Ananas comosus (L.) Merr., Bromeliaceae
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Introduction

Ananas comosus, otherwise known as the pineapple, belongs to the family Bromeliaceae. It is also known as the piña by the Spanish, abacaxi by the Portuguese, ananas by the Dutch and French, as well as nanas in Southern Asia and the East Indies (Morton, 1987). While the family Bromeliaceae includes approximately 2,000 species, the genus Ananas consists of 2 species: A. macrodontes and A. comosus. Of these 2 species, the more common species is A. comosus (Sanewski 2011) (Figure 1). It is native to Central and South America but is grown in other areas such as Hawaii, South Africa, China, India, Kenya, Thailand, Malaysia, and the Philippines (Tochi et al. 2008). Bromelain is a proteolytic enzyme obtained from the stem of the pineapple that exhibits therapeutic properties such as preventing malignant cell growth and platelet aggregation, thrombus formation, anti-inflammatory and wound-healing action, and increased permeability of drugs (Maurer 2001). Other constituents besides stem bromelain include fruit bromelain, ananain, and comosain (Rowan, Buttle, and Barrett 1990).

Botanical Description

Pineapple is indigenous to the tropical and subtropical regions, especially southern Brazil and Paraguay. It is essential for the pineapple to grow in these regions due to the favorable temperatures ranging from 65°F to 95°F; low temperatures can potentially delay growth as well as cause the fruit to taste acidic. In addition, high elevations can also induce acidity. The
Volatile compound | Aroma
---|---
4-hydroxy-2,5-dimethyl-3(2H)-furanone | Sweet, caramel, fruity, burnt. Strawberry and pineapple at low conc
4-methoxy-2,5-dimethyl-3(2H)-furanone | Sweet, caramel, fruity, musty, savoury
Ethyl 2-methyl butanoate | Green, apple, fruity
Methyl 2-methyl butanoate | Fruity, apple
Methyl butanoate | Fruity, apple
Ethyl 3-(methyl thio) propanoate | Pineapple
Methyl 3-(methyl thio) propanoate | Sulfurous, pineapple
Ethyl 2-methyl propanoate | Sweet, fruity
Methyl 3-propanoate | Fruity, pineapple
Methyl propanoate | Fruity, pineapple
octalactone | Creamy, coconut
decalactone | Sweet, coconut, peachy
hexalactone | Sweet, creamy, coconut, herbaceous
vanillin | Vanilla
1-(E,Z)-3,5-undecatriene | Fresh, green, pineapple
octanol | Citrus
Methyl hexanoate | Fruity, pineapple
Ethyl hexanoate | Fruity, pineapple
3-methylbutyl acetate | Fresh, fruity. Banana and pear at low conc

**Table 1. Major compounds in pineapple aroma.** This is a list of the compounds that give the pineapple its sense of aroma and flavor (Source: Sanewski 2011).

The primary pollinator of the pineapple plant is the hummingbird. Hard seeds can be present in the fruit if the flowers are pollinated; however, if they are not, few seeds will be present (Morton 1987). There are several pests and diseases that can infect the pineapple including mealy bugs and rats. Bud rot, fruit core rot, and heart rot are diseases that are also common. Bud rot is rotting of the stem and the eventual death of the plant while fruit core rot is seen in fruits that turn brown in the inside and are smaller in size. Heart rot epiphytes grow on other plants and objects. The pineapple belongs to the terrestrial branch (Okihiro 2009, 76).

The pineapple plant is an herbaceous perennial ranging from 2.5 to 5 ft high with a short stem of pointy, waxy green leaves that are 20 to 72 in. long (Pineapple 1996). The stem begins to elongate near the apex during blooming time and small purple or red flowers appear. Known as the “crown” of the pineapple, this clump of firm, short leaves grows after the stem develops. Developing from the flowers is the cone shaped fruit that is 12 or more in. in height (Morton 1987).

The pineapple fruit is composed of many small fruitlets, which determine the pineapple’s size. In general, fruit size can be as little as 100 g to as much as 7 kg. Most pineapples range from yellow to orange skin; however, there are also cream, pink, and red skinned pineapples. The yellow, green, and red skin color is due to carotenoids, remaining chlorophyll, and anthocyanins, respectively. The yellow flesh color is also a result of carotenoids similar to the skin. The sweet flavor of the pineapple is because of the sucrose content. However, it is important to note that the smaller the fruit, the sweeter it is. Flesh and skin volatile compounds establish the pineapple’s distinctive aroma (Sanewski 2011). **Table 1** lists some of the major compounds that contribute to the pineapple’s aroma and flavor.
is when the leaves begin to redden and the edges become brown and wilt. To avoid bud rot, the plant should not be cut in a way as to allow fungus to infect it. Controlling mealy bug invasion and removing the crown in the rainy season can prevent fruit core rot. In addition, proper drainage and elevation of the plant can ensure safety from heart rot (Pineapple: Pests and Diseases 2011).

Five common pineapple cultivars include the ‘Perola’, ‘Queen’, ‘Manzana’, ‘Red Spanish’, and ‘Cayenne’ illustrated in Figure 1 (Sanewski 2011). The ‘Perola’ is a yellow, large, and cylindrical pineapple with no spines and is popular in Venezuela and Columbia. The ‘Queen’ is prevalent in South Africa, Queensland, and the Philippines. It is cone-shaped, golden-yellow with more fragrance and flavor than other cultivars. However, it matures early, requires thinning, and has a low yield. A minor cultivar in Columbia is the ‘Manzana.’ In addition to these is the popular cultivar in Florida, the West Indies, Venezuela, and Mexico known as the ‘Red Spanish.’ Resistant to rotting, it ranges from having orange to red skin and represents 85% of commercial planting in Puerto Rico. Due to its cone-shaped form, orange skin, mildly acidic flavor, and canning properties, the ‘Cayenne’ is known worldwide despite its lack of ability to withstand disease (Morton 1987).

Traditional uses

Traditional medicinal uses

The pineapple has been used traditionally for a variety of ailments particularly in Central and South America (Taussig and Batkin 1988). The juice was not only consumed as a diuretic but also gargled for sore throats and to prevent seasickness. Because unripe pineapples are poisonous, it was traditionally taken for abortion and removal of intestinal worms. The pineapple root in the form of dried powder was used to heal edema in Africa while the rind was topically applied to fractures and hemorrhoids. Even today, compounds in the pineapple are commonly used to treat edema as well as to reduce pain and inflammation. In Panama, the leaf juice was used to promote menstruation, remove worms, and cleanse the intestine (Morton 1987).

Food uses

Pineapples are also commonly used in food. The flesh of the fruit can be eaten alone, in desserts, salads, pies, cakes, puddings, or made into sauces. Malayans add the pineapple in their curries while the Filipinos use extracted pulp in a dessert called nata de piña. The pineapple cannot be frozen because the flavors are subsequently extinguished. Because pineapples contain a proteolytic enzyme called bromelain, either the pineapple or the enzyme is commonly used as a meat tenderizer to break down protein. The canning of pineapples has significantly increased its demand and made it one of the leading fruits worldwide. Hawaii alone supplied 70% of the world’s canned pineapple for about a decade starting in 1970 until the company, Dole, transferred its operation to the Philippines due to increased production costs (Morton 1987).

Ethnobotanical uses

Native Americans cultivated the pineapple in Mexico and the West Indies before the arrival of Christopher Columbus. Columbus and his crewmembers saw the pineapple for the first time in 1493 in Guadeloupe. Inhabitants of the Caribbean set pineapples outside their homes to represent friendship and hospitality. As a result, Europeans in Spain and England
The pineapple’s flowers were commonly used as a source for flower arrangements (Source: Sanewski 2011). Illustrated the fruit in carvings on doorways (Morton 1987). Pineapple ware such as pots, mugs, cups, and bowls were even sold in colonial America (Okihiro 2009, 164).

In addition to its medicinal value, the pineapple was used for many other applications. The juice was used as a cleanser for knife blades and scrubbing boat decks (Morton 1987). The flowers of the plant could be used as an ornamental or flower arrangement illustrated in Figure 2. The fruit itself was also used as a means to decorate the home. For example, George and Martha Washington adorned their wall lamp with a pineapple on top illustrated in Figure 3 (Okihiro 2009, 166). In the Philippines, the natives extract fiber from the leaves in order to make fabric (Pineapple: Pests and Pesticides, 2011).

**Harvesting**

Pineapple harvesting requires an enormous amount of experience; in addition to size and color, other factors must be taken into account. Before the pineapple reaches maturity, starch is converted into sugars in a span of a few days. During the summer, crop is harvested when the skin shows a light green color because sugar content and volatile flavors begin to develop. However, the winter crop takes approximately one month longer to reach maturity; therefore, fruits are harvested when the base is covered with a light yellow pigment. In spite of this, winter pineapple is more acidic and has lower sugar content than summer pineapple. In addition, if the fruit is overripe, it is not as flavorful and is more likely to perish. Usually after the stem is cut, a 3% solution of benzoic acid is applied to the stem in order to protect the fruit from rain and dew. Pineapples should not be stored for more than six weeks although storage life can be extended by immersing the fruit in a wax solution with fungicide (Morton 1987).
Figure 4. Structure of bromelain. This illustrates the complete structure of the 2 oligosaccharides in bromelain. (Source: Ishihara et al. 1979)

Chemistry and Pharmacology

One of the main constituents in the pineapple is a cysteine protease known as stem bromelain (Figure 4). It is an aqueous extract from the stem and sometimes fruit of pineapples that is prepared by centrifugation, ultrafiltration, and lyophilization. This complex process yields a yellow powder. However, when in an aqueous solution, bromelain can degenerate due to self-digestion; therefore, α₂-macroglobulin, a plasma protein, is added to prevent deterioration (Maurer 2001). The majority of research has been conducted on bromelain and many of the therapeutic effects are attributed to it. However, there are also other cysteine proteases such as fruit bromelain also known as bromelin, ananain, and comosain. Ananain and comosain are found in the stem along with stem bromelain. Bromelain is a proteolytic enzyme comprised of a mixture of components including peroxidase, acid phosphatase, protease inhibitors, and organically bound calcium (Orsini 2006). Used as complementary medication to glucocorticoids, antirheumatics, and immunomodulatory agents, proteolytic enzymes’ low toxicity provides the capability for the treatment of inflammatory conditions. They consist of a broad range of therapeutic effects such as antiedematous, anti-inflammatory, antithrombotic, and fibrinolytic activities. These proteolytic enzymes also help regulate immune cells and cytokine production as well as functions of adhesion molecules on blood and endothelial cells (Maurer 2001). Table 2 lists the components found in Ananas comosus.

Biological Activity

In vitro

Pineapple’s main therapeutic component, bromelain, has been studied in many in vitro and in vivo studies. In vitro studies have found that not only is bromelain degraded in blood plasma by protease inhibitors, but oral administration may facilitate bromelain in preserving its proteolytic activity (Orsini 2006).

Researchers stimulated mouse ileum to induce contractions and then administered bromelain, resulting in the inhibition of contractions. This suggests bromelain inhibits intestinal motility. This discovery could help bromelain become a leading drug in regulating intestinal motility in intestinal inflammation as well as diabetes (Borrelli et al. 2011). Bromelain also hinders tumor growth by 90% in Lewis lung carcinoma, YC-lymphoma, and MCA-1 ascitic tumor even after destruction of the proteolytic activity by heat. This indicates that another factor is responsible for the anticancer effect observed in pineapple (Taussig and Batkin 1988). Bromelain also reduces platelet adhesion to endothelial cells as well as platelet aggregation. In addition, it has the ability to stimulate plasminogen to produce plasmin, which can then cleave fibrin and decrease fibrin levels (Maurer 2001).
Bromelain also has an antisecretory effect. Diarrhea is caused by the activation of the cAMP, cGMP, or calcium-dependent signaling pathways in the large intestine. Using rabbit ileum, researchers found that bromelain prevents changes in these pathways (Mynott et al. 1997).

**In vivo**

A common question is whether bromelain is absorbed after oral ingestion; researchers found that 40% of labeled bromelain is absorbed from the intestine (Maurer 2001). Bromelain’s anticancer effect was tested in vivo as well in mice subjected to ultraviolet radiation. Those fed bromelain showed retardation of the growth of lesions (Goldstein et al. 1975). Baez et al. also studied a number of tumor lines in vivo including P-388 leukemia, sarcoma (S-37), Ehrlich ascitic tumor, Lewis lung carcinoma, MB-F10 melanoma, and ADC-755 mammary adenocarcinoma. All were administered bromelain intraperitoneally and all had an increase in survival rate besides MB-F10 melanoma (Baez et al. 2007).

Bromelain also has the capability of reducing existing edemas as well as preventing the formation of new edemas (Maurer 2001). Oral bromelain not only reduces swelling and pain but also reduces the time it takes to heal by half. Experiments explored the anti-inflammatory effect of bromelain on edemas in rats along with eight other drugs, including aspirin, and found that bromelain was the most effective in terms of a reduction in inflammation (Taussig and Batkin 1988). Further experiments found similar results of bromelain’s potency in comparison to other drugs even when applied intraperitoneally (Smyth, Brennan, and Martin 1962).

**Components of Ananas comosus**

**Plant**
- 2,5-dimethyl-4-hydroxy-3(2H)-furanone (1.2 ppm)
- 5-hydroxytryptamine
- acrylic acid
- anasagric acid
- beta-methyl-thiopropionic-acid-ethyl-ester
- beta-methyl-thiopropionic-acid-methyl-ester
- ergosterol peroxyde
- ferulic acid (200-760 ppm)
- p-coumaric acid (330-730 ppm)
- stigmast-5-ene-3(beta-7-alpha-diol
- tetrahydro-alpha-alpha-5-trimethyl-5-vinylfurfuryl-alc

**Fruit**
- Acetic acid (.49 ppm)
- Acetoxyacetone
- Alpha-linolenic acid (620-4592 ppm)
- Amyl caproate
- Asparagine (1251 ppm)
- Glacetyl
- Bromelain
- Bromelin
- Butyl formate
- Chavicol (.27 ppm)
- Delta octalactone (.3 ppm)
- Dimethyl malonate (.06 ppm)
- Esters (1-250 ppm)
- Ethyl acetate (3-120 ppm)
- Ethyl acrylate (.77 ppm)
- Ethyl alcohol (60 ppm)
- Ethyl-beta-acetoxyhexanoate Ethyl-beta-hydroxyhexanoate Ethyl-beta-methylthiopropionate Ethyl butyrate
- Ethyl caproate (.77 ppm)
- Ethyl caprylate
- Ethyl formate
- Ethyl isobutyrate
- Ethyl isovalerate (.39 ppm)
- Ethyl lactate

**Table 2. Components in Ananas comosus** (Duke 2010).
Topical bromelain is used for debridement of third degree burns without removing unburned tissue; a study was done on rats with experimental burns in which topical bromelain helped remove damaged tissue with no side effects (Klaue, Aman, and Romen 1979). Bromelain is especially beneficial because it prevents bacterial growth, contamination, and infection to the healthy tissue by removing the burnt tissue (Rosenberg et al. 2004).

**Mechanism of action**

Bromelain has a number of therapeutic uses implicating that it must have multiple mechanisms (Taussig and Batkin 1988). The anti-platelet and anti-inflammatory effects are related to bromelain’s proteolytic activity. However, the anticancer and burn debridement properties are due to some other unknown factor in bromelain. A possible mechanism of action has been proposed for the anticancer property of bromelain which stimulates differentiation of leukemic cells possibly leading to apoptosis of tumor cells (Maurer 2001).

Bromelain’s mechanism of action is partially due to the activity of two types of prostaglandins: pro-inflammatory prostaglandins and anti-inflammatory prostaglandins. Pro-inflammatory prostaglandins stimulate inflammation, platelet aggregation, and vasoconstriction. Anti-inflammatory prostaglandins have the opposite effect. Bromelain is a pro-inflammatory prostaglandin inhibitor that is similar to aspirin but weaker so it does not promote bleeding. Bromelain activates plasminogen, which induces plasmin production. Plasmin subsequently cleaves fibrin, which inhibits pro-inflammatory prostaglandins. Consequently the ratio between pro-inflammatory and anti-inflammatory prostaglandins shifts in favor of anti-inflammatory prostaglandins. This leads to the activation of adenyl cyclase and the production of c-AMP. Anti-inflammatory prostaglandins generally lead to increased c-AMP production, inhibited platelet aggregation, inhibited inflammation, dilated blood vessels and smooth muscles, and increased tissue permeability; this mechanism is illustrated in Figure 5 (Taussig and Batkin 1988).

**Figure 5. Biosynthesis of prostaglandins and bromelain effect.** This diagram illustrates how bromelain and aspirin affect prostaglandins (Source: Taussig and Batkin 1988).
Clinical Studies

Pain and Inflammation

Bromelain demonstrates both analgesic and anti-inflammatory properties (Brien et al. 2004). Patients given bromelain felt less pain linked to mediolateral epistomy (Zatuchni and Colombi 1967) and bradykinin (Bodi 1966). Furthermore, bromelain reduces mild knee pain and helps improve general well-being in patients given 200 or 400 mg of oral bromelain (Walker et al. 2002). It has been widely used for inflammation ever since its discovery and is commonly used for rheumatoid arthritis, thrombophlebitis, hematomas, oral inflammations, diabetic ulcers, rectal and perirectal inflammations, oral and plastic surgery (Taussig and Batkin 1988). Researchers found that patients suffering from arthritis with joint swelling when administered bromelain report reduction in swelling, pain, and soreness (Walker et al. 2002). Previous studies have indicated that bromelain may serve as an alternative treatment to NSAIDs for patients suffering from osteoarthritis (Brien et al. 2004). However, the required dosage is unclear; while one study used between 60 and 160 mg of oral bromelain per day (Cohen and Goldman 1964), another study administered 1890 mg of oral bromelain (Tilwe et al. 2001) per day both of which reported reduced pain and swelling. Adverse reactions must also be taken into consideration when assigning dosage. While one study using 945 mg of oral bromelain per day reported gastrointestinal problems and subsequent drop-outs (Singer, Singer, and Oberleitner 2001), the previously mentioned study administering 1890 mg of oral bromelain per day reported no drop-outs or safety issues (Tilwe et al. 2001). Bromelain’s use in the treatment of osteoarthritis is promising; however, more studies must be conducted in order to identify an optimum dosage.

Cancer

Bromelain is shown to have an anticancer effect; however, studies verifying this have primarily been in vivo. Nevertheless, its activity was tested in a few clinical studies. Twelve patients with different tumors were treated with oral bromelain and were found to have a decrease in ovarian carcinoma, breast cancer, and metastases. Another study found tumor regressions in patients administered high doses of bromelain simultaneously with chemotherapeutic agents such as vincristine. Both studies found that at least 2.4 g per day of bromelain was necessary and dosages less than 1000 mg were insufficient (Taussig and Batkin 1988).

Antibiotics

It has been shown that bromelain can enhance the absorption of antibiotic drugs. It increases tissue permeability yielding enhanced diffusion of the antibiotic after subcutaneous or intramuscular application (Maurer 2001). Researchers found that patients treated with bromelain and antibiotics had an increase in serum and tissue levels of amoxicillin (Tinozzi and Venegoni 1978). Twenty-three patients with pneumonia, bronchitis, staphylococcus infections, thrombophlebitis, as well as other conditions were administered bromelain with antibiotic therapy. These patients previously did not react to antibiotic therapy but after simultaneous bromelain treatment, 22 of the patients responded (Neubauer 1961).

Burn debridement

One of bromelain’s few topical treatments is its effectiveness in the debridement of third degree burns. Patients with second and third degree burns were treated with Debridase, a multienzyme combination containing bromelain. Debridement
of the eschar was achieved after only one to two applications (Rosenberg et al. 2004). Eschar is burnt and traumatized tissue that can prevent proper assessment of the burn’s depth and lead to bacterial growth, contamination, and infection. Surgical removal is not only painful and results in significant bleeding but it also requires frequent doses of anesthesia (Tochi et al. 2008). Bromelain can achieve the same end result with no blood loss and few side effects (Rosenberg et al. 2004).

**Circulation**

By inhibiting platelet aggregation, bromelain can serve as an important treatment in cardiac medicine. Patients with a high platelet count or history of heart attack and stroke were treated with oral bromelain leading to a decrease in platelet aggregation (Heinecke, Waal, and Yokoyama 1972). Researchers suggest the activity is due to the activation of plasminogen followed by an increase in fibrinolytic activity, therefore blocking fibrin production (Orsini 2006). Bromelain also inhibits thrombus formation due to its inhibition of platelet aggregation and decreased fibrin production (Tochi et al. 2008).

**Contraindications**

According to the U.S. Federal Drug Administration, bromelain is generally recognized as safe (Orsini 2006). It has low toxicity and few side effects associated with it (Maurer 2001). Possible adverse effects of bromelain include gastrointestinal problems, headache, fatigue, dry mouth, skin rash, and allergic reactions (Orsini 2006). However, these effects are uncommon in the general population; a study found a 1.8% prevalence of side effects after bromelain administration (Maurer 2001). It is important to note that higher doses of bromelain will lead to a greater likelihood of exhibiting side effects (Orsini 2006). Since unripe pineapples were used as an abortifacient in the past, pregnant women should limit intake unless used for that purpose (Morton 1987). Consumption of pineapples can also cause allergic reactions in which symptoms include itching, rashes, abdominal pain, vomiting, and diarrhea (Kabir, Speelman, and Islam 1993). The blood glucose response in diabetic patients after pineapple consumption is significantly higher than other fruits such as mango and chico. Due to the increased glucose response and pineapple’s identification as a fruit with a high glycemic index (GI), it is suggested that diabetic patients limit intake to moderate amounts (Guevarra and Panlasigui 2000).

Bromelain can potentially increase bleeding when taken with aspirin and warfarin due to its anticoagulant properties. In addition, there is very little research conducted on the drug safety of bromelain in children; most clinical studies focus on adults. Therefore, children should not be given bromelain supplements due to the lack of studies in children. There is also little information on bromelain’s effects at high doses, taken long term, or taken in combination with other medication (Orsini 2006). More research is needed for bromelain’s use as an established compound for medicinal purposes.

**Current Use in Allopathic and CAM Therapies**

Bromelain is an extract that yields a yellow powder (Maurer 2001) available in the form of a powder, tablet, cream, or capsule (Orsini 2006). Bromelain is also available in multienzyme combinations in Debridase, Phlogenzym, Wobenzym, and Traumanase (Orsini 2006) (Figure 6). Other trade names include Ananase, Bromelain, Resolvit, Extranase,
and Inflamex (Sittig 2007). The German Commission E recommends 80-320 mg of bromelain two to three times per day. However, if used for arthritis, 500-2000 mg per day should be consumed; for injuries, 500 mg should be consumed four times per day. In order to use bromelain for its anticancer activity, at least 2.4 g per day must be consumed (Taussig and Batkin 1988). Bromelain is a popular supplement in European countries such as Germany; the German Commission E approved bromelain to be used simultaneously with other therapeutic agents in the treatment of inflammations of the nose and sinuses due to surgery (American Cancer Society 2011). It is also recommended to consume the bromelain herbal supplements on an empty stomach to reduce reactions with other foods (University of Maryland Medical Center 2011).

Discussion

*Ananas comosus* is an important plant with many ethnobotanical and even more medicinal uses. Its primary constituent, bromelain, is not only an anti-tumor agent, but prevents platelet aggregation and hence thrombus formation. It is an analgesic as well as an anti-inflammatory agent used in a number of conditions such as rheumatoid arthritis, oral inflammations, ulcers, and plastic surgery. Although it can promote antibiotic drug absorption, one of the most important capabilities of bromelain is its use in burn debridement of second and third degree burns. Bromelain is generally recognized as safe and there are very few if any side effects due to it, which can possibly occur at very high doses. However, research is limited in bromelain’s use in children as well as the required dosage to view its effects. With more research, *A. comosus* can serve as an important plant for the treatment of dermatological disorders, inflammatory conditions, as well as cancer treatments in the future.

References Cited


