B., Sohila, S., Kanagesan, S., and Ramesh, R. (2016). Potential role of bromelain in clinical and therapeutic applications. Biomedical Reports, 5(3), 283-288.
- Ryan, R. E. (1967). A double-blind clinical evaluation of bromelains in the treatment of acute sinusitis. Headache, 7(4), 13-17.
- Saikia, B. (2006). Ethno medicinal plants from Gohpur of Sonitpur district, Assam. Indian Journal of Traditional Knowledge, 5(4), 529-30.
- Salisbury, R. E. (1990). In-thermal burns. In: Plastic Surgery, Vol.1 (Ed. J.C. McCarthy). Saunders, Philadelphia. pp.787-830.
- Salve, R. S., and Ray, S. (2020). Comprehensive study of different extraction methods of extracting bioactive compounds from pineapple waste : A review. The Pharma Innovation Journal, 9(4), 327-340.
- Secor Jr, E. R., Singh, A., Guernsey, L. A., et al. (2009). Bromelain treatment reduces CD25 expression on activated CD4+ T cells in vitro. International Immunopharmacology, 9(3), 340-346.
- Secor, E. R., Carson, W. F., Cloutier, M. M., Guernsey, L. A., Schramm, C. M., Wu, C. A., & Thrall, R. S. (2005). Bromelain exerts anti-inflammatory effects in an ovalbumin-induced murine model of allergic airway disease. Cellular Immunology, 237, 68–75.
- Seligman, B. (1969). Oral bromelains as adjuncts in the treatment of acute thrombophlebitis. Angiology, 20, 22-26.
- Selzer, A., Kelly, J. J., Vannitamby, M., Walker, P., Gerbode, F., & Kerth, W. J. (1967). The syndrome of mitral insufficiency due to isolated rupture of the chordae tendineae. The American Journal of Medicine, 43, 822–836.
- Shahid, S. K., Turakhia, N. H., Kundra, M., Shanbag, P., Daftary, G. V., & Schiess, W. (2002). Efficacy and safety of phlogenzym-A protease formulation, in sepsis in children. Journal of Association Physicians India, 50, 527-531.
- Sheridan, R. L., Tompkins, R. G., & Burke, J. F. (1994). Management of burn wounds with prompt excision and immediate closure. Journal of Intensive Care Medicine, 237, 68-75.
- Shibayama, Y. (1986). An experimental study into the cause of acute haemorrhagic gastritis in cirrhosis. The Journal of Pathology, 149, 307–313.
- Stopper, H., Schinzel, R., Sebekova, K., & Heidland, A. (2003). Genotoxicity of advanced glycation end products in mammalian cells. Cancer Letters, 190, 151–156.
- Tang, P. L., & Hassan, O. (2020). Bioconversion of ferulic acid attained from pineapple peels and pineapple crown leaves into vanillic acid and vanillin by Aspergillus niger I-1472. BMC Chemistry, 14(7). https://doi.org/10.1186/s13065-020-0663-y.
- Tassman, G. C., Zafran, J. N., & Zayon, G. M. (1964). Evaluation of a plate proteolytic enzyme for the control of inflammation and pain. Journal of Dental Medicine, 19, 73-77.

- Vazhappilly, C. G., Ansari, S. A., Al-Jaleeli, R., Al-Azawi, A. M., Ramadan, W. S., Menon, V., Hodeify, R., Siddiqui, S. S., Merheb, M., Matar, R., et al. (2019). Role of flavonoids in thrombotic, cardiovascular and inflammatory diseases. Inflammopharmacology, 27, 863-869.
- Walker, A. F., Bundy, R., Hicks, S. M., & Middleton, R. W. (2002). Bromelain reduces mild acute knee pain and improves well -being in a dose -dependent fashion in an open study of otherwise healthy adults. Phytomedicine, 9, 681–686.
- Zalavadiya, I., & Ganatra, T. (2022). Bromelain's properties and therapeutic applications : A review. GIS Science Journal, 9, 2025-2032.