

Graviola supplement research studies, benefits, risks, side effects, testimonies, how well does it benefit cancer treatment or prevention? What is the right dosage?

by Ray Sahelian, M.D. (March 15, 2014)

Graviola tree, also known as soursop, is found in the Amazon jungle and some of Peru, Brazil or the Caribbean islands. The *Annona muricata* tree produces a delicious fruit which is widely consumed by indigenous peoples. (There seems to be some confusion regarding calling the graviola fruit Brazilian pawpaw or papaw since fruits from other plant species may also be called pawpaw, such as the tropical fruit papaya (*Carica papaya*.) The fruit and the leaves are used in traditional medicine for their tranquilizing and sedative properties.

What does the research say

As of 2014, I cannot find any research with graviola supplements done with humans. There are dozens of laboratory tests done in test tubes and a few on animals. Some of these studies show it to have anti-viral, anti-parasitic and potent anti- cancer properties. However we do not know if it has the same benefits if ingested as a supplement in humans.

My opinion

Until human trials are done, it is difficult to make any recommendations with certainty. Does it work well when taken as a supplement? What is the ideal dosage? How often should it be taken and for how long? Does graviola have side effects that we are not aware of if taken daily for many months or years? These are questions that still need to be answered through rigorous research. However, some of the studies regarding graviola's anti-cancer potential are intriguing and certainly worthwhile to further explore. In the meantime, it is prudent to take breaks from use, for instance two days off each week. one full week off each month, and one full month off every three months.

Suggested Use: As a dietary supplement, take 1 graviola capsule daily or as directed by a health care professional. Take breaks from use, for instance two days off a week and one week off per month.

What's in the fruit, seed and leaf ?

The pulp contains 81% moisture, 3% titratable acidity and 24% non-reducing sugar. Graviola seed contains 8% moisture, 2% crude protein, 13% ash, 8% crude fiber, 20% fat and 47% carbohydrate. The seed also contains 0.2% water soluble ash, 0.8% titratable acidity and 17 mg calcium / 100 grams.

There are quite a number of compounds in the fruit with exotic names. Some of these include acetogenins, muricins, annonuricine and muricapentocin, muricatocins A and B, and many others including annopentocins A, B, and C. The leaves contain monotetrahydrofuran acetogenins such as annonuricins A and B, gigantetrocin A, annonacin-10-one, muricatetrocins A and B, annonacin, and goniotalamicin.

Cancer prevention or treatment

Although laboratory research with graviola and cancer looks promising, little is known about the role graviola supplements would play in human cancer prevention or treatment. It is difficult to say whether graviola herb or extract is effective, what the appropriate dosage would be, how long treatment would be needed, which cancers it is suited for, and how it combines with pharmaceutical anti-cancer drugs.

Curr Top Med Chem. 2013. Anti cancer activity on Graviola, an exciting medicinal plant extract vs various cancer cell lines and a detailed computational study on its potent anticancerous leads. Many naturally occurring compounds have very complicated structures that present great challenges to chemists wishing to determine their structures or replicate them. Graviola has wide potent anticancerous agents coined acetogenins which play a key role towards many varieties of cancer. Acetogenins are potent inhibitors of NADH oxidase of the plasma membranes of cancer cells. Potent leads were taken for the study through literature survey, major types of cancer targets were identified. Phytochemicals such as Anonaine, Friedelin, Isolaureline, Annonamine, Anomurine, Kaempferol, Asimilobine, Quercetin, Xylopin were clustered and the highly clustered compounds such as Annonamine, Kaempferol termed to be a potential lead for the study. Further study on experimental analysis may prove the potentiality of these compounds. In the experimental analysis, Graviola leaves were collected, and the extracted components were tested against the HeLa cell line and PC3 cell line. HeLa cells treated with 75 µg of a crude leaf extract of *A. muricata* showing 80% of cell inhibition. Further investigation of other experimental studies may confirm that these potential lead could make a great impact in which it could help to accelerate the pipeline of drug discovery.

If you had cancer would you, personally, use graviola herb as a treatment?

There are many types of cancer and for some, modern medicine has a good treatment option. It depends on the type of cancer, the stage, what kind of therapy modern medicine offered, and what kind of available laboratory, animal, or human research was available at the time regarding the potential benefits of the herbal option.

Breast cancer

Nutr Cancer. 2011. Selective growth inhibition of human breast cancer cells by graviola fruit extract in vitro and in vivo involving downregulation of EGFR expression. In the mouse xenograft model, a 5-wk dietary treatment of GFE (200 mg/kg diet) significantly reduced the protein expression of EGFR, p-EGFR, and p-ERK in MDA-MB-468 tumors and inhibited tumor growth.



My wife has breast cancer and is taking graviola along with her chemo treatments. The herbal product has worked miracles, it's taken away the pain in the sternum and the tumors on her liver have shrunk in size.

I would be very happy if graviola was the natural treatment that is actually helping with the pain and liver tumor shrinkage, but since she is taking chemotherapy treatments at the same time, how do we know it is the graviola supplement use that is responsible for the liver tumor shrinkage?

Colon cancer

My father involve with adenocarcinoma of colon and metastatic complication to liver. He is under chemotherapy from 5 weeks ago. Please send me some information about graviola and it's anticancer effect. Will this herbal product help him?

It is not possible to know since human studies are lacking.

Five novel mono-tetrahydrofuran ring acetogenins from the seeds of *Annona muricata* J Nat Prod. 1996.

Cis-annonacin, cis-annonacin-10-one, cis-goniothalamycin, arianacin, and javoricin were isolated. Cis-annonacin was selectively cytotoxic to colon adenocarcinoma cells (HT-29) in which it was 10,000 times the potency of adriamycin.

Pancreatic cancer

Cancer Lett. 2012. Graviola: a novel promising natural-derived drug that inhibits tumorigenicity and metastasis of pancreatic cancer cells in vitro and in vivo through altering cell metabolism. The present study was aimed at evaluating the potential of a novel plant-derived product as a therapeutic agent for pancreatic cancer (PC). The effects of an extract from the tropical tree *Annona Muricata* was evaluated for cytotoxicity, cell metabolism, cancer-associated protein/gene expression, tumorigenicity, and metastatic properties of PC cells. Our experiments revealed that graviola induced necrosis of PC cells by inhibiting cellular metabolism. The expression of molecules related to hypoxia and glycolysis in PC cells (i.e. HIF-1 α , NF- κ B, GLUT1, GLUT4, HKII, and LDHA) were downregulated in the presence of the extract. In vitro functional assays further confirmed the inhibition of tumorigenic properties of PC cells. Overall, the compounds that are naturally present in a graviola extract inhibited multiple signaling pathways that regulate metabolism, cell cycle, survival, and metastatic properties in PC cells. Collectively, alterations in these parameters led to a decrease in tumorigenicity and metastasis of orthotopically implanted pancreatic tumors, indicating promising characteristics of the natural product against this lethal disease.

Prostate cancer

Two years ago my nephew was scheduled for surgery after a positive biopsy for prostate cancer. While awaiting surgery he took graviola supplements for two months. His tumors disappeared and his PSA dropped to 2 and his surgery was cancelled. His checkups remain fine. His PSA is now less than 2.

I was told by what I believe is a reliable person that JAMA had an article in it about the benefits of graviola extract for cancer. He didn't know the date of the Journal. I can't find



any info on the article, etc.

We searched Medline and did not find any human graviola cancer studies mentioned in JAMA.

Near the beginning of this year, I had a PSA of 11 after being followed for 4 or 5 years with a PSA in the range of 5 to 7 by my personal urologist who retired a full year before the PSA of 11 was obtained. I had been seeing him for regular checkups every 6 months prior to his retirement; however, after his retirement it was a full year before I had the next one obtained by my family physician. I saw another urologist, a much younger man, who had much difficulty in listening to anything I said and so when he began to talk about a biopsy and the possibility of surgery without answering any of my questions, I went to the Univ of Chicago Center for Advanced Medicine. This led to a biopsy with a negative finding for cancer; however, there were "markers" present suggesting a need for further biopsy and that there would be a 50% chance of finding the presence of cancer. So during the ensuing 6 to 7 weeks, I initially set and did nothing other than my usual activity and then, I decided to take a look at the internet discussions relative to alternative methods of treatment other than surgery and radiation. I discovered that which you had to say about graviola and ordered a 100 capsule supply and I began taking it on that day using the dosage of 1 per day for 5 days each week with one week off during the month and 1 month after each 3 months. Meanwhile 3 weeks later, I had the 2nd biopsy with a finding that I was cancer free and although there were a very few "markers" present, they were not significant at this time. I don't know if it helped or not. It does not seem to have caused any negative side effects.

This is interesting, please keep me updated on your future results and I wish you the best outcome.

Depression

Isoquinoline derivatives isolated from the fruit of *Annona muricata* as 5-HT₂ and 5-HT_{1A} receptor agonists in rats: unexploited antidepressive (lead) products.

J Pharm Pharmacol. 1997.

Extracts of the graviola plant have been shown to inhibit binding of [³H]rauwolscine to 5-HT₂ and 5-HT_{1A} receptors in calf hippocampus, including three alkaloids, annonaine, nornuciferine and asimilobine. Our results imply that the fruit of graviola possesses antidepressive effects, possibly induced by compounds annonaine, nornuciferine and asimilobine.

Herpes simplex

Effect of the extract of *Annona muricata* and *Petunia nyctaginiflora* on Herpes simplex virus.

J Ethnopharmacol. 1998.

Annona muricata and *Petunia nyctaginiflora* were screened for their activity against Herpes simplex virus-1 (HSV-1). The minimum inhibitory concentration of ethanolic extract of graviola and aqueous extract of *P. nyctaginiflora* was found to be 1 mg/ml.



Prostate gland

I am a 58 year old man, who has had a PSA elevated, benign for years, it has continually gone higher and higher, it went to 13. I went through all the biopsies, non cancerous. I went on a 3 capsules graviola herb per morning, 3 capsules per evening for 3 months went and retested and it was almost undetectable. I went off it now for approx two years, and now the PSA is back to 10, so starting again the herbal product, just wanted you to know, I did not take other peoples word and this is not something someone else said they did. It did cause some nausea and loose bowels, but I know it works. I used 3 capsules of Gravola Max, AM, PM, for three months, took my rising PSA from from 13 to 0.01, almost undetectable, and THAT is the ONLY thing that did it, it was rising for 5 years till then, just info only for your benefit.

Graviola extract

I have heard that some companies sell a graviola extract, but whether an extract offers benefits beyond that of regular graviola whole powder is not known.

Graviola and atypical Parkinson's disease symptoms, side effects, caution, safety and toxicity

There have been a few reports that regular ingestion of graviola fruit for decades by residents of Guadeloupe and other Caribbean countries may lead to atypical Parkinsonian type symptoms. Until this is clarified, it is a good idea to follow the suggestions of frequent breaks from the use of graviola supplements as suggested earlier in this article.

The mitochondrial complex I inhibitor annonacin is toxic to mesencephalic dopaminergic neurons by impairment of energy metabolism.

Neuroscience. 2003.

The death of dopaminergic neurons induced by systemic administration of mitochondrial respiratory chain complex I inhibitors such as 1-methyl-4-phenylpyridinium (MPP+); given as the prodrug 1-methyl-1,2,3,6-tetrahydropyridine) or the pesticide rotenone have raised the question as to whether this family of compounds are the cause of some forms of Parkinsonism. We have examined the neurotoxic potential of another complex I inhibitor, annonacin, the major acetogenin of *Annona muricata*,. When added to mesencephalic cultures, annonacin was much more potent than MPP(+) and as effective as rotenone in killing dopaminergic neurons.

Graviola fruit concerns, potential toxicity, danger

As you can read in detail in the research updates above, there is a concern that consuming the graviola fruit for prolonged periods (many years in a row or perhaps a lifetime) may increase the risk for a form of Parkinson's Disease. This is not known for certain at this time but to be cautious, it would be best to take holidays from use of graviola and not eat the fruit for months at a time without a break. However, there is some encouraging safety results from a rodent study.

Good news about graviola

J Basic Clin Physiol Pharmacology, December 2013. Toxicological evaluation of the



lyophilized fruit juice extract of *Annona muricata* in rodents. Graviola fruit juice is widely consumed either raw or after processing in tropical countries because of its very juicy, creamy and sweet character including its medicinal importance. The safety of the fruit was investigated in Sprague-Dawley rats for acute and 60-day subchronic toxicity effects. There was no mortality recorded up to 2000 mg/kg following acute administration. There were no significant changes in vital organ weights and hematological and biochemical parameters. However, significant reduction in platelet count and packed cell volume was observed at 2000 and 400 mg/kg, respectively, which was reversed after cessation of treatment. Interestingly, subchronic oral administration (80, 400 or 2000 mg/kg) significantly increased sperm count and motility in comparison to vehicle-treated control. Long-term treatment induced significant increases in the levels of glutathione, superoxide dismutase (SOD) and catalase, respectively, in the liver and kidney. Conversely, 2000 mg/kg produced significant increase in malondialdehyde level with decreased SOD activity in the brain. The study established that graviola did not induce any significant toxic effect, indicating that it is safe in rats following oral administration for 60 consecutive days.

Quantification of acetogenins in *Annona muricata* linked to atypical parkinsonism in guadeloupe.

Mov Disord. 2005.

Atypical parkinsonism in Guadeloupe has been associated with the consumption of fruit and infusions or decoctions prepared from leaves of *Annona muricata*, which contains annonaceous acetogenins, lipophilic inhibitors of complex I of the mitochondrial respiratory chain. An average fruit is estimated to contain about 15 mg of annonacin, a can of commercial nectar 36 mg, and a cup of infusion or decoction 140 microg. As an indication of its potential toxicity, an adult who consumes one fruit or can of nectar a day is estimated to ingest over 1 year the amount of annonacin that induced brain lesions in rats receiving purified annonacin by intravenous infusion.

Annonacin, a lipophilic inhibitor of mitochondrial complex I, induces nigral and striatal neurodegeneration in rats: possible relevance for atypical parkinsonism in Guadeloupe. J Neurochem. 2004.

Annonaceae family plants contain a class of powerful, lipophilic complex I inhibitors, the annonaceous acetogenins. To determine the neurotoxic potential of these substances, we administered annonacin, the major acetogenin of graviola, to rats. Annonacin inhibited complex I in brain homogenates in a concentration-dependent manner, and, when administered systemically, entered the brain parenchyma and decreased brain ATP levels. In the absence of evident systemic toxicity, we observed neuropathological abnormalities in the basal ganglia and brainstem nuclei. There was loss of dopaminergic neurones in the substantia nigra, and cholinergic and dopamine neurons in the striatum, accompanied by a significant increase in the number of astrocytes and microglial cells. The distribution of the lesions was similar to that in patients with atypical parkinsonism.

I noticed you mention potential toxicity. If studies have been done over years spanning lifetimes, did these Parkinsonian graviola eaters die of cancer ever? Do you think death

likelihood from colon adenocarcinoma has greater morbidity over Parkinson's? What is the morbidity window for persons with pancreatic, lung, bone, bladder cancer versus Parkinson's of the lifespans of persons studied leading to your 'potential toxicity' report? Is the toxicity of cancer less or greater than the toxicity of the plant? If you had cancer, would you consume graviola?

These are good questions and there are no easy answers since there is little research addressing these issues. Different cancers have different causes and treatments. If I had a form of cancer that had no good pharmaceutical options, I would certainly explore the use of graviola or other herbal and plant remedies.

Emails

Q. In 2003 I met Dr. Jerry McLaughlin, emeritus professor of pharmacognosy of Purdue. Dr. McLaughlin lectured about his work with the Annonaceous acetogenins. Among these are the molecules from *Annona muricata* (graviola) and *Asimina triloba* (paw paw). He distinguished these species mainly because of the difference in bioassay activity and the difference in tumor inhibition in mice. He reported on a human trial in the US of an extract from *Asimina triloba* (paw paw) that had 94 participants with diagnosed cancer. Later that year, I videotaped his lecture. I then posted the parts on an educational website called pawpaw dot tv. Although he is the former editor of the Journal of Natural Products and has published 70 papers in peer-reviewed journals concerning Annonaceous acetogenins, he has not had success thus far in finding a publisher. I wanted you to be aware that there is a significant difference in activity levels of the double ring compounds (e.g. bullatacin) found in *Asimina triloba*, and the single ring compounds found in *Annona muricata* (annonacin). Much of the popular writing from sources on the internet fails to distinguish the difference. This causes a misleading information to be put forward about the biological use of the two herbs. You may wish to refer to his published review of Annonaceous acetogenins found in the 1999 Journal of Natural Products.

Q. I was reading up on one of the herbs and came across this explanation graviola, also known as soursop, is a small tree from the Amazon jungle and some of the Caribbean islands. The graviola tree (*Annona muricata*) produces a delicious fruit commonly called paw-paw, which is widely consumed by indigenous peoples'. I was reading up on products concerning the immune system and came across this write up and was abit confused as you say in the above that the soursop is a small tree and produces fruit commonly called paw-paw but they are both different fruits are you aware of that? I live in Australia and we grow both fruit trees the soursop tree similar to the custard apple fruit and the paw-paw tree which has a few varieties both grown in Queensland.

A. We're not completely sure about this since we are not botanists but rather focus on the clinical effects of herbs and plant extracts, but it appears that in Brazil the graviola fruit is called Brazilian paw paw, and in Australia paw-paw is distantly related to soursop (*Annona muricata*), and in Australia the tropical papaya, *Carica papaya*, is also known as pawpaw. The main point is that the plant we are focused on this page is graviola, *annona muricata*. If there are botanists familiar with this topic who would like to enlighten us, we would appreciate it.



My uncle is afflicted with squamous cell lung cancer which has also spread to other parts of the body. He is currently undergoing chemotherapy which is not helping him much. The toxicity is so high that his WBC count reaches dangerous levels after every chemo session. Where could I purchase Graviola online? I wanted your recommendation on using Graviola to help him survive longer. I have read the standard dosage on your webpage. 1 per day for 5 days each week with one week off during the month and 1 month after each 3 months. Would you recommend a similar dosage? I would appreciate any help, and of course, I understand that you are not making any guarantees.

It is not possible to predict how this supplement will interact with chemotherapy drugs and or whether it will offer any help in treating lung cancer since human studies are not available. I am not in a position to offer individual advice, but if his doctor approves this herbal product can be used.

I live in Uruguay, and I have an hepatic carcinoma. I have been drinking graviola leaf infusions (using 4 leaves per cup of water) once a day for seven months. Although I completely trust its healing properties, I do not know about its administration quantities, how often should I consume it, if I should take brakes in between its usage, etc. and would appreciate if you could guide me on this. The leaves I am using are brought to me directly from Brazil.

Unfortunately there is not enough research on this topic to know the answers to any of these questions. Also, most of the studies I have seen in a laboratory have been done with the fruit rather than with the leaf.

I am taking your graviola, and have found it to be fantastic. I also take terazosin, on the days I take the terazosin, I do not take the natural product. Is there an issue if I take both regarding blood pressure?

I am not aware of studies regarding this combination nor have I treated patients who have taken both together. I doubt if there would be any serious interactions but I can't be sure.

Source : <http://www.raysahelian.com/graviola.html>

www.MacaPUNCH.ch



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