

Introduction

Soursop is the fruit of *Annona muricata*, a broad leaf, flowering, evergreen tree native to Mexico, Cuba, Central America, the Caribbean, and northern South America, primarily Colombia, Brazil, Peru, Ecuador, and Venezuela.

[Picture Credit: Soursop Tree and Fruit]



Today, it is also grown in some areas of Southeast Asia, as well as in some Pacific islands. It was most likely brought from Mexico to the Philippines by way of the Manila-Acapulco Galleon trade. It is in the same genus as the chirimoya and the same family as the pawpaw (Wikipedia).

Soursop is also known as Graviola (Hoax-Slayer).

Nutritional Facts of Soursop (Graviola)

Nutritional Facts per 100g

Calories		66
Total Fat		0,3g
Saturated fat		0,1g
Polyunsaturated fat		0,1g
Monounsaturated fat		0,1g
Cholesterol		0mg
Sodium		14mg
Potassium		278mg
Total Carbohydrate	17g	
Dietary fibre		3,3g
Sugar		14g
Protein		1g

[Picture Credit: Soursop Fruit]



Vitamin A*		0%
Vitamin C*		34%
Calcium*	1%	
Iron*		3%
Vitamin B ₆ *		5%
Vitamin B ₁₂ *		0%
Magnesium*		5%

*Per cent Daily Values are based on a 8 000 kj diet. The daily values may be higher or lower depending on a person's kilojoule needs.

Scientific Research on Soursop (Graviola) and Cancer

According to an animal study by Yan, *et al.* (2015), the leaves of *Annona muricata*, commonly known as Graviola, are rich in flavonoids, isoquinoline alkaloids and annonaceous acetogenins and confers protection against prostate cancer.

Defining *in vitro*, *in vivo* and *ex vivo*

In vitro (Latin: *in glass*) studies in experimental biology are those that are conducted using components of an organism that have been isolated from their usual biological surroundings in order to permit a more detailed or more convenient analysis than can be done with whole organisms. Colloquially, these experiments are commonly called 'test tube experiments'.

In contrast, ***in vivo*** studies are those that are conducted with living organisms in their normal intact state, while ***ex vivo*** studies are conducted on functional organs that have been removed from the intact organism (Wikipedia).

A brief discussion of the three (3) other peer-reviewed scientific papers

In a study by Torres, *et al* (2012) researching the anti-cancer properties of Soursop, it was found that the compounds that are naturally present in a Graviola extract inhibited multiple signalling pathways that regulate metabolism, cell cycle, survival, and metastatic properties in pancreatic cancer cells. The study showed the promising characteristics of the natural product against this lethal disease.

Dai, *et al* (2011) studied the effects of Soursop (Graviola) on breast cancer. Their data showed that dietary Graviola fruit extract (GFE) induced significant growth inhibition of MDA-MB-468 cells *in vitro* and *in vivo* through a mechanism involving the EGFR/ERK signalling pathway, suggesting that GFE may have a protective effect for women against EGFR-overexpressing breast cancer.

In his study, Cassileth (2008) found that Graviola demonstrated anticancer effects *in vitro*, but has not been studied in humans. Despite the lack of human data, many websites promote graviola to cancer patients based on traditional use and on the *in vitro* studies. Caution is, however, required as there is no evidence of safety or efficacy in this regard.

According to Cancer Research UK studies on Graviola extract has shown its ability to kill some types of liver and breast cancer cells that are resistant to particular chemotherapy drugs. However, there haven't been any large scale studies in humans. So it is not known yet whether it can work as a cancer treatment or not. Overall, there is no evidence to show that Graviola works as a cure for cancer. Many

sites on the internet advertise and promote Graviola capsules as a cancer cure, but none of them are supported by any reputable scientific cancer organisations (Cancer Research UK).

Bioassay-guided fractionation of the fruit powder of graviola (*Annona muricata*) yielded three novel compounds: muricins J, K, and L. The compounds are all C35 Annonaceous acetogenins with a mono-tetrahydrofuran ring and four hydroxyls. Their structures were elucidated by spectral methods and chemical modification after isolation via chromatographic techniques and HPLC purification. These three acetogenins demonstrated an antiproliferative against human prostate cancer PC-3 cells. (Sun, et al., 2014).

Chan, W-J. J., McLachlan, A.J., Hanrahan, J.R. & Harnett, J.E. 2020.

Objectives: *Annona muricata*, also known as graviola, soursop and guanabana, has been widely utilised for the treatment of a range of cancers. The mechanism of action and the efficacy of *A. muricata* and its constituents in the treatment of cancer have been comprehensively reviewed. The aim of this systematic review was to summarise the available literature that reports on factors related to the safety and tolerability of *A. muricata* leaf extract and its acetogenins.

Methods: In-vitro, preclinical animal studies and human studies of any design written in any language were included. Studies that evaluated *A. muricata* leaf extract and its constituents were searched through the databases Pubmed, Medline and Embase from inception to April 2019. The elaborated item 4 of Consolidated Standards of Reporting Trials statement and Animals in Research: Reporting In vivo Experiments guidelines were used to evaluate the quality of the studies.

Key findings: The results suggest that *A. muricata* and its constituents have hepatoprotective, neurotoxic, antinociceptive, anti-ulcerative and chemopreventive effects. The dose and duration used in animal studies demonstrating toxicity may not directly translate into the effects in humans. Studies included in this review were judged to be of medium to high quality.

Conclusions: The overall outcome of the current review suggests that *A. muricata* has a favourable safety and tolerability profile. Future studies investigating its use in people diagnosed with a range of cancers are warranted.

Claims Made in Support of Soursop's Ability to Treat Cancer

The following anti-cancer claims are listed on various websites regarding Soursop (Graviola):

[Picture Credit: Soursop Juice]

- Cures cancer - by eating the fruit of soursop helps to attack the cancer cells safely and naturally without side effects such as nausea, weight loss or hair loss
- Increases immune response - substances contained in soursop fruit such as acetogenins, annocatacin, annocatalin, anno-hexocin, annonacin, anomuricin, anomurine, anonol, caclourine, gentisic acid, gigantetronin, linoleic acid, muricapentocin, make the body kill malignant cancer cells
- Soursop leaf can kill malignant cells for 12 types of cancer, including colon, breast, prostate, lung and pancreatic cancer



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November 2020

- Soursop is 10 000 times stronger in slowing the growth of cancer cells compared to adriamycin and chemotherapy

- [Picture Credit: Soursop Leaves]

- Soursop leaves is very effective for cancer of the prostate, pancreas and lung
- Soursop attacks cancer cells effectively because it does not harm healthy cells
- Soursop does not cause extreme nausea, weight loss and hair loss



(Yang, *et al.*, 2015; Deep, *et al.*, 2016).

Naik, A.V. & Sellappan, K. 2020.

Purpose: The present study evaluates the *in-vitro* anti-tumorigenic potential of leaf methanol extracts of *Annona muricata* (LMAM).

Materials and methods: The cytotoxic activity was assessed in MCF-7 cells by MTT assay at various concentrations ranging from 25-250µg/mL. MCF-7 cells were treated with 50 and 100 µg/mL LMAM for 24 h. To detect LMAM-induced apoptosis; Hoescht 33342 staining along with Cell cycle analysis, Annexin-PI probe as well as oxidative stress damage by reactive oxygen species (ROS) measurements were determined using flow cytometric analysis. While caspase-3 expression levels were studied employing the qRT-PCR method.

Results: LMAM exhibited significant inhibition of MCF-7 cells with an IC₅₀ value of 85.55 µg/mL. Hoescht staining showed marked morphological features characteristic of apoptosis in LMAM treated cells. Cell cycle analysis confirmed the proven capability of LMAM showing a 30% rise in G₁ phase upon treatment with 100 µg/mL LMAM, thus inducing cell cycle arrest at G₁ phase and a rise in sub G₀-G₁ population paralleled with a decrease in S phase. Flow cytometric analysis with Annexin V-FITC-PI staining indicated an increase in the early and late apoptotic population with a 3.38% and 19.47% rise respectively when treated with 100 µg/mL LMAM. Treatment with 100 µg/mL LMAM caused an increase in intracellular ROS with MFI value 3334.08. Upregulation of caspase-3 was observed with a 2.18 and 32.47 fold increase compared to control in MCF-7 cells cultured at 50 µg/mL and 100 µg/mL LMAM respectively suggesting caspase-dependent apoptosis.

Conclusion: LMAM proved as a potent ethno-chemopreventive agent and a potential lead in cancer treatment attributable to the synergistic interactive properties of phytoconstituents.

Rady, I., Bloch, M.B., Chamcheu, R.N., Banang Mbeumi, S., Anwar, M.R., Mohamed, H., Babatunde, A.S., Kuate, J.R., Noubissi, F.K., El Sayed, K.A., Whitfield, G.K. & Chamcheu, J.C. 2018.

“Graviola (*Annona muricata*) is a small deciduous tropical evergreen fruit tree, belonging to the Annonaceae family, and is widely grown and distributed in tropical and subtropical regions around the world. The aerial parts of graviola have several functions: the fruits have been widely used as food confectionaries, while several preparations, especially decoctions of the bark, fruits, leaves, pericarp, seeds, and roots, have been extensively used in traditional medicine to treat multiple ailments including cancers by local communities in tropical Africa and South America. The reported therapeutic benefits of graviola against various human tumors and disease agents in *in vitro* culture and preclinical animal model systems are typically tested for their ability to specifically target the disease, while

exerting little or no effect on normal cell viability. Over 212 phytochemical ingredients have been reported in graviola extracts prepared from different plant parts. The specific bioactive constituents responsible for the major anticancer, antioxidant, anti-inflammatory, antimicrobial, and other health benefits of graviola include different classes of annonaceous acetogenins (metabolites and products of the polyketide pathway), alkaloids, flavonoids, sterols, and others. This review summarizes the current understanding of the anticancer effects of *A. muricata* and its constituents on diverse cancer types and disease states, as well as efficacy and safety concerns. It also includes discussion of our current understanding of possible mechanisms of action, with the hope of further stimulating the development of improved and affordable therapies for a variety of ailments.”

Kim, J.Y., Dao, T.T.P., Song, K., Park, S.B., Jang, H., Park, M.K., Gan, S.U. & Kim, Y.S. 2018.

“*Annona muricata* L., known as graviola, is an evergreen plant of the tropical regions and is a rich source of natural products. Graviola has various biological activities, and it is best known for its anticancer activity. This study aimed to investigate the effects of crude graviola extract *in vitro* on breast cancer cells; in particular, we aimed to identify an agent against triple negative breast cancer (TNBC). We used the TNBC MDA-MB-231 cell line as the experimental model and the ER(+) non-TNBC MCF-7 breast cancer cell line as the control. We identified annonaceous acetogenins, including annonacin isomers, characteristic to this plant by using liquid chromatography tandem mass spectrometry (LC/MS/MS). We observed a significant decrease in the cell viability in both cell lines within 48 h, whereas impaired cell motility and invasiveness were observed only in the MDA-MB-231 cell line. While the MCF-7 cells showed an ER-dependent mechanism of apoptosis, the apoptosis of MDA-MB-231 cells was governed by an intrinsic apoptotic pathway triggered by graviola leaf extract (GLE).”

Warnings Against Graviola

The following warnings against graviola have been made recently by reputable scientists, scientific groups and institutions:

- Cancer Research UK does not support the use of graviola to treat cancer. Their advice is to be very cautious about believing information or paying for any type of alternative cancer therapy on the internet (Cancer Research UK).
- Extracts of graviola show antiviral, antiparasitic, antirheumatic, astringent, emetic, antileishmanial and cytotoxic, antinociceptive, anti-inflammatory, antihyperglycemic and anticancer effects *in vitro* and *in vivo*. However, human data are lacking. Alkaloids extracted from graviola may cause neuronal dysfunction and degeneration leading to symptoms of Parkinson's disease.
- Some side effects follow from graviola's areas of bioactivity. Studies on animal subjects have demonstrated that the plant can dilate blood vessels and lower blood pressure, so those whose blood pressure is already low, or are already on medication to reduce hypertension, should consult their physician before taking graviola (Wright). Also, a large dose taken at one time can cause nausea and vomiting.
- Graviola's purported anti-cancer potency comes largely from its ability to reduce the supply of adenosine triphosphate (ATP) to cancer cells. ATP often provides metabolic energy to healthy cells as well, and some nutritional supplements, notably Coenzyme Q10, are known for increasing ATP. For this reason, CoQ10 may neutralize the effect of graviola and they should not be taken together.

FDA Warns Against Soursop (Graviola)

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In April 2017, the Food and Drug Association (FDA) sent out warning letters to 14 companies, advising them to change or remove the fraudulent claims regarding Graviola on their websites. The FDA forwarded warning letters to all companies selling/distributing Graviola because unsubstantiated claims are made that Graviola can cure cancer.

The FDA warned that if the companies do not comply, the FDA may take further legal action to prevent their products from reaching consumers.

The Position of the Cancer Association of South Africa (CANSA)

While CANSA does not dispute the fact that Soursop (Graviola) may demonstrate anti-cancer properties in laboratory tests, that it may have a protective effect for women against EGFR-overexpressing breast cancer and that it shows promising characteristics of fighting cancer cells and providing protection against prostate cancer (*in vitro*), it cannot at present, advance or promote the use of Soursop (Graviola) in any form for the treatment of cancer until there is sufficient scientific evidence of its safety and efficacy in this regard until such time as additional peer-reviewed research has been published in support of the anti-cancer properties of Graviola.

Medical Disclaimer

This Fact Sheet and Position Statement is intended to provide general information only and as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet and Position Statement. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet and Position Statement.

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Soursop Juice

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Soursop Fruit

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Soursop Leaves

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Soursop Tree and Fruit

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