

## Potential Benefits of Soursop in Combating Cancer: A Review

Jasmitha B. G.<sup>1</sup> and Honnabyraiah M. K.<sup>2</sup>

<sup>1</sup>Department of Fruit Science, College of Horticulture, GKVK campus, Bengaluru, Karnataka

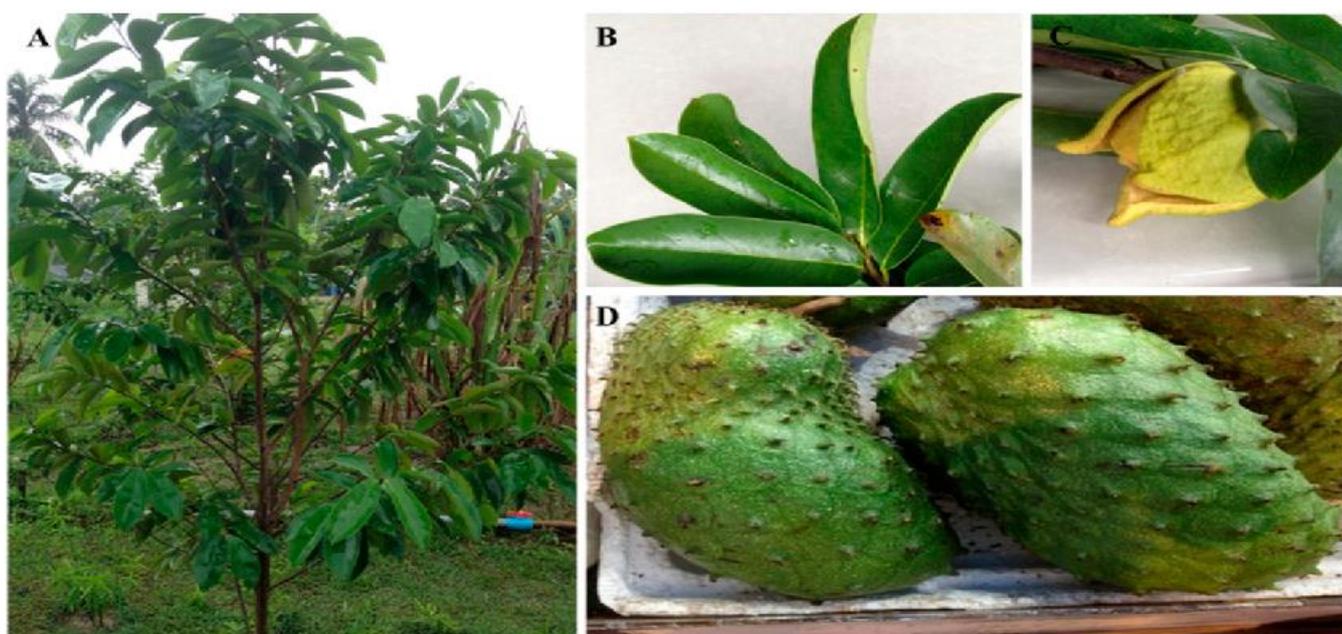
<sup>2</sup>Professor and Head, Department of Fruit science, College of Horticulture Yalachahalli, Mysuru, Karnataka

### SUMMARY

*Annona muricata* is a species of the genus *Annona* of the custard apple tree belongs to the family, Annonaceae, which has edible fruit. The fruit is usually called soursop due to its slightly acidic taste when ripe. Soursop is a tropical plant, it has been used in the ethno medicine as treatment to a range of diseases, from common cold to treat cancer. Numerous studies conducted on various parts of soursop plant, validate its use as anti-cancer. Many investigations in different types of cancers have revealed that soursop induces cytotoxicity either through inhibition of ATP synthesis by blocking the mitochondrial complexes, or by promotion of apoptosis through up regulation of Bax (Bcl-2 associated X protein) and down regulation of Bcl2 (Bcl-2 – B-cell lymphoma). Interestingly, the constituent phytochemicals are also found to down regulate the oncogenes responsible, for example EGFR (Epidermal Growth Factor Receptor) down regulation in the case of breast cancer.

### INTRODUCTION

The incidence of cancer is in increasing trend each year, which generates more concerns regarding the efficacy of the current treatment options. This led patients to seek alternatives to complement or to replace surgery, chemotherapy and radiotherapy. Cancer being a catastrophe of the frame of higher multicellular organisms consequential from the abnormal cell proliferation, attains modifications in the statement of copious amendments, prompting dysregulation of conventional cell programming concerned with cell division and cell separation. This upshot, resulting in uneven cell replication and cell passing that stimulates the development of a tumour. Although major breakthroughs have been achieved in the field of surgery, chemotherapy and radiotherapy, many still express concerns regarding these methods of treatment due to their limitations and, most noticeably, their side effects. Apart from the obvious toxicity induced by chemotherapy, another side effect that might appear following radiotherapy is hypothyroidism.



**Fig 1:** (A) Soursop tree (B) Leaves (C) Flower (D) Fruit

These issues, among others, have created a significant distrust towards cancer management procedures in hospitals and have caused patients to seek treatment elsewhere, especially from traditional medications, whether as a complementary treatment alongside conventional medications or as a way to improve their health without the treatments offered by hospitals. Complementary and alternative medicine is defined as means of treatment that are outside the scope of modern medicinal treatment. These treatments may be used as therapeutic and

preventative agents to assist in combating physical or mental illnesses. They have been widely used for generations to treat illnesses prior to the arrival of modern medicine. Since the establishment of modern medicine, complementary and alternative medicine has been used in conjunction with current treatment methods in certain countries to help and assist patient recovery.

#### **Phyto constituents:**

The most prominent constituent chemicals reported are alkaloids, phenols, flavonoids and acetogenins. *In vitro* studies, conducted on both crude extracts as well as the isolated phytochemicals of soursop, help to classify these compounds to be potent against microbes, inflammation, protozoans, reactive oxygen species (ROS), insects, and/or tumorigenic cells. Researches further suggested that it has potent properties as contraceptive, anti-ulcer, wound healing, hepatoprotective, anxiolytic, anti-hypertensive, anti-icteric and hypoglycaemic activities. The unique class of compounds *i.e.*, acetogenins have been reported to hold a major share in the plant phytochemical concentration and the subsequent medicinal value. Acetogenins, also called Annonaceous acetogenins (AGEs), are found only in the plants belonging to the Annonaceae family. Acetogenins, usually of C35/C37, are metabolic derivatives of C32/C34 long chain fatty acids, *via* the polyketide pathway.

#### **Anticancer activity:**

In recent years, acetogenins have drawn significant scientific interest due to the remarkable structures and broad spectrum of biological activities. AGEs have been successful in actively inducing death in cancer cells, that are resistant even to prescribed chemotherapeutic drugs (Tundis *et al.*, 2017).

#### **Breast Adenocarcinoma**

Several studies revealed that the ethanol extracts of soursop leaves downregulate EGFR eventually leading to selective inhibition of cells constituting the BC. This indicates EGFR as a rational breast cancer therapy target (Dai *et al.*, 2011). Adding to this, xenograft mice model studies reported a reduced tumor growth in breast upon treatment with the fruit extract. A promising observation was made *in vivo* when the soursop leaves were found to protect from the development of a DMBA – induced breast cancer, by preventing DNA damage (Minari and Okeke, 2014).

#### **Cervical and Ovarian Carcinomas**

The study revealed that the acetogenins from soursop have growth inhibitory and cytotoxic effect on cervical cancer cell line. Its leaf acetogenins inhibited HeLa cell growth. The decrease in cell viability can be attributed to either cell death or cell cycle arrest. The mechanism of cell cycle distribution is also associated with some of cellular protein especially the tumor suppressor protein p53. It was observed that acetogenins from *Annona muricata* elevated the levels of p53 found in the nucleus, upon treatment. And this group of phytochemicals is with an outstanding potency to prevent cervical cancer development (Parama *et al.*, 2013).

#### **Colorectal Carcinoma**

Jaramillo *et al.* (2000) demonstrated the potent inhibition of HT-29 and HCT-116, cell lines of colon cancer, apart from the lung cancer cell lines, A-549. These cells were treated using an ethyl acetate extract of soursop leaves. The mechanism of action suggested by this study was that the extracts induced apoptosis, *via* the mitochondria mediated pathway, in the cell lines subjected to treatment. A subsequent arrest of the cells at G1 phase of cell cycle was reported. The Leaf extract inhibited profoundly the migration and invasion of colon cancer cells (Zorofchian *et al.*, 2014).

#### **Leukaemia**

Several investigations have also been done to check the ability of ethanol extracts of soursop leaves for its cytotoxicity potential and capacity of inducing apoptosis in K562 cancer cells, a chronic myelogenous cell line. The activity of Caspase-3 was remarkably enhanced during the apoptosis stimulated by the extract at a low quantity. Terminal deoxynucleotidyl transferase-mediated dUTP nick-end labelling (TUNEL) assay results

verified the process of apoptosis. The Caspase-3 activity and TUNEL assay reports endorsed that soursop leaf phytochemicals extracted using ethanol induced apoptosis in K562 cell lines. Ezirim *et al.* (2013), thus concluded that soursop could be considered as a natural source for the preparation of proapoptotic drugs.

## CONCLUSION

The anticancer property of soursop has been prominent and this has been validated by a majority of studies done on this plant. Overall, this review summarizes the reported significance of the soursop plant and providing insight across the laboratory analyses as well as the clinical case studies carried out to validate its activity against different types of cancers. The current review is longed to be a source of spur for the scientists to further conduct *in vitro/ in vivo* investigations of the biological activities of soursop to attain an understanding for the development of novel pharmaceutical agents.

## REFERENCES

- Dai Y, Hogan S, Schmelz EM, Ju YH, Canning C and Zhou K (2011). Selective growth inhibition of human breast cancer cells by graviola fruit extract *in vitro* and *in vivo* involving downregulation of EGFR expression. *Nutr. Cancer*, 63: 795801.
- Ezirim AU, Okochi VI, James AB, Adebeshi OA, Ogunnowo S and Odeghe O (2013). Induction of apoptosis in myelogenous leukemic k562 cells by ethanolic leaf extract of *Annona muricata*. *Ind. J. Drugs and Dis.*, 2: 241-247.
- Jaramillo MC, Arango GJ, González MC, Robledo SM and Velez ID (2000). Cytotoxicity and antileishmanial activity of *Annona muricata* pericarp. *Fitoterapia*, 71: 183-186.
- Minari JB and Okeke U (2014). Chemopreventive effect of *Annona muricata* on DMBA-induced cell proliferation in the breast tissues of female albino mice. *Egyptian J. Med. Human Gen.*, 15: 327-334.
- Parama AO, Artanti AN, Fitria MS, Agustina E and Prayitno A (2013). *Annona muricata* Linn Leaf Induce Apoptosis in Cancer Cause Virus. *J. Cancer Therapy*, 4: 1244-1250.
- Prasad, S.K., Varsha, V. and Devananda, D., 2019. Anti-cancer properties of *Annona muricata* (L.): A Review. *Medicinal Plants-International Journal of Phytomedicines and Related Industries*, 11(2), pp.123-134.
- Tundis R, Xiao J and Loizzo MR (2017). *Annona* species (Annonaceae): a rich source of potential antitumor agents? *Ann. N Y Acad. Sci.*, 1398: 30-36.
- Zorofchian MS, Kadir HA, Paydar M, Rouhollahi E and Karimian H (2014a). *Annona muricata* leaves induced apoptosis in A549 cells through mitochondrial-mediated pathway and involvement of NF-kappa B. *BMC Complement Altern Med.*, 14: 299.