



## PHARMACOLOGICAL ACTIVITY OF PINEAPPLE (ANANAS COMOSUS): A COMPREHENSIVE REVIEW

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### ABSTRACT:

Pineapple is a sub-tropical fruit grown in India, Bangladesh, Malaysia, Sri Lanka, Maldives and many more. It has a juicy taste and flavour and has been used from the historical ages and used for different purposes like cardiovascular effects, antianginal, wound healing, anticancer, osteoarthritis, antidiarrheal, and anti-aging properties. There are different important phytoconstituents available in different parts of pineapple like root, peel, core, and leaves like flavonoids, terpenoids, glycosides, carbohydrates, amino acids, and many more. Most important is Bromelain which is a very good enzyme having proteolytic activity, burn wound healing activity, and good digestive properties. Due to enormous uses in versatile pharmacological profiles, there are numerous formulations that have also been discovered. These formulations are overcoming the side effects of synthetic drugs and playing a crucial role in herbal drug technology. Bromelain is a complex enzyme and different amino acids are present in it. Many researchers are trying to isolate and are trying to establish unknown pharmacological activity. The pineapple is a magic fruit and many more are yet to be discovered.

**Keywords:** Pineapple, tropical fruit, different pharmacological activity, bromelain, phytoconstituents, isolation.

## 1. INTRODUCTION

A tropical fruit, pineapple is a member of the Bromeliaceae family. It is mostly consumed raw but can also be processed into juice, drinks, jams, and jellies (1). The *Ananas comosus* is a herbaceous perennial that may reach heights of 1.0 to 1.5 meters (3.3 to 4.9 feet), while it can occasionally reach much higher heights. The plant itself is visually striking, with a short, stocky stem and stiff, waxy leaves. When it blossoms, the separate fruits of the flowers come together to form a pineapple. Commercial growers "Following the first fruit, the main stem's leaf axils produced side shoots, which are known as suckers by Commercial growers (2). Pineapple is one of the most beneficial fruits for producing value-added compounds such as antioxidants, organic acids, bromelain, and phenolic compounds, according to its physicochemical makeup and nutritional value.(3). Pineapple stems are the source of the potent chemoresponsive proteolytic enzyme bromelain. It is isolated and purified using a variety of techniques and contains several thiol endopeptidases. Though scientists have also shown that it has antibacterial and anticancer properties, it is most typically utilized as an anti-inflammatory medication.(4)

Kingdom	Plantae
Clade	Tracheophytes
Clade:	Angiosperms
Clade:	Monocots
Clade:	Commelinids
Order	Poales
Family	Bromeliaceae
Subfamily	Bromelioideae
Genus	Ananas
Species	comosus

### **Pineapple: A Brief Historical Overview**

It's vital to give a little historical recap before getting into pineapple's pharmacological properties. The scientific name for pineapple is *Ananas comosus*, and it has long been used in traditional medical systems for medicinal purposes. Pineapple was employed as a medicine by ancient societies like the Mayans and Native Americans.

They utilized pineapple to treat a variety of illnesses because it had anti-inflammatory and digestive qualities. In recent years, modern scientific research has validated these traditional claims and uncovered additional pharmacological activities of pineapple(5).

Pineapple exhibits significant antioxidant activity due to its high content of vitamin C and other antioxidants. These antioxidants neutralize the free radicals which are harmful for our body, reducing oxidative stress and potential damage to cells and tissues. Moreover, pineapple contains a variety of polyphenolic compounds and flavonoids that contribute to its antioxidant activity(6). The antioxidant activity of pineapple has been demonstrated in various studies. For example, a study conducted by Das et al. investigated the antioxidant potential of silver

nanoparticles synthesized using the outer peel extract of *Ananas comosus*(7).The results showed that the pineapple peel extract exhibited strong antioxidant activity, indicating its potential as a natural antioxidant source.

**Dyslipidemia Effects of Pineapple** Pineapple has been studied for its potential anti-obesity and anti-dyslipidemia effects(8).One study conducted by Kondo et al. explored the effects of pineapple extract on obesity in high-fat diet-induced obese mice. The study found that treatment with pineapple extract resulted in a reduction in body weight, fat accumulation, and plasma lipid levels. Furthermore, pineapple extract was shown to improve glucose tolerance and insulin sensitivity in the obese mice.

Pineapple possesses potent anti-inflammatory activity, attributed to the presence of bromelain, a complex mixture of enzymes. Bromelain has been extensively studied for its anti-inflammatory effects and has shown promise in various inflammatory conditions.

### **Pharmacological Activities of Pineapple peels**

Pineapple peels, the discarded outer layer of the pineapple fruit, have gained attention in recent years for their potential pharmacological activity. Various studies have indicated that pineapple peels possess several pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. These activities can be attributed to the presence of bioactive compounds such as phenolic compounds, flavonoids, vitamins, and enzymes in pineapple peels.

**Antimalarial activity:** In the Traditional medicine system, pineapple peels are a well-known component(9). From the traditional knowledge, the application of Pineapple peels either in isolation or conjugated with other medicinal plants used for the treatment of malaria, Autoimmune disease like Rheumatoid arthritis, gastric problem and fever like typhoid(9).

**Antioxidant activities:** Pineapple peels have been found to possess antioxidant activity(35). Pineapple peels with ethanol show highest antioxidant activity instead of methanolic extract(36). *Ananas comosus* peels contain various phenolic compounds such as catechin, epicatechin, gallic acid, ferulic acid which are responsible for antioxidant activities(10). These compound are also liable for inhibitory effects pineapple peels extract opposed both gram(-) bacteria(*Salmonella typhimurium*, *E.coli*) and gram(+)bacteria(*Staphylococcus aureus*, *Bacillus cereus*)(37)

**Antirheumatic activity:** Pineapple peels with methanol extract also exhibit anti- rheumatic activity(10). In a study, by lowering the levels of prostaglandin PGE2 and CRP in the serum of arthritic rats and raising the level of the level of SOD, CAT, and GPx in the liver, kidney, and spleen, pineapple peels demonstrate their anti-rheumatic properties(31).

**In memory impairment and alcohol induce toxicity:** Additionally, *Ananas comosus* fruit peel extract has been evaluated for its potential to mitigate memory impairment, anxiety-like behavior and oxidative stress resulting from a high-fat diet in rats (11). The methanolic extract of pineapple peels under alcohol-induced oxidative stress has been shown to positively modulate lipid peroxidation, catalase activities, and liver biomarker levels of blood plasma, indicating its protective potential in the management of alcohol-induced toxicity(12).

**Antimicrobial activity:** According to a study, AgNPs synthesizing using pineapple peels extract has shown antimicrobial activity. Ions of metallic silver are highly reactive in nature when it is ionized in water. By the electrostatic interaction force metallic silver ions interact

with the microorganism and generate reactive oxygen species(ROS). This can lead to rupture of the cell wall of the microorganism(34).

### **Pharmacological Activities of Pineapple stem**

Pineapple stem is known for its culinary uses, but recent research has also highlighted its pharmacological potential(13).Bromelain is a multiple endopeptidase of thiol which is derived from the pineapple stem or fruit(14).

**Antifungal activity:** The antifungal properties of pineapple stem have been shown against a range of fungal infections, including as *Pythium* sp., *Fusarium verticillioides*, *Fusarium oxysporum*, and *Fusarium proliferatum*(38,39,40). Stem bromelain poses strong antifungal activity to protect the plant from phytopathogen and its possible application as a crop protective agent(15). Furthermore, it has been shown that pineapple stem waste obtained during the production of bromelain has moderate bioactivities against fungal development, maybe as a result of the presence of benzoic acid(41).

**Anti-cancer activity:** Bromelain, a proteolytic enzyme found in pineapple stems, has been found to have anticancer properties and may be used as a therapeutic agent. Research has demonstrated that the stem of the pineapple, or bromelain, has antitumoral properties and suppresses the proliferation of many types of cancer cells, such as HeLa cells for cervical cancer, U251 cells for glioblastoma, Caco-2 cells for colon adenocarcinoma, A2780 cells for ovarian cancer, and HT29 cells for colon cancer. (42,43,44,45). Studies have shown that bromelain inhibits the growth of cells, increases apoptosis, and downregulates signaling pathways including Akt and ERK that are important in the progression of cancer(46). In colorectal cancer cells, bromelain has antiproliferative and proapoptotic activities. It also has chemopreventive effects on colon carcinogenesis in vivo(16).

**Anti-inflammatory activity:** According to a study Stem bromelain inhibits the intestinal motility and it can be used as lead compound of a drug development which can control the intestinal motility in diabetes and inflammation(17). Pineapple stem residue contains Feruloyl Oligosaccharide Ester which shows anti microbial activity(18).

### **Pharmacological Activities of Pineapple(Fruit):**

The tropical fruit pineapple is known for its distinct scent and sweet flavor. It also poses various pharmacological activities that significantly increase our health benefits.

**Anti-inflammatory activity:** Pineapple consists of an enzyme called bromelain, which exhibits anti-inflammatory properties. Bromelain reduces inflammation by inhibiting a variety of pro-inflammatory molecules, such as prostaglandins and cytokines(19). These anti-inflammatory properties make pineapple a potential therapeutic option for conditions characterized by inflammation, such as arthritis and sinusitis.

**Anti-tumor activity:** Bromelain shows antitumor activity as bromelain exhibit immunomodulatory activity by increasing the damage immune cytotoxicity of monocytes against tumor cells and stimulate the release of various cytokines such as TNF $\alpha$ , interleukin (II)-1 $\beta$ , II-6, and II-8(20). It has been shown that bromelain also reduces the adverse effects of a variety of antibiotics. Bromelain is used in the treatment of burns, infection in the skin as well as vaccine preparation(20).

**Antioxidant activity:** Bromelain extract with methanol contains protein, terpenoids, carbohydrates, lipids, peptides and amino acids(24). It showed highest antioxidant activity and

provided a protection of our human body from disease induced by free radicals without any side effects(21,22.). By reducing the oxidative chain reaction, antioxidants reduce the oxidative stress(22).

**Anti-platelet activity:** By in-vitro and in-vivo analysis showed that administration of bromelain enzymes prevents aggregation of blood platelets and reduces the angina pectoris(23). Platelet aggregation was inhibited by the purified bromelain extract, with an aggregation percentage of 49.70% and an inhibition percentage of 46.89%(47). Furthermore, in vitro, the pure bromelain demonstrated antiplatelet activity with a percentage of inhibition of 77.994% and a percentage of aggregation of 20.892%.Moreover, research on bromelain that was separated from pineapple core revealed that it can lengthen the bleeding period, suggesting that it may have antiplatelet properties(48). According to these results, bromelain from pineapple may have antiplatelet properties and be used medicinally to stop platelet aggregation.

**Hepatoprotective activities:** It has been found that pineapples possess hepatoprotective activity.In rats fed a high-cholesterol diet, daily pineapple consumption has been proven to lower weight growth, blood lipid profiles, and cardiac risk factors(49). In rats given a high-cholesterol diet, pineapple fruit consumption has also been shown to enhance vascular function and decrease hepatic steatosis(50).

**Antidepressant activities:** In rats given a high-cholesterol diet, pineapple fruit consumption has also been shown to enhance vascular function and decrease hepatic steatosis(51).Additionally, pineapple juice prevented the hypothermia brought on by reserpine, confirming the antidepressant properties of the fruit(52).Furthermore, pineapple juice decreased malondialdehyde (MDA) levels and suppressed the activity of monoamine oxidase (MAO) enzymes, indicating its potential to regulate neurotransmitter levels and oxidative stress, both of which are linked to depression(53).

#### **Miscellaneous activity:**

- It has been shown that bromelain also reduces the adverse effects of a variety of antibiotics.
- Bromelain is used in the treatment of burns, infection in the skin as well as vaccine preparation(20).
- According to a study bromelain is used in the treatment of ulcerative colitis(23).
- Different ethnobotanical studies state that pineapple juice is used to control the birth and fertility by the Indian people(24).
- Crude bromelain has an antibacterial activity particularly against the E.coli and Streptococcus pyogenes(25).
- Pineapple contains Vit B or Thiamine which allows our cell to transform the carbohydrate into ATP(26).
- Manganese is found in pineapple which is essential for our body for the development of bone(26).
- One of the common sources of alpha-hydroxy acids is pineapple which is used in various skin creams for the treatment of wrinkles(26).

#### **Pharmacological activity of Pineapple leaves:**

**Antioxidant activity:** Pineapple leaves have also been found to possess pharmacological properties. An antioxidant is a molecule that stops the free radical chain reactions which can cause damage to cells. According to a study pineapple leaf extract with ascorbic acid shows antioxidant activity(27). Pineapple consists of non enzymatic antioxidants such as Vit E, Vit C, Carotenoids and polyphenol (29).

**Anti-Inflammatory activity:** Pineapple leaf extract possessed notable inhibition of the denaturation of protein and proteinase activity(28). It also restrained the secretion of TNF $\alpha$ , prostaglandin and interleukin-1 $\beta$ . For that reason it was identified that pineapple leaf extract shows anti-inflammatory activity(28).

**Absorption promoter:** Pineapple leaf extract rich with a variety of phenolic acid such as caffeic acid and p-coumaric acid. A study suggests that this phenolic acid has better absorption properties under an acidic environment as well as being fully absorbed into the whole intestine(30). It can be incorporated into sustained release formulation to improve the absorption(30)

#### **Pharmacological activity of Pineapple roots:**

**Antioxidant activity:** The antioxidant activity of the pineapple roots exhibit due to the presence of flavonoids and phenolic compounds(32). These compounds scavenge free radicals and protect cells from oxidative damage.

**Antimalarial activity:** In addition, pineapple roots have shown weak antimalarial activity against Plasmodium berghei in mice(33). Furthermore, pineapple roots have demonstrated potential as an immune stimulant, suggesting their use in relieving the symptoms of malaria.

**Anti-rheumatic activity:** Pineapple roots have shown activity against rheumatoid arthritis. Studies have indicated that pineapple roots possess inhibitory activities against Cox-2 and PGE2, which are involved in the pathogenesis of rheumatoid arthritis.

## **2. CONCLUSION**

Pineapple has pharmacological activity that makes it a promising candidate for more study and investigation in the field of natural medicines. This includes its antioxidant capacity, anti-inflammatory effects, anti-diabetic activity, and anti-cancer capabilities. The primary pharmacological or biological effects of Ananas comosus, or pineapple, and its variants were summarized in this review study. The review articles focuses on each and every parts of pineapple's and their specific pharmacological actions, emphasizing its capacity to act as an antioxidant, as well as its anti-inflammatory, anti-microbial, anti-cancer, and hepatoprotective qualities.

## **3. REFERENCES**

1. Twum, L.A. and Pare, A. (2019). Optimization of Flour Blends for Domestic and Industrial Application. Current Journal of Applied Science and Technology, 32(4), pp.1–10. doi:<https://doi.org/10.9734/cjast/2019/40852>.
2. Debnath, P., Dey, P., Chanda, A. and Bhakta, T. (2012). A Survey on Pineapple and its medicinal value. Scholars Academic Journal of Pharmacy (SAJP) Scholars Academic & Scientific Publishers, [online] (1). Available at: [https://saspublishers.com/media/articles/SASP11\\_24-29\\_vMVRj7M.pdf](https://saspublishers.com/media/articles/SASP11_24-29_vMVRj7M.pdf).
3. Mohd Ali, M., Hashim, N., Abd Aziz, S. and Lasekan, O. (2020). Pineapple (Ananas comosus): A comprehensive review of nutritional values, volatile compounds, health benefits, and potential food products. Food Research International, 137, p.109675. doi:<https://doi.org/10.1016/j.foodres.2020.109675>.
4. Chakraborty, A.J., Mitra, S., Tallei, T.E., Tareq, A.M., Nainu, F., Cicia, D., Dhama, K., Emran, T.B., Simal-Gandara, J. and Capasso, R. (2021). Bromelain a Potential Bioactive

- Compound: A Comprehensive Overview from a Pharmacological Perspective. *Life*, 11(4), p.317. doi:<https://doi.org/10.3390/life11040317>.
5. Suarez, Angelica Faith L., et al. "In Situ Spatiotemporal Mapping of 3 -Hydroxy-3-Methylglutaryl-Coa Reductase (HMGCR) Inhibitor in Pineapple (*Ananas Comosus*) Fruit Tissue by MALDI Mass Spectrometry Imaging." *Frontiers*, Frontiers, 31 Mar. 2023, [www.frontiersin.org/articles/10.3389/fntpr.2023.1160541/full](http://www.frontiersin.org/articles/10.3389/fntpr.2023.1160541/full).
  6. Azevedo da Paixão, J., Fernando de Araújo Neto, J., Oliveira do Nascimento, B., Mota da Costa, D., Brandão, H.N., Duarte Souza, F.V., Hilo de Souza, E., Lovatti Alves, Q., Lima Erling, S.B. and Pereira de Lima David, J. (2021). Pharmacological Actions of *Ananas comosus* L. Merrill: Revision of the Works Published from 1966 to 2020. *Pharmacognosy Reviews*, [online] 15(29), pp.57–64. doi:<https://doi.org/10.5530/phrev.2021.15.6>.
  7. Industrial applications of *Ananas comosus* wastes as valuable and utilizable products- A review. (2022). *Indian Journal of Natural Products and Resources*. doi:<https://doi.org/10.56042/ijnpr.v13i3.53857>.
  8. Seenak, P., Kumphune, S., Malakul, W., Chotima, R. and Nernpermpisooth, N. (2021). Pineapple consumption reduced cardiac oxidative stress and inflammation in high cholesterol diet-fed rats. *Nutrition & Metabolism*, 18(1). doi:<https://doi.org/10.1186/s12986-021-00566-z>.
  9. Ajayi, A.M., Coker, A.I., Oyebanjo, O.T., Adebanjo, I.M. and Ademowo, O.G. (2022). *Ananas comosus* (L) Merrill (pineapple) fruit peel extract demonstrates antimalarial, anti-nociceptive and anti-inflammatory activities in experimental models. *Journal of Ethnopharmacology*, 282, p.114576. doi:<https://doi.org/10.1016/j.jep.2021.114576>.
  10. Das, G., Patra, J.K., Debnath, T., Ansari, A. and Shin, H.-S. (2019). Investigation of antioxidant, antibacterial, antidiabetic, and cytotoxicity potential of silver nanoparticles synthesized using the outer peel extract of *Ananas comosus* (L.). *PLOS ONE*, 14(8), p.e0220950. doi:<https://doi.org/10.1371/journal.pone.0220950>.
  11. Ajayi, A.M., John, K.A., Emmanuel, I.B., Chidebe, E.O. and Adedapo, A.D.A. (2021). High-fat diet-induced memory impairment and anxiety-like behavior in rats attenuated by peel extract of *Ananas comosus* fruit via atheroprotective, antioxidant and anti-inflammatory actions. *Metabolism Open*, 9, p.100077. doi:<https://doi.org/10.1016/j.metop.2021.100077>.
  12. Okafor, O., Erukainure, O.L., Ja, A., RO Adejobi, Owolabi, F. and SB Kosoko (2011). Modulatory effect of pineapple peel extract on lipid peroxidation, catalase activity and hepatic biomarker levels in blood plasma of alcohol-induced oxidative stressed rats. 1(1), pp.12–14. doi:[https://doi.org/10.1016/s2221-1691\(11\)60060-9](https://doi.org/10.1016/s2221-1691(11)60060-9).
  13. Nitta, T., Arai, T., Takamatsu, H., Inatomi, Y., Murata, H., Inuma, M., Tanaka, T., Ito, T., Asai, F., Ibrahim, I., Nakanishi, T. and Watabe, K. (2002). Antibacterial Activity of Extracts Prepared from Tropical and Subtropical Plants on Methicillin-Resistant *Staphylococcus aureus*. *Journal of Health Science*, 48(3), pp.273–276. doi:<https://doi.org/10.1248/jhs.48.273>.
  14. Varilla, C., Marcone, M., Paiva, L. and Baptista, J. (2021). Bromelain, a Group of Pineapple Proteolytic Complex Enzymes (*Ananas comosus*) and Their Possible Therapeutic and Clinical Effects. A Summary. *Foods*, 10(10), p.2249. doi:<https://doi.org/10.3390/foods10102249>.
  15. López-García, B., Hernández, M. and Segundo, B.S. (2012). Bromelain, a cysteine protease from pineapple (*Ananas comosus*) stem, is an inhibitor of fungal plant pathogens. *Letters in Applied Microbiology*, 55(1), pp.62–67. doi: <https://doi.org/10.1111/j.1472-765x.2012.03258.x>.

16. Romano, B., Fasolino, I., Pagano, E., Capasso, R., Pace, S., De Rosa, G., Milic, N., Orlando, P., Izzo, A.A. and Borrelli, F. (2014). The chemopreventive action of bromelain, from pineapple stem (*Ananas comosus* L.), on colon carcinogenesis is related to antiproliferative and proapoptotic effects. *Molecular nutrition & food research*, [online] 58(3), pp.457–65. doi:<https://doi.org/10.1002/mnfr.201300345>.
17. Borrelli, F., Capasso, R., Severino, B., Fiorino, F., Aviello, G., De Rosa, G., Mazzella, M., Romano, B., Capasso, F., Fasolino, I. and Izzo, A.A. (2011). Inhibitory effects of bromelain, a cysteine protease derived from pineapple stem (*Ananas comosus*), on intestinal motility in mice. *Neurogastroenterology & Motility*, 23(8), pp.745-e331. doi:<https://doi.org/10.1111/j.1365-2982.2011.01735.x>.
18. Ishihara, Masanobu & Hasegawa, Mayu & Taira, Toki & Toyama, Seizen. (2000). Isolation and Antimicrobial Activity of Feruloyl Oligosaccharide Ester from Pineapple Stem Residues.. *Nippon shokuhin kagaku kogaku kaishi*. 47. 23-29. 10.3136/nskkk.47.23.
19. Chakraborty, A.J., Mitra, S., Tallei, T.E., Tareq, A.M., Nainu, F., Cicia, D., Dhama, K., Emran, T.B., Simal-Gandara, J. and Capasso, R. (2021). Bromelain a Potential Bioactive Compound: A Comprehensive Overview from a Pharmacological Perspective. *Life*, 11(4), p.317. doi:<https://doi.org/10.3390/life11040317>.
20. Maurer, H.R. (2001). Bromelain: biochemistry, pharmacology and medical use. *Cellular and Molecular Life Sciences*, 58(9), pp.1234–1245. doi:<https://doi.org/10.1007/p100000936>.
21. Saksri, T. and Kumpun, S. (2019). Antioxidant activity of pineapple (*Ananas comosus*). *International academic multidisciplinary research conference in amsterdam 2019*, [online] pp.110–113.
22. Saptarini, N.M., Rahayu, D. and Herawati, I.E. (2019). Antioxidant Activity of Crude Bromelain of Pineapple (*Ananas comosus* (L.) Merr) Crown from Subang District, Indonesia. *Journal of Pharmacy & Bioallied Sciences*, [online] 11(Suppl 4), pp.S551–S555. doi:[https://doi.org/10.4103/jpbs.JPBS\\_200\\_19](https://doi.org/10.4103/jpbs.JPBS_200_19).
23. 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), pp.283–288. doi:<https://doi.org/10.3892/br.2016.720>.
24. Azevedo da Paixão, J., Fernando de Araújo Neto, J., Oliveira do Nascimento, B., Mota da Costa, D., Brandão, H.N., Duarte Souza, F.V., Hilo de Souza, E., Lovatti Alves, Q., Lima Erling, S.B. and Pereira de Lima David, J. (2021). Pharmacological Actions of *Ananas comosus* L. Merrill: Revision of the Works Published from 1966 to 2020. *Pharmacognosy Reviews*, [online] 15(29), pp.57–64. doi: <https://doi.org/10.5530/phev.2021.15.6>.
25. Ali Abdulrahman Ali, Mohammed Adamu Milala, Isa Adamu Gulani. Antimicrobial Effects of Crude Bromelain Extracted from Pineapple Fruit (*Ananas comosus* (Linn.) Merr.). *Advances in Biochemistry*. Vol. 3, No. 1, 2015, pp. 1 -4. doi: 10.11648/j.ab.20150301.11
26. Debnath, P., Dey, P., Chanda, A. and Bhakta, T. (2012). A Survey on Pineapple and its medicinal value. *Scholars Academic Journal of Pharmacy (SAJP) Scholars Academic & Scientific Publishers*, [online] (1). Available at: [https://saspublishers.com/media/articles/SASP11\\_24-29\\_vMVRj7M.pdf](https://saspublishers.com/media/articles/SASP11_24-29_vMVRj7M.pdf).
27. Sahu, D., Yadav, B., Verma, S., Yadav, A.P., Tilak, V.K. and Maurya, S.D. (2020). ANTIOXIDANT ACTIVITY Antioxidant Activity and Phytochemical Analysis of Leaf Extracts of Pineapple. *Journal of Drug Delivery and Therapeutics*, 10(5), pp.165–167. doi:<https://doi.org/10.22270/jddt.v10i5.4397>.



28. Kargutkar, S. and Brijesh, S. (2017). Anti-inflammatory evaluation and characterization of leaf extract of *Ananas comosus*. *Inflammopharmacology*, 26(2), pp.469–477. doi:<https://doi.org/10.1007/s10787-017-0379-3>.
29. Ajagun-Ogunleye, M.O. and Ebuehi, O.A.T. (2020). Evaluation of the anti-aging and antioxidant action of *Ananas sativa* and *Moringa oleifera* in a fruit fly model organism. *Journal of Food Biochemistry*, 44(11). doi:<https://doi.org/10.1111/jfbc.13426>.
30. Dang, Y. and Zhu, C. (2015). Genomic Study of the Absorption Mechanism of p-Coumaric Acid and Caffeic Acid of Extract of *Ananas Comosus* L. Leaves. *Journal of Food Science*, 80(3). doi:<https://doi.org/10.1111/1750-3841.12774>.
31. Kargutkar, S. and S Brijesh (2016). Anti-rheumatic activity of *Ananas comosus* fruit peel extract in a complete Freund's adjuvant rat model. *Pharmaceutical Biology*, 54(11), pp.2616–2622. doi:<https://doi.org/10.3109/13880209.2016.1173066>.
32. Azevedo da Paixão, J., Fernando de Araújo Neto, J., Oliveira do Nascimento, B., Mota da Costa, D., Brandão, H.N., Duarte Souza, F.V., Hilo de Souza, E., Lovatti Alves, Q., Lima Erling, S.B. and Pereira de Lima David, J. (2021). Pharmacological Actions of *Ananas comosus* L. Merrill: Revision of the Works Published from 1966 to 2020. *Pharmacognosy Reviews*, [online] 15(29), pp.57–64. doi: <https://doi.org/10.5530/phrev.2021.15.6>.
33. Popp, F.D., Wefer, J.M., Rosen, G. and Noble, A.C. (1967). Investigations of Philippine plants for alkaloids, antimalarial agents, and antineoplastic agents. *Journal of Pharmaceutical Sciences*, 56(9), pp.1195–1197. doi:<http://doi.org/10.1002/jps.2600560936>.
34. Baran, A., Keskin, C., Baran, M.F., Huseynova, I., Khalilov, R., Eftekhari, A., Irtegun-Kandemir, S. and Kavak, D.E. (2021). Ecofriendly Synthesis of Silver Nanoparticles Using *Ananas comosus* Fruit Peels: Anticancer and Antimicrobial Activities. *Bioinorganic Chemistry and Applications*, 2021, pp.1–8. doi:<https://doi.org/10.1155/2021/2058149>.
35. Hendri Hendri, Zulfah Zakhiah and Rikhsan Kurniatuhadi (2023). Antibacterial Activity of Pineapple Peel Eco-enzyme (*Ananas comosus* L.) on Growth *Pseudomonas aeruginosa* and *Staphylococcus epidermidis*. *Jurnal Biologi Tropis*, 23(3), pp.464–474. doi:<https://doi.org/10.29303/jbt.v23i3.5272>.
36. Purwati, E., & Raharjeng, S. W. (2023). Aktivitas antibakteri sabun padat ekstrak kulit buah nanas (*Ananas comosus* L.) PADA *Escherichia coli*. *Jurnal Ilmiah Manuntung*, 9(1), 71–78. <https://doi.org/10.51352/jim.v9i1.670>
37. Lubaina, A.S., Raveendran, R., Nair, R.R. and Kumar, P. (2023). In vivo anti-inflammatory potential, minimum inhibitory concentration and minimum bactericidal concentration of ferulic acid, isolated from pineapple waste. *Applied Biological Research*, 25(1), pp.36–43. doi:<https://doi.org/10.5958/0974-4517.2023.00004.6>.
38. Ninsuwan, K., Nimnuan, J., Watcharakitti, J., Siritwong, C., Amornsakchai, T., & Smith, S. M. (2023). Antifungal Activity of Water-Based Adhesives Derived from Pineapple Stem Flour with Apple Cider Vinegar as an Additive. *Polymers*, 15(7), 1735. <https://doi.org/10.3390/polym15071735>
39. López-García, B., Hernández, M., & Segundo, B. S. (2012). Bromelain, a cysteine protease from pineapple (*Ananas comosus*) stem, is an inhibitor of fungal plant pathogens. *Letters in Applied Microbiology*, 55(1), 62–67. <https://doi.org/10.1111/j.1472-765x.2012.03258.x>
40. Sales, M. D. C., Costa, H. B., Fernandes, P. M. B., Ventura, J. A., & Meira, D. D. (2016). Antifungal activity of plant extracts with potential to control plant pathogens in pineapple. *Asian Pacific Journal of Tropical Biomedicine*, 6(1), 26–31. <https://doi.org/10.1016/j.apjtb.2015.09.026>

41. Tawata, S., Taira, S., Kobamoto, N., Zhu, J., Ishihara, M., & Toyama, S. (1996). Synthesis and antifungal activity of cinnamic acid esters. *Bioscience, Biotechnology, and Biochemistry*, 60(5), 909–910. <https://doi.org/10.1271/bbb.60.909>
42. Pant, B., Chand, K., Paudel, M. R., Joshi, P. R., Thapa, B. B., Park, S. Y., Shakya, S., Thakuri, L. S., Rajbahak, S., Sah, A. K., Baniya, M. K., Gurung, P. R., Maharjan, L., & Rajbhandari, P. (2021). Micropropagation, antioxidant and anticancer activity of pineapple orchid: *Dendrobium densiflorum* Lindl. *Journal of Plant Biochemistry and Biotechnology*, 31(2), 399–409. <https://doi.org/10.1007/s13562-021-00692-y>
43. Raeisi, E., Shahbazi-Gahrouei, D., & Heidarian, E. (2019). Pineapple extract as an efficient anticancer agent in treating human cancer cells. *SciSpace - Paper*. <https://typeset.io/papers/pineapple-extract-as-an-efficient-anticancer-agent-in-381cqp3dk3>
44. Báez, R., Lopes, M. T. P., Salas, C., & Hernández, M. (2007). In Vivo Antitumoral Activity of Stem Pineapple (*Ananas comosus*) Bromelain. *Planta Medica*, 73(13), 1377–1383. <https://doi.org/10.1055/s-2007-990221>
45. Romano, B., Fasolino, I., Pagano, E., Capasso, R., Pace, S., De Rosa, G., Milić, N., Orlando, P., Izzo, A. A., & Borrelli, F. (2013). The chemopreventive action of bromelain, from pineapple stem (*Ananas comosus*L.), on colon carcinogenesis is related to antiproliferative and proapoptotic effects. *Molecular Nutrition & Food Research*, 58(3), 457–465. <https://doi.org/10.1002/mnfr.201300345>
46. Gani, M. B. A., Nasiri, R., Almaki, J. H., Majid, F. a. A., Marvibaigi, M., Amini, N., Chermahini, S. H., & Mashudin, M. (2015). In vitro antiproliferative activity of fresh pineapple juices on ovarian and colon cancer cell lines. *International Journal of Peptide Research and Therapeutics*, 21(3), 353–364. <https://doi.org/10.1007/s10989-015-9462-z>
47. Musfiroh, F. F., Setiasih, S., Handayani, S., Hudiyo, S., & Ilyas, N. M. (2018). In Vivo antiplatelet activity aggregation assay of bromelain fractionate by ethanol from extract pineapple core (*Ananas comosus*[L.] merr.). *IOP Conference Series: Materials Science and Engineering*, 299, 012017. <https://doi.org/10.1088/1757-899x/299/1/012017>
48. Du, L., Sun, G., Zhang, X., Liu, Y., Prinyawiwatkul, W., Xu, Z., & Shen, Y. (2016). Comparisons and correlations of phenolic profiles and anti-oxidant activities of seventeen varieties of pineapple. *Food Science and Biotechnology*, 25(2), 445–451. <https://doi.org/10.1007/s10068-016-0061-3>
49. Seenak, P., Kumphune, S., Malakul, W., Chotima, R., & Nernpermpisooth, N. (2021). Pineapple consumption reduced cardiac oxidative stress and inflammation in high cholesterol diet-fed rats. *Nutrition & Metabolism*, 18(1). <https://doi.org/10.1186/s12986-021-00566-z>
50. Namwong, A., Kumphune, S., Seenak, P., Chotima, R., Nernpermpisooth, N., & Malakul, W. (2022). Pineapple fruit improves vascular endothelial dysfunction, hepatic steatosis, and cholesterol metabolism in rats fed a high-cholesterol diet. *Food & Function*, 13(19), 9988–9998. <https://doi.org/10.1039/d2fo01199a>
51. Milind, P., & Pooja, G. (2010). Eat pineapple a day to keep depression at bay.
52. Ademosun, A. O., & Oboh, G. (2017). Effect of pineapple, orange and watermelon juices on phosphodiesterase, monoamine oxidase and angiotensin-I converting enzyme activities in rat heart and brain homogenates. *Oriental Pharmacy and Experimental Medicine*, 17(3), 269–276. <https://doi.org/10.1007/s13596-017-0279-5>
53. Dureja, H., Kumar, V., & Sangwan, V. (2023). Therapeutic Application of Pineapple: a review. *Recent Advances in Food, Nutrition and Agriculture*, 14(2), 107–125. <https://doi.org/10.2174/2772574x14666230522114039>