

**LACTONES, POLYKETIDES AS NEUROTOXIN IN ONCOGENIC GENINS OF  
SOURSOP: A HOLISTIC MIRACLE****Astha P. Sanyal, Vidhi V. Patel, Vaibhavi N. Akhani, Megha R. Baranda and Prof. Dr. Dhrubo Jyoti Sen\***Department of Pharmaceutical Chemistry, Shri Sarvajani Pharmacy College, Gujarat Technological University,  
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**ABSTRACT**

*Soursop also known as graviola and (Hanuman Phal/Laxman Phal) in Hindi is a fruit that has its origin in the forests of South America, Africa and Southeast Asia. This is an evergreen broad leaved tree whose every part is useful and has medicinal properties. This fruit is extremely delicious with a sharp aroma and a sweet-sour taste which is basically a combination of the taste of pineapple and strawberry. Recently, it has gained attention and popularity due to its natural cancer cell killing properties. Apart from its anti-cancer properties, it has several other medical benefits. Soursop leaves are the most beneficial parts of this tree. They have the Acetogenin containing compounds namely bulatacin, asimisin and squamosin. Acetogenin acts as an anti-feedent. Thus, they are often used in killing insects and pests which die by consuming these leaves even in small amounts. Scientific research conducted by The National Cancer Institute has proved that Soursop leaves can effectively attack and destroy cancer cells. In addition to this, they are also used in the treatment of several other diseases.*

**Health Benefits of Soursop Leaves**

*Soursop leaves are rich in several compounds including protein, calcium, fructose, fat, vitamins A and B and the like. Thus, the leaves have excellent medicinal properties making them usable as an ingredient in several herbal health products. The health benefits of soursop leaves are as follows.*

- 1. Treatment of Cancer: Soursop leaves can inhibit cancer cells and cure cancer more quickly and effectively than chemotherapy which results in several side effects besides being expensive. In fact, research has proved that soursop has an active ingredient that is 10000 times stronger than chemotherapy in fighting cancer cells. Thus, soursop leaves can treat different types of cancers including prostate, lung and breast cancers. For treatment, boil 10 soursop leaves in 3 cups of water until only one cup of water remains, strain and cool it and drink this concoction every morning for 3-4 weeks to determine improvement in the condition. Soursop leaves cancer treatment is one of the most potent cures till date.*
- 2. Treatment of Uric Acid: Eating soursop leaves can greatly help in treating gout. In fact, many alternative medicines use soursop leaves for the treatment of gout. For this purpose, take 6 to 10 soursop leaves which are old but still green and wash them clean. Boil the leaves in 2 cups of water and simmer until one cup of water remains. This concoction should be taken twice a day i.e. morning and evening for maximum benefits.*
- 3. Treatment of Back Pain: Back pain is commonly experienced these days, particularly while exercising. Using chemical drugs for back pain can cause side effects. Soursop leaves are an effective herbal remedy for treating back pain without any negative effect. You can boil 20 pieces of soursop leaves in 5 cups of water until only 3 cups of water are left. Drink  $\frac{3}{4}$  cup of this concoction once in a day for relief.*
- 4. Treatment of Eczema and Rheumatism: Rheumatic diseases are commonly observed in elderly people, causing great pain. Soursop leaves are a natural treatment for arthritis pain. For this purpose, mashes the soursop leaves until they become smooth and apply on the areas of the body affected by pain due to arthritis and eczema, regularly twice a day.*
- 5. Treatment of Diabetes: The limit of normal sugar levels ranges from 70 mg to 120 mg. The nutrients in soursop leaves are believed to stabilize blood sugar levels in the normal range. Besides, the extracts of soursop leaves can be used as one of the natural diabetes remedies. All this makes these leaves beneficial for diabetics.*
- 6. Boosts the Immune System and Prevents Infections: The nutrient content of soursop leaves is believed to boost the immune system and avoid infections in the body. Boil 4/5 soursop leaves in 4 cups of water until one cup water remains and drink this concoction regularly once in a day for beneficial results. In addition to the benefits mentioned above, soursop leaves are extremely effective in inhibiting the growth of bacteria, virus, parasites and tumor development. Their healing properties make them capable of being used as an anti-seizure medication. They are also capable of reducing fever and lowering high blood pressure. They help in*

treating inflammation and swollen feet. They aid in digestion and improve appetite. Soursop leaf consumption on a regular basis helps in improving stamina and facilitating quick recovery from diseases.

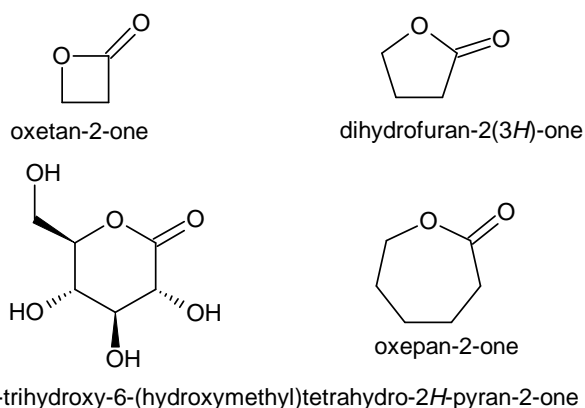
7. **Skin Benefits of Soursop Leaves:** Due to their medicinal properties soursop leaves are extremely beneficial for health. As pointed out earlier, they are used in the treatment of some of the deadliest diseases. The leaves offer some skin benefits as well.
8. **Treatment of Boils:** Ulcer is a skin disorder that is characterized by immense pain and even has the risk of catching infection. Boils can occur on the body or on the face, thus interfering with your skin health and beauty. Soursop leaves are a natural remedy to cure ulcers. You can pick some young soursop leaves and place them on the body affected by ulcers.
9. **Treatment of Eczema:** As already stated earlier, soursop leaves can treat eczema in a natural way. You can mash a few soursop leaves and apply it on the affected areas twice a day regularly. This will help in alleviating the pain caused by eczema besides treating it. A pulp made with fresh soursop leaves and rose water when applied on the skin can be very useful in preventing the occurrence of blackheads and other skin problems too.
10. **Hair Benefits of Soursop Leaves:** Get rid of Lice. All of us long for healthy and damage free hair. But unfortunately, the unhealthy lifestyle coupled with exposure to harmful chemicals and environmental pollutants is responsible for several hair problems like dandruff, split ends, hair loss, pre mature greying etc. Natural ingredients and herbal products can be very effective in combating these problems. As far as soursop leaves are concerned, much is not known about their benefits for hair. However, soursop leaves have the capability to inhibit the growth of parasites, besides other medicinal properties. Thus, applying a soursop leaf decoction on your hair can help you to get rid of head lice.

**KEYWORDS:** Lactone, Polyketide, Genin, Neurotoxin, Mycotoxin, Acetogenin, Bullatacin, Uvaricin.

## INTRODUCTION

They are characterized by linear 32- or 34- carbon chain containing Oxygenated Functional groups including Hydroxyles, Ketones, Epoxide, Tetrahydrofuran and

tetrahydropyranes. They are often terminated with a lactone or butenolide. Over 400 members of this family of compound have been isolated from 51 different species of plants.



**Figure-1: Lactones:  $\beta$ -propiolactone (oxetan-2-one),  $\gamma$ -butyrolactone (dihydrofuran-2(3H)-one), D-glucono- $\delta$ -lactone (3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-one,  $\epsilon$ -caprolactone (oxepan-2-one)**

**Lactones** are cyclic esters of hydroxycarboxylic acids, containing a 1-oxacycloalkan-2-one structure, or analogues having unsaturation or heteroatoms replacing one or more carbon atoms of the ring. Lactones are formed by intramolecular esterification of the corresponding hydroxycarboxylic acids, which takes place spontaneously when the ring that is formed is five- or six-membered. Lactones with three- or four-membered rings ( $\alpha$ -lactones and  $\beta$ -lactones) are very reactive, making their isolation difficult. Special methods are normally required for the laboratory synthesis of small-ring lactones as well as those that contain rings larger than six-membered. Lactones are usually named according to the precursor acid molecule (*aceto*=2

carbons, *propio*=3, *butyro*=4, *valero*=5, *capro*=6, etc.), with a *-lactone* suffix and a Greek letter prefix that specifies the number of carbons in the heterocycle — that is, the distance between the relevant -OH and the -COOH groups along said backbone.<sup>[1-3]</sup>

The first carbon atom after the carbon in the -COOH group on the parent compound is labelled  $\alpha$ , the second will be labeled  $\beta$ , and so forth. Therefore, the prefixes also indicate the size of the lactone ring:  $\alpha$ -lactone=3-membered ring,  $\beta$ -lactone=4-membered,  $\gamma$ -lactone=5-membered, etc. The other suffix used to denote a lactone is *-olide*, used in substance class names like butenolide, macrolide, cardenolide or bufadienolide.

**Polyketides** are a class of secondary metabolites produced by certain living organisms in order to impart to them some survival advantage. Many mycotoxins produced by fungi are polyketides. Structurally, polyketides are complex organic compounds that are often highly active biologically. Many pharmaceuticals are derived from or inspired by polyketides. Polyketides are usually biosynthesized through the decarboxylative condensation of malonyl-CoA derived extender units in a similar process to fatty acid synthesis (a Claisen condensation). The polyketide chains produced by a minimal polyketide synthase are often further derivatization and modified into bioactive natural

products. Polyketides are structurally a very diverse family of natural products with diverse biological activities and pharmacological properties.<sup>[4-6]</sup>

They are broadly divided into three classes: type I polyketides (often macrolides produced by multimodular megasynthases), type II polyketides (often aromatic molecules produced by the iterative action of dissociated enzymes) and type III polyketides (often small aromatic molecules produced by fungal species). Polyketide antibiotics, antifungals, cytostatics, anticholesteremic, antiparasitics, cococcidistats, animal growth promoters and natural insecticides are in commercial use.

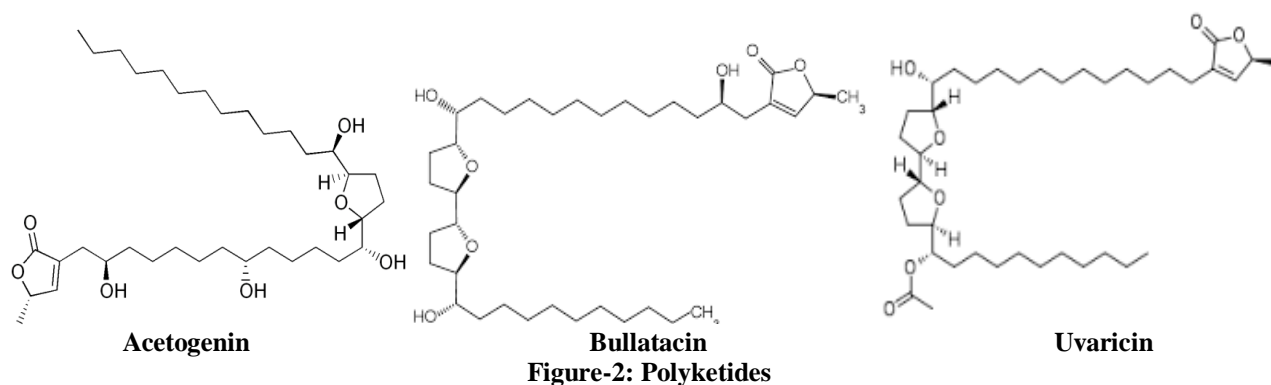


Figure-2: Polyketides

**Acetogenins** are a class of polyketide natural products found in plants of the family Annonaceae. They are characterized by linear 32- or 34-carbon chains containing oxygenated functional groups including hydroxyls (-OH), ketones (=CO), epoxides (-CH<sub>2</sub>-CH<sub>2</sub>-O), tetrahydrofurans (C<sub>4</sub>H<sub>8</sub>O) and tetrahydropyrans (C<sub>5</sub>H<sub>10</sub>O). They are often terminated with a lactone or butanolide. Over 400 members of this family of compounds have been isolated from 51 different species of plants. Examples include: Annonacin, Annonins, Bullatacin, Uvaricin.<sup>[7,8]</sup>

Acetogenins have been investigated for their potential therapeutic use in treating cancer, but this potential is tempered with concerns about neurotoxicity. Well over half of all cancer patients pursue some sort of complementary and alternative medical treatments. Neither purified acetogenins nor crude extracts of the pawpaw or the Brazilian pawpaw (*Asimina triloba*, Annonaceae) have been approved by the FDA for cancer treatment, but they have exhibited antitumor efficacy both in animal models and in a limited number of clinical studies. There is a lack of rigorously controlled clinical trials, casting doubt of the efficacy of acetogenins. Both the Pawpaw extract and acetogenins appear to inhibit HIF-1 activation by blocking the hypoxic induction of nuclear HIF-1 $\alpha$  protein. Annonacin is a neurotoxic chemical compound found in some fruits such as the paw paw (custard apple), soursop and others from the family Annonaceae. It is a member of the class of compounds

known as acetogenins. Annonacin is a neurotoxin that is believed to be responsible for the incidence of atypical parkinsonism in the Caribbean island of Guadeloupe where consumption of soursop and pawpaw is common. Studies in rodents indicate that consumption of annonacin (3.8 and 7.6 mg per kg per day for 28 days) caused brain lesions consistent with Parkinson's disease. Along with other acetogenins, annonacin blocks mitochondrial complex (NADH-dehydrogenase), which is responsible for the conversion of NADH to NAD<sup>+</sup> and the build-up of a proton gradient over the mitochondrial inner membrane.

This effectively disables a cell's ability to generate ATP via an oxidative pathway, ultimately forcing a cell into apoptosis or necrosis. Based on basic polyketide synthesis, the biosynthesis of annonacin is likely accomplished by a modular polyketide synthase (PKS). Not much is known other than this about the domains responsible for the biosynthesis of annonacin. The biosynthesis likely involves the use of 17 modules consisting of a number of enzymes commonly found in PKS. These include the acyl carrier protein (ACP), acetyl transferase (AT), ketosynthase (KS), malonyl transferase (MT; which can come carrying a variety of functionalities), ketoreductase (KR), dehydratase (DH), and enoyl reductase (ER). An example of the possible modular biosynthetic pathway detailing the combination of these enzymes and the subsequent modules can be seen in the figure below.<sup>[9-11]</sup>



In 2010 the French food safety agency, Agence française de sécurité sanitaire des produits de santé, concluded that, based on the available research findings, "it is not possible to confirm that the observed cases of atypical Parkinson syndrome are linked to the consumption of *Annona muricata*," calling for further study on potential risks to human health. Soursop is the fruit of *Annona muricata*, a broadleaf, flowering, evergreen tree native to Mexico, Cuba, Central America, the Caribbean islands of Hispaniola and Puerto Rico, and northern South America, primarily Colombia, Brazil, Peru, Ecuador, Venezuela. Soursop is also produced in all tropical parts of Africa, especially in Eastern Nigeria, Mambilla Plateau and The Democratic Republic of Congo, Southeast Asia and the Pacific. It is in the same genus, *Annona*, as cherimoya and is in the Annonaceae family.<sup>[13]</sup>





It cured cancer probably reduce it to zero healthy cell formation, immune system prevention of abnormal cellular division cleaning abnormal tissue growth anti-tumor agents, anti-tumors, antimicrobial. No side effects like chemotherapy.



Figure-4: Soursop.

The soursop is adapted to areas of high humidity and relatively warm winters; temperatures below 5°C (41°F) will cause damage to leaves and small branches, and temperatures below 3°C (37°F) can be fatal. The fruit becomes dry and is no longer good for concentrate. The flavour has been described as a combination of

strawberry and pineapple, with sour citrus flavour notes contrasting with an underlying creamy flavour reminiscent of coconut or banana. Soursop is widely promoted (sometimes as "graviola") as an alternative cancer treatment. There is, however, no medical evidence that it is effective.<sup>[14]</sup>

Table-1: Nutrition values.

Nutritional value per 100 g (3.5 oz)			
Energy 276 kJ (66 kcal)		Vitamins	
Carbohydrates	16.84 g	Folate (B <sub>9</sub> )	(4%), 14 µg
Sugars	13.54 g	Choline	(2%), 7.6 mg
Dietary fibers	3.3 g	Vitamin C	(25%), 20.6 mg
Fat	0.3 g	Minerals	
Protein	1 g	Calcium	(1%), 14 mg
Vitamins		Iron	(5%), 0.6 mg
Thiamine (B <sub>1</sub> )	(6%), 0.07 mg	Magnesium	(6%), 21 mg
Riboflavin (B <sub>2</sub> )	(4%), 0.05 mg	Phosphorus	(4%), 27 mg
Niacin (B <sub>3</sub> )	(6%), 0.9 mg	Potassium	(6%), 278 mg
Pantothenic acid (B <sub>5</sub> )	(5%), 0.253 mg	Sodium	(1%), 14 mg
Vitamin B <sub>6</sub>	(5%), 0.059 mg	Zinc	(1%), 0.1 mg

**Neurotoxicity:** The Memorial Sloan-Kettering Cancer Center cautions, "alkaloids extracted from graviola may cause neuronal dysfunction". The compound annonacin, which is contained in the seeds of soursop, is a neurotoxin associated with neurodegenerative disease and research has suggested a connection between consumption of soursop and atypical forms of Parkinson's disease due to high concentrations of annonacin. LD<sub>50</sub>=0.018µM to dopaminergic neurons by annonacin (one of the acetogenins in Soursop), which is 100 fold more toxic than 1-methyl-4-phenylpyridinium (MPP), 700 fold more than coreximine, twice rotenone. Average fruit contains 15mg of annonacin. In 2010 the French food safety agency, Agence française de sécurité sanitaire des produits de santé, concluded that, based on the available research findings, "it is not possible to confirm that the observed cases of atypical Parkinson syndrome are linked to the consumption of *Annona muricata*," calling for further study on potential risks to human health.<sup>[15]</sup>

**Alternative cancer treatment:** The Memorial Sloan-Kettering Cancer Center lists cancer treatment as one of the "purported uses" of soursop. According to Cancer Research UK, "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" and "there is no evidence to show that graviola works as a cure for cancer" and consequently they do not support its use as a treatment for cancer. The Federal Trade Commission in the United States determined that there was "no credible scientific evidence" that the extract of soursop sold by Bioque Technologies "can prevent, cure, or treat cancer of any kind." Cancer Research UK also released a statement about the alleged cancer "cure" that included these sentences: "Overall, there is no evidence to show that graviola works as a cure for cancer. In laboratory studies, graviola extracts can kill some types of liver and breast cancer cells that are resistant to particular chemotherapy

drugs. But there haven't been any large scale studies in humans. So we don't know yet whether it can work as a cancer treatment or not. 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. We do not support the use of graviola to treat cancer." In 2008, a court case relating to the sale in the UK of Triamazon, a soursop product, resulted in the criminal conviction of a man under the terms of the UK Cancer Act for offering to treat people for cancer. A spokesman for the council that instigated the action stated, "it is as important now as it ever was that people are protected from those peddling unproven products with spurious claims as to their effects."

## CONCLUSION

Graviola (*Annona muricata*) is a rainforest tree, classified under the pineapple family Annonaceae. The Annonaceae are a family, the custard apple family, of flowering plants consisting of trees, shrubs, or rarely lianas. With 105 accepted genera and about 2500 known species, it is the largest family in the Magnoliales. Several genera produce edible fruit, most notably *Annona*, *Anonidium*, *Asimina*, *Rollinia* and *Uvaria*. Its type genus is *Annona*. The family is concentrated in the tropics, with few species found in temperate regions. About 900 species are Neotropical, 450 are Afro-tropical, and the other species Indo-malayan. Also known as soursop or raintree or Brazilian paw paw, it is found in the belt extending from Central America to South America, including parts of Brazil. This small evergreen tree with large glossy dark green leaves grows to a height of 5-6 meters. The edible fruit is heart-shaped, yellow green in color and white inside. Graviola has gained much importance because of acetogenins, a group of potential anti-cancer agents, found in this plant. Graviola has been purported to have a number of uses, especially therapeutic. Leaves, seeds, bark, fruits and roots are the traditionally used parts of this tree. Listed are some of the traditional and herbal uses of this tree: 1. Leaves are used for headaches and insomnia. The leaves also contain antioxidants known to fight inflammation and insomnia. 2. Cooked leaves, applied topically, fight rheumatism and abscesses. In certain regions of Brazil, the oil of the leaves and unripe fruit is mixed with olive oil and used externally for neuralgia, rheumatism and arthritis pain.

The fruit and fruit juice are used as de-worming and anti-parasitic agents, as an astringent for diarrhea and dysentery, to cool fevers and to increase mother's milk after childbirth.

The compound annonacin in the seeds and leaves of many Annonaceae including *Annona muricata* (soursop), is a neurotoxin and it seems to be the cause of a neurodegenerative disease. The disorder is a so-called tauopathy associated with a pathologic accumulation of tau protein in the brain. Experimental results demonstrate that the plant neurotoxin annonacin is responsible for this

accumulation. Compared to the species from the Neotropics, very little is known about many species from Indomalaya. Only a few attempts have been made for the phylogeny-based reclassification of the family, and those have been hampered by the Neotropic bias in the available information, with the most of the work having been done on genera and tribes.

1. The seeds are crushed and used against internal and external parasites, head lice, and worms. However, it is important to note research has shown that seeds and roots contain certain toxins that could cause atypical Parkinson's disease, so this herbal remedy is best avoided.

2. Tea made from Graviola leaves has long been used in the Amazon region to treat liver and stomach disorders.

3. A tea made from the bark, leaves, and roots are used as a sedative, antispasmodic, to calm the nerves, to reduce high blood pressure.

**Health Benefits of Graviola:** Most studies regarding health benefits of Graviola have been conducted on laboratory animals and have not been confirmed in humans. Graviola is best known for its anti-cancer properties. Researchers are very enthusiastic about Graviola being an alternative medicine to be used as supportive therapy for cancers, such as breast cancer, prostate cancer, liver cancer, lung cancer, pancreatic cancer, and lymphoma. It is one of the most studied properties of the tree and so far it has shown positive results. However, always consult your doctor before using Graviola for any therapy.

**Pancreatic cancer:** An increased metabolic activity and glucose concentration in the tumor cell has been linked to aggressive pancreatic cancer. One study published in the journal Cancer Letters showed that Graviola extract containing acetogenins acted in a way to decrease ATP production thus leading to death of cancer cells. Incidentally, the researchers found that it does not affect the healthy cells. Acetogenin have been investigated for their potential therapeutic use in treating cancer, but this potential is tempered with concerns about neurotoxicity. Well over half of all cancer patient pursue some sort of complementary and alternative medicinal treatments. Neither purified acetogenins nor crude extracts of the pawpaw or the Brazilian pawpaw (*Asimina triloba*, annonaceae) have been approved by the FDA for cancer treatment, but they have exhibited antitumor efficacy both in animal models. Pawpaw extract and acetogenins appear to inhibit HIF-1 activation by blocking hypoxic induction nuclear HIF-1  $\alpha$  protein.

**Lung cancer:** Adriamycin is sometimes used as the chemotherapy drugs for cancers including lung cancer and blood cancers. A Japanese study done on lab animals found that annonacin (acetogenin) could inhibit the growth of cancer cells in the lungs as much as Adriamycin, if not better. However, R. Webster Kehr, at Independent Cancer Research Foundation, warns that Graviola can be especially dangerous for lung cancer

patients and brain cancer patients where a clustered amount of cancer dead cells (lysing) can be very dangerous.

**Breast cancer:** Researchers found that fruit extract of Graviola could successfully inhibit the growth of a gene that directly expresses cell growth (oncogene EGFR) which frequently over-expresses in breast cancer.

**Analgesic and anti-inflammatory properties-** A study published in the International Journal of Molecular Sciences on experimental animals supported these traditional uses for analgesic and anti-inflammatory activities, suggesting a potential for therapeutic purposes. However, the researchers suggested further studies to be conducted to ensure its safe usage.

**Diabetes:** Graviola has been found to be beneficial in cases of diabetes. A Nigerian study revealed that leaf extract of Graviola significantly reduced blood glucose concentration in experimental animals, possibly by enhancing the effects of insulin and adrenalin. No human trials have yet been done, therefore its use for this purpose cannot be recommended.

**High blood pressure:** Studies have shown Graviola to be a hypotensive (reduces blood pressure), vasodilator (widens the blood vessels) and cardio depressant (decreases heart rate and contractility). If you are using drugs for your high blood pressure, check with your doctor before taking Graviola as your medication may need adjusting.

There is no evidence that taking Graviola in pregnancy and lactation is safe. Consult your doctor regarding the use of this alternative medicine. Graviola comes from a tree in the rain forests of Africa, South America, and Southeast Asia. Its scientific name is *Annona muricata*. It is also known as custard apple, cherimoya, guanabana, soursop and brazilian paw paw. The active ingredient is thought to be a type of plant compound (phytochemical) called annonaceous acetogenins. Overall, there is no evidence to show that graviola works as a cure for cancer. In laboratory studies, graviola extracts can kill some types of liver and breast cancer cells that are resistant to particular chemotherapy drugs. But there haven't been any studies in humans. So we don't know whether it can work as a cancer treatment or not. 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. People in African and South American countries have used graviola to treat infections with viruses or parasites, rheumatism, arthritis, depression, and sickness. We know from research that some graviola extracts can help to treat these conditions. In many countries, people use the bark, leaves, root, and fruits of this tree for traditional remedies.

**Arrhythmia:** *A. muricata* is among the ethno medicine employed to treat arthritic pain an in-vivo study on

different doses (3, 10, 30 and 100 mg/kg) of ethanolic extract from *A. muricata* activity in complete Freund's adjuvant (CFA)-induced arthritic activity in rats according to the results, oral administrations of the extract reduce the edema dose dependent manner after two weeks for injection. Because the extract at higher dose significantly suppressed TNF- $\alpha$  and IL-1 $\beta$  expressions in local tissue the arthritic activity of *muricata* leaves contribute to the suppressions of pro-inflammatory cytokines. Hence, the anti-arthritic potential of *A. muricata* was substantiated by the findings of this *in-vivo* study. To evaluate the antihypertensive properties of *A. muricata* leaves, aqueous leaf extract (9.17-48.5 mg/kg) was administered to normotensive Sprague-Dawley rats. The results demonstrated that treatments of rats with the leaf extract significantly decreased blood pressure in a dose-dependent manner without affecting heart rates. This effect suggested to be induced through peripheral mechanism involving the antagonism of Ca<sup>+2</sup>.

**Possible side effects of graviola:** We don't know much about how graviola affects the body. But some researchers are concerned that particular chemicals present in graviola may cause nerve changes and movement disorders when taken in large amounts. The nerve changes may cause symptoms similar to Parkinson's disease. Laboratory research has found that some substances in graviola cause nerve damage and that these substances can cross into the brain from the bloodstream. One research study has shown that people in the Caribbean who had large amounts of graviola in their diet were more likely to develop particular nerve changes and were also more likely to have hallucinations. It is unlikely that drinks or foods containing graviola could harm you when taken as part of a normal diet. But always talk to your doctor before taking any kind of complementary or alternative therapy. Although seeds and roots of graviola too contain acetogenins that help in cancer therapy, they are best avoided because other chemicals present in these parts have shown neurotoxic effects similar to atypical Parkinson's disease.

**Ethno medical use:** All portions of the *A. muricata* tree, similar to other *Annona* species including *A. squamosa* and *A. reticulata* are extensively used as traditional medicines against an array of human ailments and disease, especially cancer and parasitic infection.

**Other uses:** The bark has properties enough to fight the most fearsome fungus. Unripe fruit has been used to treat diarrhea and dysentery. The leaves, roots, and stems have been shown clobber in bacteria grown in laboratory culture. Seeds are known to be seed parasites packing. Roots bark has been used to tame raging fevers. A leaf extract stood its ground against malaria. The fruit used as a natural medicine for arthritic pain, Neuralgia, Arthritis, Diarrhea, Fever, Malaria, Rheumatism, Skin rushes and worms and also to elevate a mother's milk after childbirth.





### How much does graviola cost?

Graviola costs more than £5 for 100 capsules. The manufacturers advise taking 2 capsules, 3 to 4 times a day. So 100 capsules could last less than 2 weeks.

10000 times stronger killer of CANCER than Chemotherapy can save many lives, fill up hopes and build confidence in the patients. The Soursop or the fruit from the graviola tree is a miraculous natural cancer cell killer 10,000 times stronger than Chemo. Why are we not aware of this? Its because some big corporation want to make back their money spent on years of research by trying to make a synthetic version of it for sale. So, since you know it now you can help a friend in need by letting him know or just drink some Soursop juice yourself as prevention from time to time. The taste is not bad after all. It's completely natural and definitely has no side effects. If you have the space, plant one in your garden. The other parts of the tree are also useful. The next time you have a fruit juice, ask for a sour sop. How many people died in vain while this billion-dollar drug maker concealed the secret of the miraculous Graviola tree? This tree is low and is called graviola! in Brazil, guanabana in Spanish and has the uninspiring name "soursop" in English. The fruit is very large and the subacid sweet white pulp is eaten out of hand or, more commonly, used to make fruit drinks, sherbets and such. The principal interest in this plant is because of its strong anti-cancer effects. Although it is effective for a number of medical conditions, it is its anti tumor effect that is of most interest. This plant is a proven cancer remedy for cancers of all types. Besides being a cancer remedy, graviola is a broad spectrum antimicrobial agent for both bacterial and fungal infections, is effective against internal parasites and worms, lowers high blood pressure and is used for depression, stress and nervous disorders. If there ever was a single example that makes it dramatically clear why the existence of Health Sciences Institute is so vital to Americans like you, it's the incredible story behind the Graviola tree. The truth is stunningly simple: Deep within the Amazon Rainforest grows a tree that could literally revolutionize what you, your doctor, and the rest of the world thinks about cancer treatment and chances of survival. The future has never looked more promising.

Research shows that with extracts from this miraculous tree it now may be possible to: (1) Attack cancer safely and effectively with an all-natural therapy that does not cause extreme nausea, weight loss and hair loss (2) Protect your immune system and avoid deadly infections (3) Feel stronger and healthier throughout the course of the treatment (4) Boost your energy and improve your outlook on life.

The source of this information is just as stunning: It comes from one of America's largest drug manufacturers, the fruit of over 20 laboratory tests conducted since the 1970's! What those tests revealed was nothing short of mind numbing. Extracts from the tree were shown to: (1) Effectively target and kill malignant cells in 12 types of cancer, including colon, breast, prostate, lung and pancreatic cancer (2) The tree compounds proved to be up to 10,000 times stronger in slowing the growth of cancer cells than Adriamycin, a commonly used chemotherapeutic drug! (3) What's more, unlike chemotherapy, the compound extracted from the Graviola tree selectively hunts down and kills only cancer cells. It does not harm healthy cells! The amazing anti-cancer properties of the Graviola tree have been extensively researched—so why haven't you heard anything about it? If Graviola extract is One of America's biggest billion-dollar drug makers began a search for a cancer cure and their research centered on Graviola, a legendary healing tree from the Amazon Rainforest. Various parts of the Graviola tree—including the bark, leaves, roots, fruit and fruit-seeds—have been used for centuries by medicine men and native Indians in South America to treat heart disease, asthma, liver problems and arthritis. Going on very little documented scientific evidence, the company poured money and resources into testing the tree's anti-cancerous properties—and were shocked by the results. Graviola proved itself to be a cancer-killing dynamo. But that's where the Graviola story nearly ended. The company had one huge problem with the Graviola tree—it's completely natural, and so, under federal law, not patentable. There's no way to make serious profits from it. It turns out the drug company invested nearly seven years trying to synthesize two of the Graviola tree's most powerful



anti-cancer ingredients. If they could isolate and produce man-made clones of what makes the Graviola so potent, they'd be able to patent it and make their money back. Alas, they hit a brick wall. The original simply could not be replicated. There was no way the company could protect its profits—or even make back the millions it poured into research. As the dream of huge profits evaporated, their testing on Graviola came to a screeching halt. Even worse, the company shelved the entire project and chose not to publish the findings of its research! Luckily, however, there was one scientist from the Graviola research team whose conscience wouldn't let him see such atrocity committed. Risking his career, he contacted a company that's dedicated to harvesting medical plants from the Amazon Rainforest and blew the whistle. Graviola 750, Maximize, Maximum International, 100 Veggie Caps, 5 bottles.

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