Crimson Publishers
Wings to the Research

Review Article

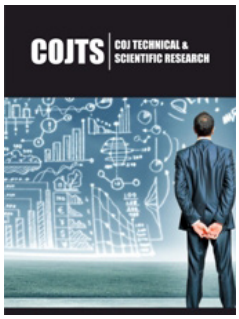
Applications of Bromelain as Biopharmaceutical Potential: A Short Review

Mohammad Hossein Karami[1,2]*, Majid Abdouss[1]* and Behzad Aghabarari[2]*

[1]Department of Chemistry, Amirkabir University of Technology, Iran

[2]Nanotechnology and Advanced Materials Department, Materials and Energy Research Center, Iran

ISSN: 2643-7066



***Corresponding authors:** Mohammad Hossein Karami, Majid Abdouss, Department of Chemistry, Amirkabir University of Technology, P.O. Box 15875-4413, Tehran, Iran
Behzad Aghabarari, Nanotechnology and Advanced Materials Department, Materials and Energy Research Center, Iran;
E-mail: HYPERLINK "mailto:karami.polymerpostdoc@gmail.com"karami.polymerpostdoc@gmail.com, HYPERLINK "mailto:phdabdouss44@aut.ac.ir"phdabdouss44@aut.ac.ir and b.aghabarari@merc.ac.ir

Submission: March 15, 2024
Published: May 23, 2024

Volume 5 - Issue 1

How to cite this article: Mohammad Hossein Karami*, Majid Abdouss* and Behzad Aghabarari*. Applications of Bromelain as Biopharmaceutical Potential: A Short Review. COJ Tech Sci Res. 5(1). COJTS. 000601. 2024.
DOI: 10.31031/COJTS.2024.05.000601

Abstract

Medicinal plants have always been seen as the best and easiest way to treat various health issues. Bromelain is a mixture of chemicals taken from pineapples and is used in many different ways, such as in medicine, health products, food, and beauty products. Br has different positive effects on the body, including: antibacterial, antioxidant, anti-cancer, healing wounds, treating burns, relieving pain, reducing inflammation, preventing blood clots and dissolving blood clots. However, many proteins can be easily damaged and changed, which can reduce their effectiveness. Tiny particles called nanoparticles can make drugs stronger and easier for the body to use. This could help with getting drugs to the right place in the body and making them more effective. This survey is to find out different ways to make Br more effective.

Keywords: Bromelain; Nanoparticles; Pineapple; Stability; Therapeutic application

Introduction

Herbal medicines such as bromelain have long been considered affordable and readily available treatments for many health conditions. The therapeutic benefits of BR are many, because in the structure of pineapple (Br) there are enzymes that lead to antibacterial, antioxidant, anti-cancer, wound healing and anti-inflammatory properties [1]. It may also reduce the risk of cancer, diabetes and cardiovascular disease. Additionally, bromelain improves antibiotic bioavailability and supports the immune system. However, storing and stabilizing bromelain is important to maximize its effectiveness [2]. Various methods have been investigated to improve the stability of bromelain, such as chemical modification, protein engineering, and use of nano systems [3]. The presence of drugs in nanometer-sized particles is a promising approach because it increases stability against enzymatic denaturation, prevents rapid clearance, and increases bioavailability. Nano drug in the body leads to increased solubility, penetration and cytotoxicity. In addition, the small size of nanoparticles leads to efficiently adsorb and interact with biomolecules [4-7]. In this review article, the study of the therapeutic properties of bromelain is discussed as a therapeutic potential in biotechnology.

Therapeutic applications of nanoparticles containing bromelain

The use of NPs to encapsulate drug molecules has been shown to improve solubility, stability, permeability, and bioavailability [8]. NPs can also be used to deliver drugs in a controlled release manner into target tissues. In one study, hydrogel particles made from starch and pectin were used to deliver a drug called Br through the gastrointestinal tract [9]. This method leads to a controlled and sustained release of Br. Another study showed that Br immobilized on gold NPs showed improved stability and specific activity, as well as increased sensitivity to inhibition by protease inhibitors. These results highlight different methods using Br nano formulations to improve treatment efficacy [10].

Toxicity and side effects

After oral administration, the body completely absorbs Br. There are no significant side effects with long-term use [11]. Even Br reduces the side effects caused by radiotherapy

and chemotherapy in cancer treatment. Br has shown promising results as a clinical treatment for human breast cancer and mucin-producing peritoneal tumors [12]. Clinical and preclinical studies have reported that the toxicity profile of Br has few toxic effects [13]. Br exhibits significant anticancer properties against ovarian and colon cancer cell lines, but is toxic to healthy cell lines. Therefore, it is essential to create a safe targeted delivery system to minimize the negative effects of Br on healthy cell lines while maximizing the toxic effects of Br on tumor sites [14]. The lethal dose (LD50) in mice is >10g/kg [15]. Another study reported no significant changes in blood coagulation parameters even after administering up to 3000 FIP units of Br per day [16]. In general, the cytotoxic effects of Br are dose-dependent [17]. Therefore, side effects at various doses should be investigated to determine optimal intake limits and effective doses. Further clinical research is needed to obtain reliable results about the toxic effects of Br on the body and normal cells.

Bioavailability and delivery system

Br is absorbed through the intestinal epithelium and has high bioavailability. In its active form, it can bind to two anti-proteinases in the blood [18]. Over the years, new methods have been developed to improve the cancer-fighting ability of Br from the lab to the patient's bedside. Improving how well the body can use Br as a healthy compound using new medical nano formulations is a very promising method. Administration of Br is performed alone or in combination with other molecules in various studies. However, one of the best delivery methods is nanoparticle formulations, which can be effectively used as a new approach for cancer chemotherapy [19]. To fight cancer, it is necessary to develop nano delivery systems that enhance protease activity or sustainably release Br (38). As a proteolytic enzyme, Br increases the binding affinity and changes the surface of the particles. Br acts as a surface conditioning agent for lacto-bionic acid-modified chitosan nanoparticles and enhances their penetration into tumor cells [20]. Studies have shown that Br nanoparticles inhibit the proliferation of MCF-7 BC cells. These nanoparticles extend lifespan, reduce cell proliferation, increase apoptosis, improve chemosensitivity and inhibit cancer cell proliferation. Br nanoparticles and pineapple nanoemulsion were more likely to be released from breast cancer cells [21-23]. Additionally, studies have shown that Br is significantly reduced when combined with nanoparticles (magnetic carbon nanoparticles). Furthermore, sustained release of synthesized magnetic carbon nanoparticles may result in significant cancer cures [24]. Br nano capsules also have a stronger antiproliferative effect than Br solution [25]. Br can be delivered to target organs using various nanostructured materials for cancer treatment and prevention [26].

Cancer therapy

Br has been found to have effects on breaking down proteins and boosting the immune system. This may help stop cancer cells from growing and spreading. Previous studies have suggested that Bromine can affect how certain qualities in cancer cells behave, possibly making it a future treatment for cancer. Bromelain is believed to affect tumors in three different ways at the cellular level [27]. Firstly, it regulates the expression of genes important for cell differentiation and proliferation. Secondly, it induces cell death through apoptosis/autophagy [28]. Lastly, it blocks the cell cycle by inhibiting necessary cyclins. In recent studies, chitosan-bromelain NPs were prepared using a cross-linking method and freeze-dried for stability. These NPs showed higher enzymatic activity and increased encapsulation rate compared to free Br. Another study investigated the antioxidant, antiproliferative, and antimigration activities of chitosan-bromelain NPs and observed inhibition in specific tumor cell lines [29]. However, the slow release of protein from the NPs may have reduced the activity of Br [30]. The combination of chitosan NPs, lacto-bionic acid, and Br was used to deliver doxorubicin specifically to tumors. This helped the doxorubicin to get into the tumors better. Tiny magnetic particles with Br and folic acid attached to them showed better ability to fight tumors than particles with just Br or folic acid by themselves [22-25]. Eudragit-coated Br-PLGA NPs showed improved antitumor effects and sustained release compared to free Br. Br formulated with PLGA NPs was shown to protect skin cells from carcinogenicity and induce apoptosis-inducing genes in a mouse model. Magnetic carbon NPs and nanotubes were used to encapsulate Br, demonstrating antitumor effects and inhibiting breast cancer cells. Overall, Br shows promise as a potential anticancer agent with various delivery systems and mechanisms of action being explored [26-30].

Conclusion

Br has demonstrated promising anti-cancer effects against breast cancer in both laboratory and animal studies. Its mechanisms include reducing inflammation, modulating the immune system, inhibiting cancer cell growth, and promoting cell death in breast cancer cells. Although there have been reports of minor side effects, Br is generally considered safe as a natural remedy. However, more research is needed to confirm its effectiveness. When used in combination with chemotherapy drugs like cisplatin, Br has shown to enhance treatment outcomes by reducing drug toxicity. Apart from its potential in treating breast cancer, Br has also been explored for its therapeutic benefits in cardiovascular diseases and skin disorders. Nanotechnology has been used to make Br stronger and more effective. Encapsulation is a good way to make it work better as a medicine. Helpful tests are needed to study the healing effects and possible risks of nanoparticles that contain Br.

Credit Authorship Contribution Statement

Mohammad Hossein Karami: Supervision, Formal analysis, Data curation, Investigation, Resources, Writing-riginal draft, Writing-review & editing, Visualization, Project administration, Methodology.

Majid Abdouss: Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Pavan R, Jain S, Shraddha, Kumar A (2012) Properties and therapeutic application of bromelain: A review. Biotechnol Res Int 2012: 976203.
2. Ataide JA, Gérios EF, Mazzola PG, Souto EB (2018) Bromelain-loaded nanoparticles: A comprehensive review of the state of the art. Adv Colloid Interface Sci 254: 48-55.
3. Rani A, Pannuru V (2016) Unanticipated behaviour of sorbitol towards the stability and activity of stem bromelain: An outlook through biophysical techniques. Process Biochem 51(8): 1028-1039.
4. Karami MH, Abdouss M, Rahdar A, Pandey (2024) Graphene quantum dots: Background, synthesis methods, and applications as nanocarrier in drug delivery and cancer treatment: An updated review. Inorg Chem Commun 161: 112032.
5. Li J, Li M, Tang J, Li X, Zhang H, et al. (2008) Resonance light-scattering spectrometric study of interaction between enzyme and MPA-modified CdTe nanoparticles. Spectrochim Acta A Mol Biomol Spectrosc 70(3): 514-518.
6. Hami Z (2021) A brief review on advantages of nano-based drug delivery systems. Ann Mil Health Sci Res 19(1): e112274.
7. Gelperina S, Kisich K, Iseman MD, Heifets L (2005) The potential advantages of nanoparticle drug delivery systems in chemotherapy of tuberculosis. Am J Respir Crit Care Med 172(12): 1487-1490.
8. Parodi A, Haddix SG, Taghipour N, Scaria S, Taraballi F, et al (2014) Bromelain surface modification increases the diffusion of silica nanoparticles in the tumor extracellular matrix. ACS nano 8(10): 9874-9883.
9. Bagga P, Ansari TM, Siddiqui HH, Syed A, Bahkali AH, et al. (2016) Bromelain capped gold nanoparticles as the novel drug delivery carriers to aggrandize effect of the antibiotic levofloxacin. EXCLI J 15: 772-780.
10. Khan S, Rizvi SMD, Avaish M, Arshad M, Bagga P, Khan MS (2015) A novel process for size controlled biosynthesis of gold nanoparticles using bromelain. Mater Lett 159: 373- 376.
11. De Sousa IP, Cattoz B, Wilcox MD, Griffiths PC, Dalgliesh R, et al. (2015) Nano particles decorated with proteolytic enzymes, a promising strategy to overcome the mucus barrier. Eur J Pharm Biopharm 97: 257-264.
12. Samaridou E, Karidi K, De Sousa IP, Cattoz B, Griffiths P, et al. (2014) Enzyme-functionalized PLGA nanoparticles with enhanced mucus permeation rate. Nano Life 4(4): 1441013.
13. Ataide JA, Gérios EF, Cefali LC, Fernandes AR, Teixeira Md C, et al. (2019) Effect of polysaccharide sources on the physicochemical properties of bromelain–chitosan nanoparticles. Polymers 11(10): 1681.
14. Kammona O, Kiparissides C (2012) Recent advances in nanocarrier-based mucosal delivery of biomolecules. J Control Release 161(3): 781-794.
15. Lü JM, Wang X, Marin-Muller C, Wang H, Lin PH, et al. (2009) Current advances in research and clinical applications of PLGA-based nanotechnology. Expert Rev Mol Diagn 9(4): 325-341.
16. Nagpal K, Singh SK, Mishra DN (2010) Chitosan nanoparticles: A promising system in novel drug delivery. Chem Pharm Bull 58(11): 1423-1430.
17. Karami MH, Pourmadadi M, Abdouss M, Kalaee MR, Moradi O, et al. (2023) Novel chitosan/γ-alumina/ carbon quantum dot hydrogel nanocarrier for targeted drug delivery. Int J Biol Macromol 251: 126280.
18. Karami M H, Abdouss M (2024) Assessing particle size and surface charge in drug carrier nanoparticles for enhanced cancer treatment: a comprehensive review utilizing dls and zeta potential characterization. PSPRJ 5(3): 000615.
19. Brito AM, Oliveira V, Icimoto MY, Nantes-Cardoso IL (2021) Collagenase activity of bromelain immobilized at gold nanoparticle interfaces for therapeutic applications. Pharmaceutics 13(8): 1143.
20. Hirche C, Almeland SK, Dheansa B, Fuchs P, Governa M, et al. (2020) Eschar removal by bromelain based enzymatic debridement (Nexobrid®) in burns: European consensus guidelines update. Burns 46(4): 782-796.
21. Karami M H, Abdouss M (2024) Recent advances of carbon quantum dots in tumor imaging. Nanomed J 11(1): 13-35.
22. Karami M H, Abdouss M, Maleki B (2024) The state of the art metal nanoparticles in drug delivery systems: A comprehensive review. Nanomed J.
23. Da Elisa Silva López R (2017) Debridement applications of bromelain: A complex of cysteine proteases from pineapple. Adv Biotechnol Microbiol 3: 555624.
24. Wu SY, Hu W, Zhang B, Liu S, Wang JM, et al. (2012) Bromelain ameliorates the wound microenvironment and improves the healing of firearm wounds. J Surg Res 176(2): 503-509.
25. Hikisz P, Bernasinska SJ (2021) Beneficial Properties of Bromelain. Nutrients 13(12): 4313.
26. Ghensi P, Cucchi A, Bonaccorso A, Ferroni L, Gardin C, et al. (2019) *In vitro* effect of bromelain on the regenerative properties of mesenchymal stem cells. J Craniofac Surg 30(4): 1064-1067.
27. Singer AJ, Taira BR, Anderson R, Mc Clain SA, Rosenberg L (2010) The effects of rapid enzymatic debridement of deep partialthickness burns with Debrase on wound reepithelialization in swine. J Burn Care Res 31(5): 795-802.
28. Karami MH, Abdouss M, Karami M (2023) Evaluation of *in vitro* and *ex vivo* models for studying the effectiveness of vaginal drug systems in controlling microbe infections: A systematic review. Clin J Obst Gynecol 6: 201-215.
29. Miranda ÍKSPB, Santana FR, Camilloto GP, Detoni CB, Souza FVD, et al (2021) Development of membranes based on carboxymethyl cellulose/acetylated arrowroot starch containing bromelain extract carried on nanoparticles and liposomes. J Pharm Sci 110(6): 2372-2378.
30. Bayat S, Zabihi AR, Farzad SA, Movaffagh J, Hashemi E, et al. (2021) Evaluation of debridement effects of bromelain-loaded sodium alginate nanoparticles incorporated into chitosan hydrogel in animal models. Iran J Basic Med Sci 24(10): 1404.