

MULTIFARIOUS PHARMACOLOGICAL POTENTIALS OF PINEAPPLE PROTEASE (BROMELAIN): A MOMENTARY GAWK

Wasi U. Khan^{1*}, Harsimran Singh² and Abul kalam Najmi¹

¹Faculty of Pharmacy, Jamia Hamdard Hamdard Nagar, New Delhi-110062.

²Sri Sai College of Pharmacy, Badhnai Pathankot, Punjab-145001.

Article Received on
01 Oct. 2016,

Revised on 24 Oct. 2016,
Accepted on 13 Nov. 2016

DOI: 10.20959/wjpr201612-7287

*Corresponding Author

Wasi U. Khan

Faculty of Pharmacy, Jamia
Hamdard Hamdard Nagar,
New Delhi-110062.

ABSTRACT

Bromelain is a crude extract from the fruit or stem of pineapple (*Ananas cosmosus* Linn.) plant that contains proteinases, which are good anti-inflammatory, anti-thrombotic and fibrinolytic properties. Among other components various closely related proteinases exhibiting actions such as inhibition of platelet aggregation, anti-cancer, mucolytic, skin debridement, digestive assistance, enhanced wound healing, cardiovascular and circulatory improvement, enhanced absorption of other drugs etc. Further, Bromelain also contains peroxidase, acid phosphatase, several protease inhibitors. It has earned

universal acceptability as a phytotherapeutic drug because of its history of safe use and minimal side effects. This communication for review deals with the applications of bromelain in the treatment of various pathological conditions.

KEYWORDS: Bromelain, *Ananus cosmosus*, proteinases.

INTRODUCTION

Pineapple (*Ananas cosmosus* Linn.) eventually carried to Central and South America, is grown in several tropical and subtropical countries including India, China, Kenya, South Africa, Malaysia.^[1] It has been used as a medicinal plant in several native cultures and bromelain has been chemically known since 1876.^[2] It is present in all parts of the plants but stem is the most common source for the commercial preparation of bromelaine.^[3] It was first introduced as therapeutic supplement in 1957, it is currently 13th most widely used herbal medicine in Germany. Although bromelain's primary constituent is a sulfhydryl proteolytic fraction, it also contains escharase (a non proteolytic components in bromelain thought to be important in the action of topical bromelain), peroxidase, acid phosphatase, protease inhibitor

and organically bound calcium.^[4] It is a mixture of sulphur containing protein digesting enzymes. The popularity of pineapple is due to its sweet-sour taste containing 15% sugar, malic acid and citric fruit acids. It also contains vitamin B1, B2, B6 and C.^[5] According to the estimation of FAO (UN) for the year 2003, Thailand, Philippines and Brazil are the top three producers along with India ranking forth in the world. Isolation and purification of bromelain can be achieved by several methods. The commercial preparation of bromelain is done by centrifugation, ultrafiltration and lyophilization. When some proteolytic fractions of bromelain are purified, they may be physiologically inactive *in vivo* under conditions where bromelain has a beneficial effect. It was found that a great deal of the physiological activity of bromelain may not be due to its proteolytic fraction.^[6]

Bromelain and Anti-inflammatory and Analgesic activity

It is result from blocking bradykinin and its modulation of prostaglandin synthesis. It achieves an anticoagulant effect through both reduced platelet aggregation, by increasing relative concentration of prostacyclin and prostaglandin E2 over the concentration of thromboxane A2 and fibrinolysis by activation of plasmin. Plasmin further suppresses inflammation by blocking the mobilization of endogenous arachidonic acid by phospholipases.^[7-11]

Bromelain and Anti-cancer activity

Several animal and human studies indicate that bromelain might have some anticancer activity.^[12-16] It is result from bromelain ability to affect T-cell activation, induce cytokinin production in circulating monocytes and enhances production of tumor necrosis factor and interleukins. As an adjunct in cancer therapy bromelain may act as immunomodulator by raising the impaired immunotoxicity of monocytes against tumor cells and by inducing the production of T-cells. Bromelain also inhibits the proliferation of different tumor cells *in vitro*. The inhibitory activity can be traced neither to the proteolytic nor to the or to the platelet aggregation- inhibitory activity.^[18]

Bromelain and Anticoagulant and Fibrinolytic activity

The conclusive evidence that bromelain prevents aggregation of blood platelets was reported.^[19] Bromelain also inhibits platelet aggregation in a dose dependent manner in *in-vitro* study.^[20] Bromelain also prevents thrombin induced human platelet aggregation and platelet adhesion to bovine endothelial cells. Furthermore, oral and intravenous application reduced thrombus formation in rat mesenteric vessels.^[21-22]

Bromelain and Anti-helminthes activity

Infections with gastrointestinal nematodes have severe consequences. Plant cysteine proteinases from pineapple have high proteolytic activities that are known to digest nematode cuticle, have low toxicity and have been used in traditional medicines against gastrointestinal nematodes for decades.^[23-25]

Bromelain and Wound healing activity

Bromelain contains more than 50 different components and is widely used as an over the counter food additives and is also used in debridement of burn eschar.^[25,26] To exert debridement action the concentration of enzyme must be 30-100 times higher than the pharmacological dose required for wound healing. They also show collagenolytic activity which is again promotes wound healing activity.^[27] Topical bromelain (35% in lipid base) has achieved complete debridement on experimental burns in rat in about 2 days, as compared with collagenase, which required about 10 days, with no side effects or damage to adjacent burned tissue.^[28-32]

CONCLUSION

This review describes pharmacological and phytochemical studies on Pineapple Protease (Bromelain) plant. Plants are widely used in traditional medicine system for curing number of pathological diseases. The large population resides in rural areas of developing and a developed country depends on medicinal plants. The present review revealed that Bromelain, crude extract of Pineapple Protease has great potential to treat cancer, helminthes and cardiac disorders. Further, anti-oxidant, anti-inflammatory, wound healing, anticoagulant, fibrinolytic and analgesic properties of crude extract of Bromelain opens a new vista towards more focused research on molecular mechanism of action involved in the treatment of various chronic disorders.

REFERENCES

1. Tochi BN, Wang Z, Xu SY, Zhang W. (Therapeutic application of Pineapple protease(Bromelain): A Review). Pak J Nutri, 2008; 7(4): 513-520.
2. Peckoldt T, Taussig SJ, Batkin S. (Bromelain, the enzyme complex of pineapple (*Ananuscocosmosus*) and its clinical application: An update). J. Ethnopharm, 1988; 22: 191-203.
3. Rowan AD, Buttle DJ, Barrett AJ. (The cysteine proteinases of the pineapple plant).Biochem J, 1990; 266: 869-875.

4. Hale LP, Greer PK, Trinch CT, James CL. (Proteinase activity and stability of natural bromelain preparations). *Int J Immunopharmacol*, 2005; 5: 783-793.
5. Gardner PT. (The relative contribution of vitamin c, carotenoids and phenolics to the antioxidant potential of fruit juices). *Food Chemistry*, 2000; 68: 471-474.
6. Taussig SJ and Nieper HA, Bromelain: its use in prevention and treatment of cardiovascular diseases, present status, *JIA PM*, 1979; 6: 139-151.
7. Sudjarwo SA. (Anti-inflammatory and analgesic effect of bromelain in mice and rat). *Universa Medicina*, 2005; 24(4): 155-160.
8. Engwerda CR. (Bromelain activates murine macrophages and natural killer cells in vitro). *Cellular Immuno*, 2001; 210: 5-10.
9. Walker AF, Bundy R, Hicks SM, Middleton. (Bromelain reduces mild acute knee pain and improves well-being in a dose dependent fashion in an open study of otherwise healthy adults). *Phytomedicine*, 2002; 9: 681-686.
10. Fitzhugh DJ, Shan S, Dewhirst MW, Hale LP. (Bromelain treatment decreases neutrophil migration to sites of inflammation). *Clin. Immunol*, 2008; 128: 66-74.
11. Gaspari L, Limiroli E, Ferrario P, Bianchi M. (In vivo and in vitro effects of bromelain on PGE2 and SP concentration in the inflammatory exudates in rats). *Pharmacology*, 2002; 65: 83-86.
12. Gerard G. (Anti-cancer therapy with bromelain). *Agressologie*, 1972; 13: 261-274.
13. Taussig SJ, Szekeres J, Batkin S. (Inhibition of tumor growth in vitro by bromelain, an extract of the pineapple plant (*Ananas cosmosus*)). *Planta Med*, 1985; 6: 538-539.
14. Batkin S, Taussig SJ, Szekeres J. (Antimetastatic effect of bromelain with or without its proteolytic and anticoagulant activity). *J Cancer Res Clin Oncol*, 1988; 114: 507-508.
15. Nieper HA. (A program for the treatment of cancer). *Krebs*, 1974; 6: 124-127.
16. Baez R, Lopes MT, Salas CE, Hernandez M. (In vivo antitumoral activity of stem pineapple (*Ananas cosmosus*) bromelain). *Planta Med*, 2007; 73: 1377-1383.
17. Chobotava K, Vernallis AB, Majid FAA. (Bromelain's activity and potential as an anticancer agent: Current evidence and perspectives). *Cancer Lett*, 2010; 290: 148-156.
18. Garbin F, Harrach T, Eckert K, Maurer HR. (Bromelain proteinase F9 augments human lymphocyte-mediated growth inhibition of various tumor cells in vitro). *Int J Oncol*, 1994; 5: 197-203.
19. Heinicke RM, Van der WM, Yokoyama MM. (Effect of bromelain on human platelet aggregation). *Experientia*, 1972; 28: 844-845.

20. Morita AH, Uchida DA, Taussing SJ. (Chromatographic fractionation and characterization of the active platelet aggregation inhibitory factor from bromelain). *Arch Int Pharm Ther*, 1979; 239: 240-350.
21. Metzigg C, Grabowska E, Eckert K, Rehse K, Maurer HR. (Bromelain protease reduce human platelet aggregation in vitro, adhesion to bovine endothelial cells and thrombus formation in rat vessels in vivo). *In vivo*, 1999; 13: 7-12.
22. Sneddon JM, Vane JR. (Endothelial derived relaxing factor reduces platelet adhesion to bovine endothelial cells). *Proc Nat Acad Sci*, 1988; 85: 2800-2804.
23. Berger J, Asenjo. (Anthelmintic activity of fresh pineapple juice). *Science*, 1990; 299-300.
24. Greets S, Gryseels B. (Drug resistance in human helminthes: current situation and lessons from livestock). *Clin. Microbiol. Rev*, 2000; 1: 333-373.
25. Stepek G, Lowe AE, Buttle DJ, et al. (In vitro and in vivo anthelmintic efficacy of plant cysteine proteinases against the rodent gastrointestinal nematodes). *Parasitology*, 2006; 132: 681-689.
26. Levine N. (Debridement of experimental skin burns of pigs with bromelain, a pineapple stem enzyme). *Plastic reconstr surg*, 1973; 52: 413-24.
27. Houck JC, Chang CM, Klein G. (Isolation of an effective debridising agent from the stem of pineapple plants). *Int. J Tissue React*, 1983; 5: 125-34.
28. Klein GKV. (Historical development of bromelain in the treatment of burn wounds). *Int Cong. Geneva*, 1983; 90-96.
29. Ahle NW, Hamlet MP. (Enzymatic frostbite eschar debridement by bromelain). *Ann Emerg Med*, 1987; 16: 1063-65.
30. Rosenberg L, Lapid O, Bogdanov BA, Glesinger R, Silberstein E, Sagi A, Judkins K, Singer AJ. (Safety and efficacy of a proteolytic enzyme for enzymatic burn debridement: a preliminary report). *Burns*, 2004; 30(8): 843-50.
31. Gurfinkel R, Lavon I, Cagnano E. (Combined ultrasonic and enzymatic debridement of necrotic eschars in an animal model). *J Burns Care Res*, 2009; 3: 505-513.
32. Krieger Y, Rosenberg L, Lapid O. (Escharotomy using an enzymatic debridement agent for treating experimental burn induced compartment syndrome in an animal model). *J Trauma*, 2005; 58: 1259-1264.