Efficacy of Graviola fruit pulp in Human Health Care Management- A narrative review

Subramaniam Sivakumar[1*] & Sanjeevi Pandarinathan[2]
[1]Department of Biochemistry, Sri Sankara Arts and Science College (Autonomous), Enathur, Kanchipuram – 631 561, TamilNadu, India.
[2]Anbil Dharmalingam Agricultural College and Research Institute, Tiruchirappalli-620 027, Tamil Nadu, India.
Corresponding Author

Received: July 23, 2018 Accepted: October 07, 2018

ABSTRACT *Peroxidase is one of the key antioxidant enzyme. Peroxidases are present in all vascular plants. Different types of peroxidases were recognized, and an ever-increasing number of functions were assigned to them, particularly in plant physiology. The peroxidase (POD) enzyme of Graviola (Annona muricata) fruit play a restricted role in enzymatic browning during ripening process. In Graviola fruit pulp juice, guaiacol peroxidase (EC 1.11.1.7) activity was reported. Graviola is used as an antispasmodic, emetic and sudorific in herbal medicine. Antioxidant activities are important to control and prevent many diseases. Graviola fruit pulp exhibited moderate antioxidant capacity. The present review is proposed to explain the potential use of Graviola fruit and its role in human health.*

Keywords: *Graviola; Annona muricata; Peroxidase; human health; herbal medicine.*

Peroxidases

Peroxidase is one of the key antioxidant enzymes. Different types of peroxidases were recognized, and an ever-increasing number of functions were assigned to them, particularly in plant physiology. Therefore, while the basic chemical reactions of peroxidase (E.C.1.11.1.7) are well established, namely that of the peroxidatic cycles involving H_20_2 and a large array of hydrogen donors (Huystee, 1987). Basically peroxidases are classified into two major classes like heme and non-heme peroxidases. Morethan 80% of known peroxidases are heme peroxidases and only 20% are non-heme peroxidases. Heme peroxidases are further divided into animal peroxidases (peroxidase-cyclooxygenase superfamily (PCOXS)) and non-animal peroxidases (peroxidase-catalase superfamily (PCATS)). The non-animal peroxidases are further divided into Class I peroxidases, Class II peroxidases and Class III peroxidases. The class I peroxidases include both prokaryotic and eukaryotic peroxidases belonging to non-animal sources. They exhibited major role in oxidative stress i.e., detoxification of ROS(H_2O_2). The class II peroxidases, exclusively containing fungal peroxidases, have major role in lignin biodegradation. The class III peroxidases are widely distributed in plant kingdom. They are involved in wide range of physiological processes such as cell wall metabolism, lignification, suberization, auxins metabolism, wound healing, reactive oxygen species (ROS) and reactive nitrogen species (RNS) metabolism, fruit growth and ripening defense against pathogens etc (Pandey et al., 2017).

The Graviola pulp is used for producing various juice blends, syrups, nectars, jams, shakes, jellies, preserves and ice creams. It is also a raw material for flakes, fruit bars, and powders (Telis-Romero et al., 2007). Peroxidases (hydrogen-peroxide oxidoreductases) are the heme-containing glycoproteins that in the presence of hydrogen peroxide catalyze the oxidation of different substrates such as polyaromatic hydrocarbons (PAHs), phenols, aromatic amines, etc., (Dunford, 1999). Peroxidases are present in almost all vascular plants and are assumed to be involved in wide range of physiological phenomena including wound healing, detoxification of heavy metals and reactive oxygen species during oxidative stress and cellular metabolic processes, defense mechanisms against pathogens, cross-linking of cell wall polysaccharides, biodegradation reactions, scavenging of hydrogen peroxide from cytosol and chloroplast. Peroxidases are present in all vascular plants. Their activity largely depends upon the factors like pH and temperature(Kalsoom*et al*., 2015).

During harvest, transport, storage and processing, mechanical injury might occur to fruits and vegetables. These mechanical injuries cause browning color in many fruits and vegetables due to the action of polyphenol oxidase and peroxidases (Bora *et al.,* 2004).

Graviola (*Annona muricata*)

The *Annona muricata* L. is known as soursop in English-speaking countries and is referred to by numerous common names like Graviola (Badrie and Schauss, 2010). Graviola found in many parts of the

world including some parts of Asia, Africa and America. This is an evergreen and flowering tree that can be stand up to 8 meters tall and yield edible fruits. Many parts of the tree are used for the treatment of different diseases in traditional medications like diabetes, hypertension, rheumatism, inflammation and parasitic infections. It belongs to the Annonaceae family and like other fruit of the genus *Annona* is a syncarp formed by the coalescence of pistils and receptacles in a large pulpy structure. It is, therefore, a compound fruit formed by a cluster of berries, whose individual carpel components remain in the peel during the entire development in the form of spurs or pulpy spines, which are curved and short (Bueso, 1980; Worrell *et al.*, 1994).

Graviola fruit pulp

Graviola fruit is a very perishable fruit. It has five days of shelf life at room temperature when it is harvested at it physiological maturity status. The fresh graviola fruit pulp contains 13.6 % of dry matter (Leterme et al., 2006).The taste of the Graviola fruit results from the combination of acids and sugars (0.65–0.85%), with its pulp containing 18% carbohydrates, 1% protein, 1% fiber and phenols, flavonols, acetogenins and vitamins B1, B2, and C, (Rice et al., 1991; Onimawo, 2002). The fruit consists of 67.5% edible pulp, 20% peel, 8.5% seeds, and 4% core by weight (Saanchez-Nieva *et al*., 1953).

Role of Peroxidase in fruit ripening

The ripening period is quite short for Graviola fruit. Many metabolic changes occur during ripening period. The ripening process causes changes in flavor, pigmentation and softening which can be qualitatively and quantitatively assessed by the activity of different enzymes like hydrolases, pectin methylesterase (PME), polygalacturonase (PG), galactosidases, amylase, polyphenol oxidase and peroxidase. One single enzyme alone is not responsible for the ripening changes but the complex interaction of enzymes responsible for the changes.

The peroxidase (POD) enzyme, play a restricted role in enzymatic browning due to the need for the availability of hydrogen peroxide for its action (Robards *et al.*, 1999). However, in the presence of small quantities of hydrogen peroxide, the phenolic substrates can be oxidized and several compounds are susceptible to oxidation by the peroxidase enzymes (Robinson, 1991).The activity of peroxidase in Graviola fruit is still high right after harvesting, but turns severely reduced in the period from the second to the fourth day (Lima *et al.*,2003). In contrast to other fruits, the activity of the POD is higher in Graviola fruit pulp. The role of POD has been studied in many fruits and vegetables like tomatoes (Loukili *et al*. 1999), olives (Saraiva *et al*. 2007) and loquats cv. Zaozhong 6 (Lin *et al*. 2007).The 4-hexylresorcinol (4-HR), oxalic acid, and L-cysteine showed inhibitory role against the peroxidase enzyme activity (Zhang and Shao, 2015). In Graviola fruit pulp juice, guaiacol peroxidase (EC 1.11.1.7) activity was reported. The exposure of Graviola fruit juice to 55^0C for 30 min was the most effective treatment in reducing POD, PME and PG activities (Rabelo *et al*., 2016).

Graviola fruit pulp in Human health

Graviola is used as an antispasmodic, emetic and sudorific in herbal medicine. Loizzo *et al*., have reported high correlation between the consumption of fruits in prevention and treatment of various diseases (Loizzo *et al*., 2012). Antioxidant activities are important to control and prevent many diseases including rheumatoid arthritis, cancer and cardio vascular diseases related to degenerative process (Almeida *et al*., 2011; Dembitsky *et al*., 2011). Graviola fruits are vital to maintain human health since it provides nutrients, and phytochemicals. Bioactive substances such as vitamin C, flavonoid, anthocyanins and carotenoids are also found in fruits among others (Cardozo *et al*., 2012).Graviola fruit pulp exhibited moderate antioxidant capacity (Padmini*et al*., 2015).

The genus Annonaceae comprises about 70 species, of which nine are indigenous to India. Graviolais widely used in traditional Indian medicine for the treatment of kidney troubles, fever, nervousness, ulcers and wounds and possesses antispasmodic, antidysenteric, and parasiticidal activity (Padma et al., 1997; Badrie and Schauss, 2010). In terms of the plant parts, the leaves are used as suppurative, febrifuge; its bark as tonic; roots as antispasmodic, parasiticidal; flowers as bechic; unripe fruit as antiscrobutic; and seeds as insecticidal, astringent, fish-poison. Within ayurvedic medicine in India, the plant is used as a bitter, tonic, abortifacient, febrifuge, for scorpion stings, high blood pressure, and as a respiratory stimulant.

Taylor reports that in Jamaica, Haiti, and the West Indies, the fruit and/or fruit juice is used for fevers, parasites and diarrhea, and as a lactagogue. In Brazil, the fruit, its juice, and crushed seeds are used as a vermifuge and anthelmintic, while the fruit and its juice alone are used to increase mother's milk (lactagogue) and as an astringent for diarrhea and dysentery (Taylor, 2002).

Graviola is popular for its edible fruit and is used as a folkloric herbal medicine in Philippines. The Graviola fruit juice is used as a diuretic and decoction of powdered immature fruits is used as dysentery remedy (Ragasa *et al*., 2012). Most of the uses of the Graviola fruit have been scientifically validated.

The World Health Organization (WHO) is reported that 84 million deaths would be attributed to cancer in the period between 2005 and 2015. In India, the National Cancer Registry programme report of 2012 – 2015 showed that 1.74 lakhs people were affected by cancer. The most predominant site of occurrence of cancer is breast in females and lung in males (HBCR, 2015).

Even though new technologies have been applied in the field of chemotherapy, surgery and radiotherapy as treatment procedures, many patients are not satisfied over these treatment methods due to their side effects. The chemotherapy results in the side effect of toxicity to heart, lung and nervous system. In some cases drugs can induce red blood cell and stem cell mutations. Chemotherapy is also considered to be more dangerous to aged cancer patients because they cause neuropathy. The radiotherapy causes discomfort and reductions in the quality of life for cancer patients. The Intensity Modulated Radiotherapy (IMRT) can cause dysphagia in cancer patients. Due to these issues, cancer patients search for the new methods for cancer treatment. In this case, cancer patients approached the traditional medications either with the normal cancer treatment procedures or as an alternative treatment procedure. Even though these traditional medications does not have effective research evidences for their usage and side effects, people willing to follow these procedures. Because of this reason, several organizations are concentrating on the usage of traditional medications using cell culture, animal studies and modern techniques. In this scenario, the present review is proposed to explain the potential use of Graviola (*Annona muricata*) pulp and its use in human health especially against cancer treatment.

Graviolafruit extract induces apoptosis in breast T47D cancer cells (Rachmani et al., 2012). Ethanol extracts of roots, fruits, or leaves inhibited proliferation via G0/G1 cell cycle arrest in leukemia HL-60 cancer cells (Moghadamtousi et al., 2014). Ethanolic extracts of roots, fruits, or leaves of Graviola also have been shown to induce apoptosis in HL-60 leukemia cancer cells through loss of Matrix metallo proteinases (MMP) (Pieme et al., 2014). Mitochondrial membrane potential loss and activation of caspases induced apoptosis in cancer cells by Graviola. Suppression of EGFR and JAK signaling leads to blockade of the PI3K, RAS and STAT pathways respectively, culminating in decreasing cell viability and metabolic catastrophe by down-regulating HIF-1α, GLUT1, GLUT4, expression, associated with decreased glucose uptake and cell cycle arrest in human cancer cells. Graviola control inflammation by inhibiting NF-kB mediated TNF-α and IL-1 expression. The expression of catalase (CAT), superoxide dismutase (SOD) and heme-oxygenase (HO-1) increased by Graviola. Graviola also destroys the drug resistant cells possibly through multidrug resistant export proteins (Qazi et al., 2018).

Conclusion

In this review article, the various publications on Graviola plant peroxidase reviewed and summarized the health benefits of Graviola fruit. Graviola fruit is useful as a processed product due to its high nutritional, medicinal and high pulp recovery nature. The pharmacokinetic and metabolomics studies have to be carried out to confirm the side effect free nature of human consumption of raw Graviola fruits (*Moghadamtousi et al., 2015)*. This review is hoped to be a source of information for researchers to further perform in vitro, in vivo and clinical investigations on the biological activities of Graviola fruit to gain insight into developing new agricultural, phytoremediation, food industrial and pharmaceutical agents. It could be concluded that the ingestion of Graviola fruit would be beneficial for living a healthy life.

References

1. Almeida, M.M.B., de Sousa, P.H.M., Arriage, A.M.C., do Prado, G. M., Magalhaes, C.E.C., Maia, G.A. and Lemos, G.A. (2011). Bioactive compounds and antioxidant activity of fresh exotic fruits from northeastern Brazil, Food Res. Int.l. 44:2155-2159.
2. Badrie N. and Schauss A.G. (2010). Soursop (Annona muricata L.): Composition, Nutritional Value, Medicinal Uses, and Toxicology, Bioactive Foods in Promoting Health. Ch.39:621-641.
3. Bora P. S., H. J. Holschuh and M. A. da Silva Vasconcelos (2004). Characterization of Polyphenol oxidase of Soursop (Annona Muricata L.) Fruit and A Comparative study of its Inhibition in Enzyme extract and in Pulp, Cienc. Tecnol. Aliment.,4(4):267-273.
4. Bueso C E (1980). Soursop, tamarind and chironja in Nagy S and Shaw P S., Tropical and Subtropical Fruits: Composition, Properties and Uses. Westiport . AVI Publishing: pp. 375 – 406.
5. Cardozo, C.J.M., Lozano, V.V., Betancur, D.P.Y., Velasquez, H.J.C. and Valenzuela, J.R.C. (2012). Physiological and physio-chemical characterization of Soursop fruit (Annona muricata L. cv. Elita), Revista Facultad Nacional de Agronomi Medellin. 65(1):6477-6486.

6. Dembitsky, V.M., Poovarodom, S., Leontowicz, H., Leontowicz, M., Vearasilp, S., Trakhtenberg, S. and Gorinstein, S. (2011). The multiple nutrition of some exotic fruits: Biological activity and active metabolites, Food Res. Int.l. 44:1671-1701.
7. Dunford, H. B. (1999). Heme peroxidases (p. 480). New York: Willey-VCH. 190-192.
8. Gaspar, Th., Penel, C., Thorpe, T., and Greppin, H. 1982. Peroxidases 1970-1980. A survey of their biochemical andphysiological roles in higher plants. Univ. Geneve. PP 324.
9. Huystee, R B V. (1987). Some Molecular Aspects of Plant Peroxidase Biosynthetic Studies. Annual Review of Plant Physiology. 38(1):205-219.
10. Kalsoom, U., Bhatti, H.N. and Asgher, M. (2015). Characterization of Plant Peroxidases and Their Potential for Degradation of Dyes: a Review. Appl Biochem Biotechnol. 176:1529. https://doi.org/10.1007/s12010-015-1674-3.
11. Leterme P , Buldgen A , Estrada F and London A M (2006). Mineral content of tropical fruit and unconventional foods of the Andes and the rain forest of Colombia. Food Chem.95:644–652.
12. Lima M A C de , Alves R E and Filgueiras H A C (2003). Avaliação da qualidade e da suscetibilidade ao escurecimento oxidativo de graviola (Annona muricata L.) durante a maturação pós-colheita. Proc Interamer Soc Trop Hort.46:23–26.
13. Lin J., Wu Z., and Peng Z. (2007). The study on purification and properties of peroxidase from loquat fruit. Journal of Sichuan Agricultural University. 25:419–424.
14. Loizzo, M.R., Tundis, R., Bonesi, M., Menichini, F., Mastellone, V., Avallone, L. and Menichini, F. (2012). Radical scavenging, antioxidant and metal chelating activities of Annona cherimola Mill. (Cherimoya) peel and pulp in relation to their total phenolic and total flavonoid contents, Journal of Food Composition and Analysis. 25:179-184.
15. Loukili A.E., Limam F., Ayadi A., Boyer N., and Ouelhazi L. (1999). Purification and characterization of a neutral peroxidase induced by rubbing tomato internodes. Physiologia Plantarum. 105: 24–31.
16. Moghadamtousi S. Zorofchian, H. Karimian, E. Rouhollahi, M. Paydar, M. Fadaeinasab, and H. Abdul Kadir. (2014). Annona muricataleaves induce G1 cell cycle arrest and apoptosis through mitochondria-mediated pathway in human HCT-116 and HT-29 colon cancer cells.Journal of Ethnopharmacology. 156:277–289.
17. Moghadamtousi, S.Z., Fadaeinasab, M., Nikzad, S., Mohan, G., Ali, H.M., Kadir, H.A., and Battino, M. (2015).Annona muricata (Annonaceae): A Review of Its Traditional Uses, Isolated Acetogenins and Biological Activities. International journal of molecular sciences.16:15625-15658. doi:10.3390/ijms160715625.
18. Moghadamtousi, S.Z.; Goh, B.H.; Chan, C.K.; Shabab, T.; and Kadir, H.A. (2013). Biological activities and phytochemicals of Swietenia macrophylla king. Molecules. 18:10465–10483.
19. Onimawo, I. A. (2002). Proximate composition and selected chemical properties of the seed, pulp and oil of soursop (Anona muricata). Plant Foods Hum. Nutr.57(2):165–171.
20. Padma, P., Chansouria, J. P. N., and Khosa, R. L. (1997). Effect of alcohol extract of Annona muricata oncold immobilization stress induced tissue lipid peroxidation. Phytother. Res.11:326–327.
21. Padmini, S.M.P.C., Samarasekera, R. and Pushpakumara, D.K.N.G., 2015. Antioxidant capacity and total phenol content of Sri Lankan Annona muricata L.. Tropical Agricultural Research, 25(2), pp.252–260. DOI:http://doi.org/10.4038/tar.v25i2.8146.
22. Pandey VP, Awasthi M, Singh S, Tiwari S, and Dwivedi UN (2017). A Comprehensive Review on Function and Application of Plant Peroxidases. Biochem Anal Biochem. 6:308. doi: 10.4172/2161-1009.1000308.
23. Pieme C. A., S. G. Kumar, M. S. Dongmo et al., (2014). Antiproliferativeactivity and induction of apoptosis by Annona muricata (Annonaceae) extract on human cancer cells.BMC Complementary and Alternative Medicine. 14(1):516.
24. Qazi Asif Khurshid, Jawed A Siddiqui, Rahat Jahan, Sanjib Chaudhary, Larry A. Walker, Zafar Syed, Dwight T. Jones, Surinder K. Batra5 and Muzafar A. Macha, (2018). Emerging Therapeutic Potential of Graviola and its Constituents in Cancers. Carcinogenesis. 39(4):522-533. doi: 10.1093/carcin/bgy024.
25. Rabelo, Marcela Cristina et al., (2016). Thermostability of Antioxidant and Deteriorative Enzymes from Soursop and Cashew Apple Juices. Rev. Bras. Frutic., Jaboticabal. 38(2):E-338.
26. Rachmani E. P. N., T. S. Suhesti, R. Widiastuti, and A. Aditiyono. (2012). The breast of anticancer from leaf extract of Annona muricata against cell line in T47D.International Journal of Applied Science and Technology. 2(1):198–200.
27. Ragasa, C.Y., Geneveve, S., Torres, O.B., Don, M.J., Shen C.C. (2012). Acetogenins from Annona muricata, Pharmacognosy Journal. 4(32):32-37.
28. Rice, R. P., Rice, L. W., and Tindal, H. D. (1991). Fruit and Vegetable Production in Warm Climate. Oxford: Macmillan Education Ltd.
29. Robards K , Prenzler P D , Tucker G , Swatsitang P and Glover W (1999). Phenolic compounds and their role in oxidative processes in fruits. Food Chem. 66:401 – 436.
30. Robinson D S (1991). Peroxidases and their signifi cance in fruits and vegetables in Fox P F , Food Enzimology., London. Elsevier Applied Science. v1:399–426.
31. Saanchez-Nieva, F., Igaravidez, L., and Lopez-Ramos, B. (1953). The preparation of soursop nectar. University of Puerto Rico Agriculture Experimental Stational Technical Paper.11:05–19.

32. Saraiva J., Nunes C., and Coimbra M. (2007). Purification and characterization of olive (Olea europaea L.) peroxidase – Evidence for the occurrence of a pectin binding peroxidase. Food Chemistry. 101:1571–1579.
33. Taylor, L. (2002). Graviola (Annona muricata). In Herbal Secrets of the Rainforest 2nd ed. Roseville, CA:Prima Publishing.
34. Telis-Romero, J., Beristain, C. I., Gabas, A. L., and Telis, V. R. N. (2007). Effect of apparentviscosity on the pressure drop during fluidized bed drying of soursop pulp. Chemical Engineering and Processing. 46: 684-694.
35. Worrell D B , Carrington C M S and Huber D J (1994). Growth, maturation and ripening of soursop (Annona muricata L.) fruit. Scient Hortic.57:07– 15.
36. Zhang X., and Shao X. (2015). Characterisation of polyphenol oxidase and peroxidase and the role in browning of loquat fruit. Czech J. Food Sci. 33:109–117. 10.17221/384/2014-CJFS.