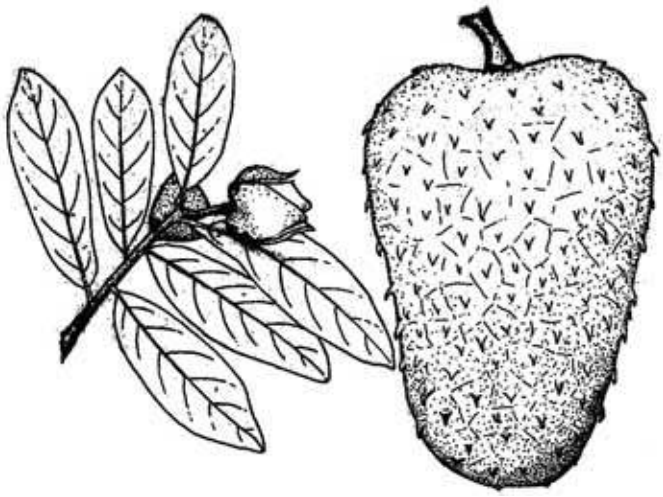
Technical Data Report

for

GRAVIOLA

Annona muricata



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Graviola

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Family: Annonaceae

Genus: *Annona*

Species: *muricata*

Synonyms: *Annona macrocarpa*, *A. bonplandiana, A. cearensis, Guanabanus muricatus*

Common Names: Graviola, soursop, guanábana, guanábano, guanavana, guanaba, corossol épineux, huanaba, toge-banreisi, durian benggala, nangka blanda, cachiman épineux

Parts Used: Leaves, fruit, seeds, bark, roots

Graviola is a small, upright evergreen tree, 5–6 m high, with large, glossy, dark green leaves. It produces a large, heart-shaped, edible fruit that is 15–23 cm in diameter, is yellow-green in color, and has white flesh inside. Graviola is indigenous to most of the warmest tropical areas in South and North America, including the Amazon. The fruit is sold in local markets in the tropics, where it is called *guanábana* in Spanish-speaking countries and *graviola* in Brazil. The fruit pulp is excellent for making drinks and sherbets and, though slightly sour-acid, can be eaten out of hand.

All parts of the graviola tree are used in natural medicine in the tropics, including the bark, leaves, roots, fruit, and fruit seeds. Different properties and uses are attributed to the different parts of the tree. Generally, the fruit and fruit juice are taken for worms and parasites, to cool fevers, as a lactagogue (to increase mother's milk after childbirth), and as an astringent for diarrhea and dysentery. The crushed seeds are used as a vermifuge and anthelmintic against internal and external parasites, head lice, and worms. The bark, leaves, and roots are considered sedative, antispasmodic, hypotensive, and nervine, and a tea is made for various disorders toward those effects.

Graviola has a long, rich history of use in herbal medicine as well as lengthy recorded indigenous use. In the Peruvian Andes, a leaf tea is used for catarrh (inflammation of mucous membranes) and the crushed seed is used to kill parasites. In the Peruvian Amazon the bark, roots, and leaves are used for diabetes and as a sedative and antispasmodic. Indigenous tribes in Guyana use a leaf and/or bark tea as a sedative and heart tonic. In the Brazilian Amazon a leaf tea is used for liver problems, and the oil of the leaves and unripe fruit is mixed with olive oil and used externally for neuralgia, rheumatism, and arthritis pain. In Jamaica, Haiti, and the West Indies, the fruit and/or fruit juice is used for fevers, parasites and diarrhea, and as a lactagogue; the bark or leaf is used as an antispasmodic, sedative, and nervine for heart conditions, coughs, grippe, difficult childbirth, asthma, asthenia, hypertension, and parasites.

Many bioactive compounds and phytochemicals have been found in graviola, as scientists have been studying its properties since the 1940s. Its many uses in natural medicine have been validated by scientific research. Several studies by different researchers demonstrated that the bark as well as the leaves had hypotensive, antispasmodic, anticonvulsant, vasodilator, smooth-muscle relaxant, and cardiodepressant activities in animals.[1,2] Researchers verified graviola leaf's hypotensive properties in rats again in 1991.[3] Several studies over the years have demonstrated that leaf, bark, root, stem, and seed extracts of graviola are antibacterial *in vitro* against numerous pathogens,[4–6] and that the bark has antifungal properties.[6,7] Graviola seeds demonstrated active antiparasitic properties in a 1991 study,[8] and a leaf extract showed to be active against malaria in two other studies (in 1990 and 1993).[9,10] The leaves, root, and seeds of graviola demonstrated insecticidal properties, with the seeds demonstrating strong insecticidal activity in an early 1940

study.[11] In a 1997 clinical study, novel alkaloids found in graviola fruit exhibited antidepressive effects in animals.[12]

In an 1976 plant screening program by the National Cancer Institute, graviola leaves and stem showed active cytotoxicity against cancer cells and researchers have been following up on these findings since.[13] Much of the cancer research on graviola focuses on a novel set of phyto-chemicals called *Annonaceous acetogenins*. Graviola produces these natural compounds in its leaf and stem, bark, and fruit seeds. Three separate research groups have isolated these acetogenin compounds in graviola which have demonstrated significant antitumorous and anticancerous properties, and selective toxicity against various types of cancer cells (without harming healthy cells) publishing eight clinical studies on their findings.[14–21] Many of the acetogenins have demonstrated selective toxicity to tumor cells at very low dosages—as little as 1 part per million. Four studies were published in 1998 which further specify phytochemicals and acetogenins which are demonstrating the strongest anticancerous, antitumorous, and antiviral properties.[22–25] Thus far, specific acetogenins in graviola have been reported to be selectively toxic to these types of tumor cells: lung carcinoma cell lines;[14,16–19] human breast solid tumor lines;[17] prostate adenocarcinoma;[22] pancreatic carcinoma cell lines;[14,22,25] colon adenocarcinoma cell lines;[14,15,25] liver cancer cell lines;[26,27,29] human lymphoma cell lines;[28] and multi-drug resistant human breast adenocarcinoma.[30]

Annonaceous acetogenins are only found in the Annonaceae family (to which graviola belongs). In general, various Annonaceous acetogenins in the plant family have been documented with antitumorous, antiparasitic, pesticidal, antiprotozoal, antifeedant, anthelmintic, and antimicrobial activities.[31] Mode of action studies in three separate laboratories have recently determined that these acetogenins are superb inhibitors of enzyme processes that are only found in the membranes of cancerous tumor cells. Purdue University, in West Lafayette, Indiana, has conducted a great deal of the research on the acetogenins, much of which has been funded by The National Cancer Institute and/or the National Institute of Health (NIH). Thus far, Purdue University and/or its staff have filed at least nine U.S. and/or international patents on their work around the antitumorous and insecticidal properties and uses of these acetogenins. In one of their reviews, titled “Recent Advances in Annonaceous Acetogenins,” they state, “Recently, we reported that the Annonaceous acetogenins can selectively inhibit the growth of cancerous cells and also inhibit the growth of adriamycin resistant tumor cells. As more acetogenins have been isolated and additional cytotoxicity assays have been conducted, we have noticed that, although most of acetogenins have high potencies among several solid human tumor cell lines, some of the derivatives within the different structural types and some positional isomers showed remarkable selectivities among certain cell lines; e.g., against prostate cancer (PC-3). We now understand the primary modes of action for the acetogenins. They are potent inhibitors of NADH: ubiquinone oxidoreductase, which is in an essential enzyme in complex I leading to oxidative phosphorylation in mitochondria. A recent report showed that they act directly at the ubiquinone-catalytic site(s) within complex I and in microbial glucose dehydrogenase. They also inhibit the ubiquinone-linked NADH oxidase that is peculiar to the plasma membranes of cancerous cells."[32]

In 1997, Purdue University published information with promising news that several of the Annonaceous acetogenins " . . . not only are effective in killing tumors that have proven resistant to anti-cancer agents, but also seem to have a special affinity for such resistant cells."[33] In several interviews after this information was publicized, the head pharmacologist in Purdue's research explained how this worked. As he explains it, cancer cells that survive chemotherapy can develop resistance to the agent originally used as well as to other, even unrelated, drugs. This phenomenon is called *multi-drug resistance* (MDR). One of the ways that cancer cells develop resistance to chemotherapy drugs is by creating an intercellular efflux pump called a *P-glycoprotein mediated pump*. These types of pumps are capable of pushing anticancer agents out of the cell before they can kill it. On average, only about two percent of the cancer cells in any given person might develop this pump—but they are the two percent that can eventually grow and expand to create multi-drug-

resistant tumors. Some of the latest research on acetogenins reported that they were capable of shutting down these intercellular pumps, thereby killing MDR tumors. Purdue researchers reported that the acetogenins preferentially killed multi-drug-resistant cancer cells by blocking the transfer of ATP—the chief source of cellular energy—into them.[34] A tumor cell needs energy to grow and reproduce, and a great deal more to run its pump and expel attacking agents. By inhibiting energy to the cell , it can no longer run its pump. When acetogenins block ATP to the tumor cell over time, the cell no longer has enough energy to operate sustaining processes—and it dies. Normal cells seldom develop such a pump; therefore, they don't require large amounts of energy to run a pump and, generally, are not adversely affected by ATP inhibitors. Purdue researchers reported that 14 different acetogenins tested thus far demonstrate potent ATP blocking properties (including several found only in graviola).[34] They also reported that 13 of these 14 acetogenins tested were more potent against MDR breast cancer cells than all three of the standard drugs (adriamycin, vincristine, and vinblastine) they used as controls.

An interesting *in vivo* study was published in March of 2002 by researchers in Japan, who were studying various acetogenins found in several species of plants. They inoculated mice with Lewis lung carcinoma cancer cells. One third received nothing, one third received the chemo-therapy drug adriamycin, and one third received the main graviola acetogenin, *annonacin* (at a dosage of 10 mg/kg). At the end of two weeks, five of the six in the untreated control group were still alive and lung tumor sizes were then measured. The adriamycin group showed a 54.6% reduction of tumor mass over the control group—but 50% of the animals had died from toxicity (three of six). The mice receiving annonacin were all still alive, and the tumors were inhibited by 57.9%—slightly better than adriamycin—and without toxicity. This led the researchers to summarize; “This suggested that annonacin was less toxic in mice. On considering the antitumor activity and toxicity, annonacin might be used as a lead to develop a potential anticancer agent.”[35] Its important to note, however, that annonacin only inhibited the normal growth of the lung tumors during this two-week period; it did not eradicate the tumors nor stop their growth altogether.

Cancer research is ongoing on these important plants and plant chemicals, as several pharmaceutical companies and universities continue to research, test, patent, and attempt to synthesize these chemicals into new chemotherapeutic drugs. In addition, researchers have reported that NADH dehydrogenase inhibitors can suppress HIV infection. As this is a familiar property of Annonaceous acetogenins, several acetogenins found in graviola and other *Annona* plants have been submitted to the NIH anti-AIDS screening program by Purdue University; research work is continuing in this area as well.

One researcher summarized his work eloquently: “At the time of preparation (August 1998) of this current review, over 350 Annonaceous acetogenins have been isolated from 37 species. Our preliminary efforts show that about 50%, of over 80 Annonaceous species screened, are significantly bioactive and are worthy of fractionation; thus, this class of compounds can be expected to continue to grow at an exponential rate in the future, provided that financial support for such research efforts can be found. With the demise of the world’s tropical rain forests, such work is compelling before the great chemical diversity, contained within these endangered species, is lost.” [34] Perhaps—if enough people believe that the possible cure for cancer or AIDS truly is locked away in a rainforest plant—we will take the steps needed to protect our remaining rainforests from destruction.

Documented Properties and Actions: Antibacterial, anthelmintic, anticancerous, anticonvulsant, antidepressant, antifungal, antimicrobial, antineoplastic, antiparasitic, antispasmodic, antitumorous, antiviral, astringent, cardiodepressant, cytotoxic, febrifuge, hypotensive, insecticide, nervine, pectoral, piscicide, sedative, stomachic, vasodilator, vermifuge

Main Phytochemicals: Annonaceous acetogenins: annocatalin, annohexocin, annomonicin, annomontacin, annomuricatin A & B, annomuricin A thru E, annomutacin, annonacin, (multiple iso, cis, one, etc.), annonacinone, annopentocin A thru C, cis-annonacin, cis-corossolone, cohibin A thru D, corepoxylone, coronin, corossolin, corossolone, donhexocin, epomuricenin A & B, gigantetrocin, gigantetrocin A & B, gigantetrocinone, gigantetronenin, goniothalamicin, iso-annonacin, javoricin, montanacin, montecristin, muracin A thru G, muricapentocin, muricatalicin, muricatalin, muri-catenol, muricatetrocin A & B muricatin D, muricatocin A thru C muricin H, muricin I, muricoreacin, murihexocin 3, murihexocin A thru C, murihexol, murisolin, robustocin, rolliniastatin 1 & 2, saba-delin, solamin, uvariamicin I & IV, xylomaticin

Traditional Remedy: The therapeutic dosage is reported to be 5–7 grams daily in capsules or tablets (in 3–4 divided dosages). A standard infusion (one cup 2–3 times daily) or a 4:1 standard tincture (2–4 ml three times daily) can be substituted if desired.

Contraindications: Graviola has demonstrated uterine stimulant activity in an animal study (rats) and should therefore not be used during pregnancy.

Graviola has demonstrated hypotensive, vasodilator, and cardiodepressant activities in animal studies and is contraindicated for people with low blood pressure. People taking antihypertensive drugs should check with their doctors before taking graviola and monitor their blood pressure accordingly (as medications may need adjusting).

Graviola has demonstrated significant *in vitro* antimicrobial properties. Chronic, long-term use of this plant may lead to die-off of friendly bacteria in the digestive tract due to its antimicrobial properties. Supplementing the diet with probiotics and digestive enzymes is advisable if this plant is used for longer than 30 days.

Graviola has demonstrated emetic properties in one animal study with pigs. Large single dosages may cause nausea or vomiting. Reduce the usage accordingly if this occurs.

One study with rats given a stem-bark extract intragastrically (at 100 mg/kg) reported an increase in dopamine, norepinephrine, and monomine oxidase activity, as well as a inhibition of serotonin release in stress-induced rats.[36] As such, the use of this plant is probably contraindicated in combination with MAO inhibitors and some prescription antidepressants. Check with your doctor first if you are taking prescription antidepressants or MAO inhibitor drugs prior to taking graviola.

Alcohol extracts of graviola leaf showed no toxicity or side effects in mice at 100 mg/kg; however, at a dosage of 300 mg/kg, a reduction in explorative behavior and mild abdominal constrictions was observed.[37] If sedation or sleepiness occurs, reduce the amount used.

Drug Interactions: None have been reported; however, graviola may potentiate antihypertensive and cardiac depressant drugs. It may potentiate antidepressant drugs and interfere with MAO-inhibitor drugs. See contraindications above.

WORLDWIDE ETHNOBOTANICAL USES

Country	Uses
Brazil	Abscess, analgesic, anthelmintic, antispasmodic, astringent, bronchitis, calmative, chest problems, cough, diabetes, diarrhea, dysentery, edema, emetic, fever, intestinal colic, liver problems, neuralgia, parasites, rheumatism
Caribbean	Antispasmodic, chill, fever, flu, indigestion, nervousness, palpitation, rash, sedative, skin disease
Curaçao	Childbirth, gallbladder, nervousness, parturition, sedative, tea, tranquilizer

Country	Uses
Haiti	Asthenia, cataplasm, cicatrizant, cough, diarrhea, emetic, fever, grippe, heart conditions, lactagogue, nervine, parasites, pediculicide, pellagra, sedative, soporific, sore, spasm, stomachic
Jamaica	Antispasmodic, asthenia, asthma, diuretic, fevers, heart conditions, hypertension, lactagogue, nervine, parasites, sedative, vermifuge
Malaysia	Astringent, boil, cough, diarrhea, dermatosis, hypertension, rheumatism, styptic
Mexico	Astringent, diarrhea, dysentery, fever, liqueur, pectoral, ringworm, scurvy
Panama	Anthelmintic, diarrhea, dyspepsia, kidney, piscicide, ulcer (stomach), vermifuge
Peru	Antiparasitic, antispasmodic, catarrh, diabetes, diarrhea, dysentery, fever, hypertension, indigestion, insecticide, lice, liver disorders, sedative, tumors (skin), ulcers (internal)
Trinidad	Depurative, fainting, flu, galactagogue, high blood pressure, hypertension, insomnia, palpitation, ringworms
West Indies	Asthma, childbirth, diarrhea, hypertension, lactagogue, parasites, worms
Elsewhere	Analgesic, antiphlogistic, arthritis, asthma, astringent, bilious, childbirth, cyanogenetic, diarrhea, dysentery, febrifuge, heart, insecticide, kidney, lactagogue, liver, malaria, pectoral, pediculicide, piscicide, ringworm, scurvy, sedative, stomach, tranquilizer

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Documented Ethnomedical Information for Graviola (Annona muricata)

Part Used / Where	Documented Use	Type Extract	Method	Ref #
Leaf Barbados	Used as a sedative.	Hot H2O Ext / Oral	Human Adult	T05032
Leaf Borneo	Used for the spleen and for fever.	Leaves / External	Human Adult	K27823
Leaf Brazil	Used for liver problems. Used as an anthelmintic and antirheumatic. Used externally for neuralgia, rheumatism and arthritis pain. Used for dysentery, intestinal colic, cough, and bronchitis. Used for abscesses, edema, rheumatism. Used for spasms, diarrhea, cough, and chest problems.	Hot H2O Ext / Oral Infusion /Oral Maceration / External Hot H2O Ext / Oral Maceration / External Decoction / Oral	Human Adult Human Adult Human Adult Human Adult Human Adult Human Adult	ZZ1024 L15585 ZZ1002 ZZ1072 ZZ1072 ZZ1099
Leaf Cook Islands	Used to treat skin rashes, skin diseases, and skin infections. Used to treat indigestion.	Decoction / External Decoction / Oral	Human Adult Human Adult	K20471
Leaf Curacao	Decoction drunk for gallbladder trouble. Used for nervousness.	Hot H2O Ext / Oral	Human Adult	A05332
Leaf Dominica	Tea is drunk by women in labor (parturition).	Hot H2O Ext / Oral	Human (pregnant)	A01962
Leaf Guatemala	Used for ringworm.	Hot H2O Ext / Oral	Human Adult	M27151
Leaf Guam	Tea used by asthma sufferers.	Hot H2O Ext / Oral	Human Adult	W01267
Leaf Guyana	Tea used as a sedative and heart tonic.	Hot H2O Ext / Oral	Human Adult	ZZ1033
Leaf Haiti	Used as an antispasmodic, sedative, and nervine. Used for grippe, coughs, and asthenia.	Not stated Decoction / Oral	Human Adult Human Adult	AA1008 T13846
Leaf Jamaica	Infusion used as an antispasmodic. Beverage prepared as a lactagogue.	Hot H2O Ext / Oral Hot H2O Ext / Oral	Human Adult Human Female	W01316

Part Used / Where	Documented Use	Type Extract	Method	Ref #
Leaf Jamaica	Used as an antispasmodic, sedative, and nervine for heart conditions, coughs, grippe, difficult childbirth, asthma, asthenia, hypertension and parasites.	Not Stated	Human Adult	ZZ1020
Leaf Madagascar	Used to treat heart palpitations, liver maladies and malaria.	Infusion / Oral	Human Adult	L15693
Leaf Malaysia	Used for high blood pressure and diarrhea. Used as an astringent and a styptic.	Decoction / Oral Leaves / External	Human Adult Human Adult	K26834 J13478
Leaf Peru	Used to treat catarrh, liver disorders, diarrhea, dysentery, fevers, hypertension, sores, internal ulcers, diabetes. Used as a sedative and antispasmodic. Used for indigestion and catarrh. Fresh leaves crushed with salt are used in a cataplasm to “ripen” malignant tumors.	Decoction / Oral Decoction / Oral Cataplasm / External	Human Adult Human Adult Human Adult	L04137 ZZ1045 ZZ1093 ZZ1093
Leaf Surinam	Claimed to be a tranquillizer.	Infusion / Oral	Human Adult	J14527
Leaf Togo	Used for malaria.	Decoction / Oral	Human Adult	M23556
Leaf Trinidad	Used to lower high blood pressure and as a galactagogue.	Hot H2O Ext / Oral	Human Adult	T05032
Leaf West Indies	Decoction used to ease delivery. Used for hypertension, worms and diarrhea. Used for difficult childbirth, asthma, hypertension, and parasites.	Hot H2O Ext / Oral Hot H2O Ext / Oral Hot H2O Ext / Oral	Human (pregnant) Human Adult Human Adult	T00701 T00701 ZZ1021
Seed Brazil	Considered emetic and astringent.	Not stated	Human Adult	ZZ1099
Seed Peru	Used to kill parasites. Crushed seeds and seed oil used as an insecticide, for skin parasites and lice.	Decoction / Oral Maceration/ External	Human Adult Human Adult	ZZ1027 ZZ1093
Bark Guyana	Tea used as a sedative and heart tonic.	Hot H2O Ext / Oral	Human Adult	ZZ1033
Bark Haiti	Used for heart conditions, coughs, and grippe.	Decoction / Oral	Human Adult	AA1008
Bark Jamaica	Used as an antispasmodic, sedative, and nervine for heart conditions, coughs, grippe, difficult childbirth, asthma, asthenia, hypertension, and parasites.	Hot H2O Ext / Oral	Human Adult	ZZ1020

Part Used / Where	Documented Use	Type Extract	Method	Ref #
Bark Peru	Used to treat diabetes. Used as a sedative and antispasmodic.	Decoction / Oral	Human Adult	ZZ1045
Bark West Indies	Used for hypertension and parasites.	Hot H2O Ext / Oral	Human Adult	ZZ1021
Fruit Haiti	Used for fevers, parasites, diarrhea and as a lactogogue.	Fruit / Oral	Human Adult	AA1008
Fruit Jamaica	Used for fevers, parasites, diarrhea and as a lactogogue.	Fruit / Oral	Human Adult	ZZ1020
Fruit West Indies	Used for fevers, parasites, diarrhea and as a lactogogue.	Fruit / Oral	Human Adult	ZZ1021
Rootbark Brazil	Considered calmative, antispasmodic, and antidiabetic.	Decoction / Oral	Human Adult	ZZ1099
Root Peru	Used to treat diabetes. Used as a sedative and antispasmodic.	Hot H2O Ext / Oral	Human Adult	ZZ1045

Documented Biological Activities for Extracts of Graviola (Annona muricata)

IN VIVO RESEARCH

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Leaf Gabon	Toxic Effect (general)	ETOH(95%) Ext	IP Mouse	100.0 mg/kg	Inactive	No toxicity noted.	K29500
Leaf Gabon	Toxic Effect (general)	ETOH(95%) Ext	IP Mouse	300.0 mg/kg	Active	Reduction in explorative behavior and abdominal constrictions observed.	K29500
Leaf + Stem Jamaica	Toxicity Assessment (quantitative)	H2O Ext	IP Mouse	Various		Minimum toxic dose 1.0 ml/animal.	A03360
Leaf Not stated	Cytotoxic / Antiproliferative Activity	Fraction: Annonacin	IP Mouse	10 mg/kg	Active	Inhibited the growth of Lewis lung carcinoma tumors by 57.9% without toxicity	AA1032
Leaf + Stem Jamaica	Uterine Stimulant Effect	ETOH(95%) Ext H2O Ext	Oral Rat Oral Rat	0.033 ml/liter 0.033 ml/liter	Active Active	Uterus (unspec.cond). Uterus (unspec.cond).	A03360
Leaf + Stem Jamaica	Hypertensive Activity	ETOH(95%) Ext H2O Ext	IV Dog IV Dog	0.1 ml/kg 0.1 ml/kg	Active Active		A03360
Bark Not stated	Cardiac Depressant Activity	H2O Ext	Rabbit	Not stated	Active	Heart	A04104
Leaf Cuba	Hypotensive Activity	H2O Ext	IV Rat	1.0 ml/animal	Active	BP fell by more than 30%.	M29843
Leaf + Stem Jamaica	Vasodilator Activity	ETOH(95%) Ext	IP Rat	0.033 ml/liter	Active	Hind Quarter (isolated)	A03360
Leaf Gabon	Anticonvulsant Activity	ETOH(95%) Ext	IP Mouse	100.0 mg/kg	Active	vs. pentylenetetrazol-induced seizures. Results significant at $P < 0.05$ Level.	K29500
Leaf Nigeria	Anticonvulsant Activity	ETOH(70%) Ext	IP Mouse	Dose Variable	Inactive	vs. metrazole-induced convulsions and vs. strychnine-induced convulsions.	T06510
Leaf Brazil	Analgesic Activity	ETOH-H2O (1:1) Ext	Intragastric Mouse	1.0 gm/kg	Inactive	vs. writhing test.	M18488

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Leaf Brazil	Analgesic Activity	ETOH-H2O (1:1) Ext	Intragastric Mouse	1.0 gm/kg	Inactive	vs. tail flick test.	M18488
Leaf + Stem Jamaica	Smooth Muscle Relaxant Activity	ETOH(95%) Ext H2O Ext	Rabbit Rabbit	3.3 ml/liter 2.2 ml/liter	Active Active	Duodenum	A03360
Leaf + Stem Jamaica	Spasmogenic Activity	ETOH(95%) Ext H2O Ext	Guinea Pig Guinea Pig	0.033 ml/liter 0.033 ml/liter	Active Active	Ileum	A03360
Leaf Cuba	Inotropic Effect Positive	Hot H2O Ext	Guinea Pig	0.032 ml/liter	Inactive	Atrium	M29843
Stembark India	Antioxidant Activity	ETOH(95%)Ext	Rat Intragastric	100.0 mg/kg	Active	vs. cold immobilization stress-induced increase in lipid peroxidation.	J10426
Stembark India	5-hydroxyindole-3-acetic Acid Inhibition	ETOH(100%)Ext	Rat Intragastric	100.0 mg/kg	Active	Brain	L19052
Stembark India	Antiulcer Activity	ETOH(100%)Ext	Rat Gastric Intubation	100.0 mg/kg	Weak Activity	Statistical data in report indicating significant results vs. cold stress-induced ulcers.	J19242
Leaf Surinam	Serotonin (5-ht) Receptor Binding Activity	CHCL3 Ext	Calf Hippocampus	100.0 mcg/ml	Weak Activity	Inhibited the binding of 3h-rauwolscine to serotonin receptors.	J10986
Fruit Surinam	Serotonin (5-HT) Receptor Binding Activity	Juice CHCL3 Ext	Calf Calf	100.0 mcg/ml 100.0 mcg/ml	Active Active	Inhibited the binding of 3h-rauwolscine to serotonin receptors.	J10986
Seed Surinam	Serotonin (5-HT) Receptor Binding Activity	MEOH Ext	Calf Hippocampus	100.0 mcg/ml	Active	Inhibited the binding of 3h-rauwolscine to serotonin receptors.	J10986
Stembark India	Dopamine Increase	ETOH(100%)Ext	Rat Intragastric	100.0 mg/kg	Active	Brain	L19052
Stembark India	Norepinephrine Level Increase	ETOH(100%)Ext	Rat Intragastric	100.0 mg/kg	Active	Brain	L19052
Stembark India	Monoamine Oxidase Activity Increase	ETOH(100%)Ext	Rat Intragastric	100.0 mg/kg	Active	Brain	L19052
Stembark India	Serotonin (5-ht) Release Inhibition	ETOH(100%)Ext	Rat Intragastric	100.0 mg/kg	Active	Brain	L19052

Documented Biological Activities for Extracts of Graviola (Annona muricata)

IN VITRO RESEARCH

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Leaf Malaysia	Epstein-barr Virus Early Antigen Induction	Ether Ext	Cell Culture	1.0 mcg/ml	Inactive	Virus - Epstein-barr (Assay designed to test for tumor promoting activity.)	J13478
Leaf Borneo	Cytotoxic Activity	ETOH(95%) Ext	Cell Culture	20.0 mcg/ml	Active	Cancer: CA-9KB. (Results significant at $p < 0.05$ level)	K27823
Leaf Costa Rica	Cytotoxic Activity	ETOH(95%) Ext	Cell Culture	ED50<20 mcg/ml	Active	Cancer: CA-9KB	X00001
Leaf USA-FL	Cytotoxic Activity	ETOH(95%) Ext	Cell Culture	ED50<20 mcg/ml	Active	Cancer: CA-9KB	X00001
Leaf Colombia	Cytotoxic Activity	ETOH(100%) Ext	Cell Culture	IC50=2.0 mcg/ml	Active	Cells-MDBK	L12082
Leaf Indonesia	Cytotoxic Activity	ETOH(95%)Ext	Cell Culture	ED50=1.9 mcg/ml	Active	Cancer: CA-Mammary-MCF-7	H24563
Leaf Indonesia	Cytotoxic Activity	Not stated	Cell Culture	IC50=0.67 mcg/ml	Active	Cancer: CA-A498	H19306
Stem Costa Rica	Cytotoxic Activity	ETOH(95%)Ext	Cell Culture	ED50<20.0 mcg/ml	Active	Cancer: CA-9KB	X00001
Leaf Taiwan	Cytotoxic Activity	ETOH(95%)Ext	Cell Culture	Not stated	Active	Human hepatoma Hep G 2,2,15	AA1009
Seed China	Cytotoxic Activity	Fractions: Acetogenins	Cell Culture	Not stated	Active	Human hepatoma Hep G(2) and 2,2,15	AA1017
Seed Korea	Cytotoxic Activity	Fractions: Acetogenins	BST	Not stated	Active	Six human tumor cell lines including prostate adenocarcinoma (PC-3) and pancreatic carcinoma (PACA-2) cell lines.	AA1020
Seed France	Cytotoxic Activity	Fractions: Acetogenins	Not stated	Not stated	Active	Murine leukemia L1210, human breast adeno-carcinoma MDA-MB231, human breast carcinoma MCF-7.	AA1031

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Leaf USA	Cytotoxic Activity	Fractions: Muricoreacin Murihexocin C	Cell Culture	Not stated	Active	Six human tumor cell lines including prostate adenocarcinoma (PC-3) and pancreatic carcinoma (PACA-2) cell lines.	H22688
Stembark USA	Cytotoxic Activity	Fractions: Acetogenins	Cell Culture	Not stated	Active	Human tumor cell lines A-549 (lung carcinoma), MCF-7 (breast carcinoma), HT-29 (colon adenocarcinoma)	AA1025
Bark USA	Cytotoxic Activity	Fraction: Gigantetronenin	Cell Culture	Not stated	Active	Human tumor cell lines.	AA1026
Leaf + Twig USA	Cytotoxic Activity	Not Stated	Cell Culture	Not stated	Active	Human tumor cell lines.	AA1023
Bark Venezuela	Cytotoxic Activity	Fraction: Xylomaticin	Cell Culture	Not stated	Active	Human solid tumor cell lines.	AA1024
Pericarp Colombia	Cytotoxic Activity	Hexane Ext Ethyl acetate Ext MEOH Ext	Cell Culture	Not stated	Active	Cancer: U-937	AA1029
Leaf Colombia	Cytotoxic Activity	MTT	Cell Culture	CC50=49.5 mcg/ml	Active	Human hepatoma 2	AA1030
Acetogenins USA	Cytotoxic Activity	Fractions: Acetogenins	Cell Culture	Not stated	Active	Murine P388 leukemia, P03, M17/adr cancer cell lines, human H8,H125 cancer cell lines, adriamycin resistant tumor cells, non-adriamycin resistant tumor cells.	AA1021
Acetogenins France	Cytotoxic Activity	Fractions: Acetogenin analogs	Cell Culture	Not stated	Active	L1210 leukemia cells (Predicts antitumor activity.)	AA1015
Leaf Cuba	Cytostatic Activity	H2O Ext ETOH Ext Ketonic Ext	Agar plate	Not stated	Active	*Neurospora crassa*	AA1013
Acetogenins USA	Cytostatic Activity	Fractions: Acetogenins	Not stated	Not stated	Active	Adriamycin resistant human mammary adenocarcinoma (MCF-7/Adr) cells.	AA1015

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Seed China	Antitumor Activity	CHC13 Ext	Cell Culture	Not stated	Active	Demonstrated antitumor activity.	AA1011
Acetogenins USA	Antiproliferative Activity	Fractions: Acetogenins	Cell Culture	Not stated	Inactive	Non-cancerous GI epithelial cell line (I18).	AA1021
Leaf Indonesia	Anticrustacean Activity	ETOH(95%) Ext	Artemia salina larvae	LC50=0.17 mcg/ml	Active	Assay system is intended to predict for antitumor activity.	H16272
Stem Puerto Rico	Cytotoxic / Anti-HIV Activity	H2O Soluble Fraction	Cell Culture	IC50<2.0 mcg/ml	Active	vs. CEM-SS Cells. Results indicate it has an anti-proliferative effect rather than a cytotoxic effect on HIV-infected cells.	L09586
Stem Puerto Rico	Antiviral Activity	H2O Soluble Fraction	Agar Plate	Not stated	Inactive	Virus - HIV	L09586
Colombia	Antiviral Activity	MTT	Cell Culture	CC50 & EC50 = 0.50 mcg/ml	Active	Virus - HSV-2	AA1030
Stembark India	Antiviral Activity	ETOH(95%) Ext	Cell Culture	1.0 mg/ml	Active	Virus- *Herpes simplex* 1	J19169
Leaf Cuba	Antifungal Activity	Acetone Ext ETOH(95%) Ext H2O Ext	Agar Plate	50%	Inactive	*Neurospora crassa*	T08589
Leaf Guatemala	Antifungal Activity	Hot H2O Ext	Broth Culture	1.0 ml	Inactive	*Epidermophyton floccosum* *Microsporum canis* *Microsporum gypseum* *Trichophyton mentagrophytes* *Trichophyton rubrum*	M27151
Stem Cuba	Antifungal Activity	Acetone Ext ETOH(95%) Ext H2O Ext	Agar Plate	50%	Inactive	*Neurospora crassa*	T08589
Leaf Dominican Republic	Antihepatotoxic Activity	Decoction	Cell Culture	1.0 mg/plate	Weak Activity	Hepatocytes (Measured by leakage of LDH and ASAT. Reduced the leakage of ASAT)	K23019

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Leaf Dominican Republic	Antioxidant Effect	H2O Ext	Cell Culture	1.0 mg/plate	Inactive	Hepatocytes (Monitored by production of malo-naldehyde.)	K23019
Leaf Dominican Republic	Radical Scavenging Effect	H2O Ext	Not stated	250.0 mg/liter	Inactive	Measured by decoloration of diphenylpicryl hydroxyl radical solution.	K23019
Stembark France	Antiparasitic Activity	MEOH Ext	In vitro	Not stated	Active	*Leishmania trypansoma*	AA1032
Pericarp Colombia	Antiparasitic Activity	Hexane Ext Ethyl Acetate Ext MEOH Ext	In vitro	Not stated	Active	*Leishmania braziliensis* *L. panamensis* *L. promastigotes*	AA1029
Seed France	Antiparasitic Activity	MEOH Ext	In vitro	Not stated	Active	*E. histolytica* *N. brasiliensis* *M. dessetae* *A. salina*	M28527
Leaf Puerto Rico	Antimalarial Activity	ETOH(95%) Ext	RBC	IC50=20.0 mcg/ml	Weak Activity	*Plasmodium falciparum W-2*	K16971
Leaf Puerto Rico	Antimalarial Activity	ETOH(95%) Ext	RBC	IC50 > 63 mcg/ml	Inactive	*Plasmodium falciparum D-6*	K16971
Leaf Togo	Antimalarial Activity	ETOH(95%) Ext	RBC	IC50=39.9 mcg/ml	Active	*Plasmodium falciparum*	M23556
Leaf Borneo	Antimalarial Activity	ETOH(95%) Ext	RBC	20.0 mcg/ml	Active	*Plasmodium falciparum D-6 & W-2. (Results significant at P < 0.01 Level)*	K27823
Leaf Cuba	Antibacterial Activity	H2O Ext	Agar Plate	Not stated	Active	*Escherichia coli* *Pseudomonas aeruginosa* *Shigella flexneri*	K09159
Stembark Papua-New Guinea	Antibacterial Activity	MEOH Ext	Agar Plate	1 mg/disc	Active	*Staphylococcus aureus* *Escherichia coli*	L03211
Stem Cuba	Antibacterial Activity	Acetone Ext	Agar Plate	Not stated	Active	*Escherichia coli* *Salmonella B* *Salmonella newport* *Salmonella typhosa* *Shigella flexneri* *Shigella flexneri 3A*	K09159

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Leaf Cuba	Antibacterial Activity	Acetone Ext	Agar Plate	Not stated	Active	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella B* *Salmonella newport* *Salmonella typhosa* *Serratia marcescens* *Shigella flexneri* *Shigella flexneri 3a* *Staphylococcus albus* *Staphylococcus aureus*	K09159
Stem Cuba	Antibacterial Activity	H2O Ext	Agar Plate	Not stated	Active	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella newport* *Salmonella typhosa* *Salmonella B* *Shigella flexneri*	K09159
Stembark Papua-New Guinea	Antibacterial Activity	ETOH(95%) Ext	Agar Plate	2-3 mcg/plate	Active Active Inactive Inactive	*Bacillus subtilis* *Staphylococcus albus* *Klebsiella pneumoniae* *Pseudomonas aeruginosa*	K15021
Leaf Papua-New Guinea	Antibacterial Activity	ETOAC Ext MEOH Ext	Agar Plate	1.0 mg/disc	Weak Activity	*Staphylococcus aureus*	L03211
Stembark Papua-New Guinea	Antibacterial Activity	ETOAC Ext	Agar Plate	1.0 mg/disc	Weak Activity	*Escherichia coli* *Staphylococcus aureus*	L03211
Leaf Cuba	Antibacterial Activity	Acetone Ext	Agar Plate	Not stated	Inactive	*Sarcina lutea*	K09159
Leaf Papua-New Guinea	Antibacterial Activity	ETOAC Ext	Agar Plate	1.0 mg/disc	Inactive	*Escherichia coli*	L03211
Leaf Cuba	Antibacterial Activity	ETOH(95%) Ext	Agar Plate	Not stated	Inactive	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella B* *Salmonella newport* *Salmonella typhosa* *Sarcina lutea* *Serratia marcescens* *Shigella flexneri* *Shigella flexneri 3a* *Staphylococcus albus* *Staphylococcus aureus*	K09159

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Leaf Trinidad	Antibacterial Activity	ETOAC Ext	Agar Plate	1000 mcg/ml	Inactive	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella typhimurium* *Staphylococcus aureus* *Staphylococcus epidermidis* *Streptococcus faecalis*	L13922
Stem Cuba	Antibacterial Activity	Acetone Ext	Agar Plate	Not stated	Inactive	*Pseudomonas aeruginosa* *Sarcina lutea* *Serratia marcescens* *Staphylococcus albus* *Staphylococcus aureus*	K09159
Leaf Cuba	Antibacterial Activity	H2O Ext	Agar Plate	Not stated	Inactive	*Salmonella B* *Salmonella newport* *Salmonella typhosa* *Sarcina lutea* *Serratia marcescens* *Shigella flexneri 3a* *Staphylococcus albus* *Staphylococcus aureus*	K09159
Leaf Trinidad	Antibacterial Activity	Pet Ether Ext	Agar Plate	1000 mcg/ml	Equiv. Equiv. Inactive Inactive Inactive	*Staphylococcus aureus* *Streptococcus faecalis* *Escherichia coli* *Salmonella typhimurium* *Staphylococcus epidermidis*	L13922
Stem Cuba	Antibacterial Activity	H2O Ext	Agar Plate	Not stated	Inactive	*Sarcina lutea* *Serratia marcescens* *Shigella flexneri 3A* *Staphylococcus albus* *Staphylococcus aureus*	K09159

Plant Part / Origin	Activity Tested For	Type Extract	Test Model	Dosage	Results	Notes / Organism Tested	Ref #
Stem Cuba	Antibacterial Activity	ETOH(95%) Ext	Agar Plate	Not stated	Inactive	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella B* *Salmonella newport* *Salmonella typhosa* *Sarcina lutea* *Serratia marcescens* *Shigella flexneri* *Staphylococcus albus* *Staphylococcus aureus*	K09159
Leaf Puerto Rico	Antimycobacterial Activity	ETOH(95%) Ext	Agar Plate	Not stated	Inactive	*Mycobacterium tuberculosis*	L12432
Stem Brazil	Molluscicidal Activity	ETOH(100%) Ext	Not stated	100.0 ppm	Inactive	*Biomphalaria glabrata*	L15585
Dried Stembark Brazil	Molluscicidal Activity	ETOH(100%) Ext	Adult snail Egg masses	LD50 = 0.97 ppm LD50 = 1.0 ppm	Active	*Biomphalaria glabrata* *Biomphalaria glabrata*	L15585
Leaf Brazil	Molluscicidal Activity	ETOH(100%) Ext	Adult Snail Egg Masses	LD50 = 1.59 ppm LD50 = 20.26 ppm	Active	*Biomphalaria glabrata*	L15585
Leaf Brazil	Molluscicidal Activity	Not stated	Adult Snail Egg Masses	LD90 < 20 ppm LD90 < 20 ppm	Active	*Biomphalaria glabrata*	AA1028
Brazil	Molluscicidal Activity	Not stated	Adult Snail Egg Masses	LD50 = 11.86 ppm LD50 = 49.62 ppm	Active	*Biomphalaria glabrata*	AA1012
Leaf + Stem India	Larvicidal Activity	H2O Ext	Not stated	0.03 gm/ml	Inactive	*Culex quinquefasciatus*	M19731
Leaf Not Stated	Insecticide Activity	ETOH(95%) Ext	Not stated	5.0%	Weak Activity	*Macrosiphoniella sanborni*	W00220
Spain	Insecticide Activity	Fraction: Squamocin	Agar plate	Not stated	Active	*L. decemlineata* *M. persicae*	AA1018
USA	Insecticide Activity	Fraction: Acetogenins	In vitro	Not stated	Active	*Blattella germanica* (L.)	AA1019
Spain	Antifeedant Activity	Fraction: Annonacin	Agar plate	Not stated	Active	*L. decemlineata*	AA1018
Root bark Taiwan	Dopaminergic modulation	Alkaloid Ext	Cell culture	18 mcg/ml	Equiv.	Dopaminergic nerve cells and GABAergic nerve cells.	AA1010

Presence of Compounds in Graviola (Annona muricata)

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Annocatalin	Misc Lactone	Leaf	Taiwan	Not stated	AA1009
Annohexocin	Misc Lactone	Leaf	Not stated	Not stated	H17799
Annomonicin	Misc Lactone	Seed	Guyana	00.00566%	H07609
Annomontacin	Misc Lactone	Seed	Guyana	00.00603%	H07609
Annomontacin, cis	Misc Lactone	Seed	Taiwan	Not stated	AA1009
Annomuricatin B	Misc Lactone	Seed	China	00.00906%	H21843
Annomuricin A	Misc Lactone Misc Lactone	Leaf Pericarp	Indonesia Colombia	00.0004% 00.0021%	H16272 L07801
Annomuricin B	Misc Lactone	Leaf	Indonesia	00.00035%	H16272
Annomuricin C	Misc Lactone	Leaf	Indonesia	00.0004%	H16273
Annomuricin E	Misc Lactone	Leaf	Indonesia	00.000235	H24563
Annomuricin-D-one, cis:	Misc Lactone	Leaf	Indonesia	00.0003%	H19306
Annomuricin-D-one, trans	Misc Lactone	Leaf	Indonesia	00.0003%	H19306
Annomutacin	Misc Lactone	Leaf	Indonesia	00.00035%	H17568
Annonacin	Misc Lactone	Pericarp Seed Seed Seed Root Leaf	Colombia Brazil USA Guyana Guinea Indonesia	00.0032% 01.0% 00.06818% 00.02674% Not stated 00.05411%	L07801 K20560 K10338 H07236 H19768 H16272
Annonacin A	Misc Lactone	Pericarp Leaf Seed Seed	Colombia Indonesia China China	00.0021% Not stated 00.00142% 00.00521%	L07801 H16274 H22999 H22999

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Annonacin B Mesitoate	Misc Lactone	Not stated	China	Not stated	H20484
Annonacin, cis:	Misc Lactone	Seed	Dominican Republic	00.00109%	H18307
Annonacin, iso:	Misc Lactone	Seed	USA	00.00277%	K10338
Annonacin, iso: 2-4-cis:	Misc Lactone	Leaf	Indonesia	Not stated	H16274
Annonacin, iso: 2-4-trans:	Misc Lactone	Leaf Seed	Indonesia China	Not stated Not stated	H16274 AA1011
Annonacin, iso: 10-one, 2,4-trans	Misc Lactone	Seed	China	Not stated	AA1011
Annonacin-10-one	Misc Lactone	Seed	USA	00.00136%	K10338
Annonacin-10-one, cis:	Misc Lactone	Seed	Dominican Republic	00.000909%	H18307
Annonacin-10-one, iso:	Misc Lactone	Seed	USA	00.00113%	K10338
Annonacin-10-one, iso: neo:	Misc Lactone	Seed	China	Not stated	H15501
Annonacin-A-one, cis-2-4: 10(r):	Misc Lactone	Leaf	Indonesia	00.00017%	H17568
Annonacin-A-one, trans-2-4: 10(r):	Misc Lactone	Leaf	Indonesia	00.00017%	H17568
Annonacinone	Misc Lactone	Seed Seed Seed Seed	Guyana Guyana Brazil Guyana	00.01811% 00.2% 01.07% 00.00697%	H07609 H07609 K20560 H07236
Annonaine	Isoquinoline Alkaloid	Fruit	Surinam	Not stated	J14527
Annopentocin A	Misc Lactone	Leaf	Indonesia (cult)	00.0004%	H19306
Annopentocin B	Misc Lactone	Leaf	Indonesia (cult)	00.0005%	H19306
Annopentocin C	Misc Lactone	Leaf	Indonesia (cult)	00.00035%	H19306
Anomuricine	Isoquinoline Alkaloid	Root Bark Leaf	Guyana Guyana Guyana	Not stated Not stated Not stated	T02076 T04073 T04073

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Anomurine	Isoquinoline Alkaloid	Root Bark Leaf	Guyana Guyana Guyana	Not stated Not stated Not stated	T02076 T04073 T04073
Anonaine	Isoquinoline Alkaloid	Fruit	Surinam	Not stated	J10986
Anonol	Alkanol C5 or More	Leaf Leaf	Dominican Republic West Indies	Not stated Not stated	A04099 W02289
Asimilobine	Isoquinoline Alkaloid	Fruit	Surinam	Not stated	J10986
Atherospermine	Isoquinoline Alkaloid	Stembark	Philippines	Not stated	A04095
Atherosperminine	Isoquinoline Alkaloid	Root Bark	Bark Bark	Not stated Not stated	T02076 T04073
Coclaurine,(+):	Isoquinoline Alkaloid	Root Bark Leaf	Guyana Guyana Guyana	Not stated Not stated Not stated	T02076 T04073 T04073
Cohibin A	Misc Lactone	Seed Root	Brazil Guinea	Not stated 00.00116%	H26434 H19768
Cohibin B	Misc Lactone	Seed Root	Brazil Guinea	Not stated Not stated	H26434 H19768
Cohibin C	Misc Lactone	Seed	Brazil	Not stated	H26434
Cohibin D	Misc Lactone	Seed	Brazil	Not stated	H26434
Corepoxylone	Misc Lactone	Seed	Brazil	00.00062%	H12235
Coreximine, (+):	Isoquinoline Alkaloid	Root	Guyana	Not stated	T02076
Coreximine, (-):	Isoquinoline Alkaloid	Bark Leaf	Guyana Guyana	Not stated Not stated	T04073 T04073
Coronin	Misc Lactone	Root	Guinea	00.0003%	H28460
Corossolin	Misc Lactone	Seed Seed Seed	Guyana Brazil Taiwan	00.00290% 01.01% Not stated	H07236 K20560 H28040

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Corossolone	Misc Lactone	Seed Seed Seed Seed	Guyana Brazil Brazil Taiwan	00.00232% 01.02% 00.00042% Not stated	H07236 K20560 H14312 H28040
Corossolone, cis	Misc Lactone	Leaf	Taiwan	Not stated	AA1009
Donhexocin	Misc Lactone	Seed	China	00.0005%	H22999
Epomuricenin A	Misc Lactone	Seed Root	Brazil Guinea	00.00278% Not stated	H14312 H19768
Epomuricenin B	Misc Lactone	Seed Root	Brazil Guinea	00.00278% Not stated	H14312 H19768
Gentisic Acid	Benzenoid	Leaf	Trinidad	Not stated	A06190
Gigantetrocin	Misc Lactone	Seed	USA	00.00221%	K10338
Gigantetrocin A	Misc Lactone	Seed	Dominican Republic	00.00181%	H12985
Gigantetrocin B	Misc Lactone	Seed	Dominican Republic	00.00136%	H12985
Gigantetrocinone, 2,4-cis	Misc Lactone	Seed	China	Not stated	AA1011
Gigantetrocinone, 2,4-trans	Misc Lactone	Seed	China	Not stated	AA1011
Gigantetronenin	Misc Lactone	Leaf	Indonesia	Not stated	H16273
Goniothalamicin	Misc Lactone	Seed Seed Leaf Seed Seed	Guyana USA Indonesia Dominican Republic Brazil	00.01660% 00.00059% Not stated 00.00568% Not stated	H07609 K10338 H16272 H18307 K20560
Goniothalamicin, cis:	Misc Lactone	Seed	Dominican Republic	00.00127%	H18307
Javoricin	Misc Lactone	Seed	Dominican Republic	00.00072%	H18307
KCL	Inorganic	Leaf Leaf	West Indies Dominican Republic	Not stated Not stated	W02289 A04099

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Lignoceric Acid	Lipid	Leaf	Dominican Republic	Not stated	A04099
Linoleic Acid	Lipid	Leaf Leaf	West Indies Dominican Republic	Not stated Not stated	W02289 A04099
Longifolicin	Not stated	Seed	China	Not stated	AA1017
Montanacin	Misc Lactone	Seed	Guyana	00.02490%	H07609
Montecristin	Misc Lactone	Root	Guinea	00.00233%	H19211
Muracin A	Misc Lactone	Seed	Taiwan	Not stated	H28040
Muracin B	Misc Lactone	Seed	Taiwan	Not stated	H28040
Muracin C	Misc Lactone	Seed	Taiwan	Not stated	H28040
Muracin D	Misc Lactone	Seed	Taiwan	Not stated	H28040
Muracin E	Misc Lactone	Seed	Taiwan	Not stated	H28040
Muracin F	Misc Lactone	Seed	Taiwan	Not stated	H28040
Muracin G	Misc Lactone	Seed	Taiwan	Not stated	H28040
Muricapentocin	Misc Lactone	Leaf	Indonesia	00.00028%	H24563
Muricatalicin	Misc Lactone	Leaf	China	Not stated	AA1027
Muricatalin	Misc Lactone	Leaf	China	Not stated	AA1027
Muricatenol	Misc Lactone	Seed	China	Not stated	AA1011
Muricatetrocin A	Misc Lactone	Seed Leaf Seed	Dominican Republic Indonesia Taiwan	00.00045% Not stated Not stated	H12985 H16272 H28040
Muricatetrocin B	Misc Lactone	Seed Leaf Seed	Dominican Republic Indonesia Taiwan	00.00045% Not stated Not stated	H12985 H16272 H28040
Muricatin D	Misc Lactone	Seed	China	00.00085%	H21114
Muricatocin A	Misc Lactone	Leaf	Indonesia	00.00045%	H16274

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Muricatocin B	Misc Lactone	Leaf	Indonesia	00.0004%	H16274
Muricatocin C	Misc Lactone	Leaf	Indonesia	Not stated	H16273
Muricin H	Misc Lactone	Seed	Taiwan	Not stated	AA1009
Muricin I	Misc Lactone	Seed	Taiwan	Not stated	AA1009
Muricine	Alkaloid-misc	Bark	Not stated	Not stated	A04104 A05062
Muricinine	Alkaloid-misc	Bark	Not stated	Not stated	A04104 A05062
Muricoreacin	Misc Lactone	Leaf	Indonesia	00.00038%	H22688
Murihexocin 3	Misc Lactone	Leaf	USA	Not stated	H17719
Murihexocin A	Misc Lactone	Leaf	USA	Not stated	H17719
Murihexocin C	Misc Lactone	Leaf	Indonesia	00.00015%	H22688
Murihexol	Misc Lactone	Seed	China	00.00035%	H22999
Murin A, epoxy:	Misc Lactone	Stembark	India	Not stated	H12242
Murisolin	Misc Lactone	Seed Seed Seed Seed	French Guiana China Brazil Guyana	00.00930% 00.00311% 00.00060% 00.0093%	H06211 H21114 H14312 H07236
N-fatty acyl tryptamines	Lipid	Seed	China	Not stated	AA1011
Oleic Acid	Lipid	Leaf Leaf	Dominican Republic West Indies	Not stated Not stated	A04099 W02289
Otivarin	Not stated	Not stated	Italy	Not stated	AA1022
Panatellin, cis	Misc Lactone	Root	Guinea	00.00216%	H21880
Reticulatacin, cis:	Misc Lactone	Root	Guinea	00.00083%	H21880
Reticuline	Isoquinoline Alkaloid	Stembark	Philippines	Not stated	A04095

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Reticuline, (+)	Isoquinoline Alkaloid	Root Bark Leaf	Guyana Guyana Guyana	Not stated Not stated Not stated	T02076 T04073 T04073
Robustocin	Misc Lactone	Seed	Brazil	00.00043%	H26304
Rolin B, epoxy:	Misc Lactone	Seed	China	00.00285%	H21114
Rolliniastatin 1	Misc Lactone	Seed	Brazil	Not stated	K20560
Rolliniastatin 2	Misc Lactone	Seed	Brazil	Not stated	K20560
Sabadelin	Misc Lactone	Seed	Guinea	00.00116%	H25221
Solamin	Misc Lactone	Seed Stembark Seed Root Seed	Brazil India Brazil Guinea French Guiana	00.00036% Not stated Not stated 00.00005% 00.00116%	H14312 H12242 K20560 K20560 H07234
Solamin, cis:	Misc Lactone	Root	Guinea	00.00216%	H21880
Tyramine, n-para-coumaroyl:	Isoquinoline Alkaloid	Leaf	Indonesia	Not stated	H17568
Uvariamicin I, cis:	Misc Lactone	Root	Guinea	00.00083%	H21880
Uvariamicin IV, cis	Misc Lactone	Root	Guinea	00.0005%	H21880
Xylomaticin	Misc Lactone	Seed	Taiwan	Not stated	AA1009

OTHER PHYTOCHEMICAL SCREENING:

Alkaloids Absent	Leaf + Stem	T05306
Alkaloids Present	Bark + Leaf + Seed	L16047
	Leaf	A04099
	Entire Plant	T06830
Hydrocyanic Acid Absent	Entire Plant	T06830
Leucoanthocyanins Present	Entire Plant	T06830
Quinones Absent	Entire Plant	T06830
Saponins Absent	Entire Plant	T06830

Literature Cited - Graviola (Annona muricata)

Please purchase the Graviola Technical Data Report to obtain these cited references. (Pages 26-38)

AA1008	
AA1009	
AA1010	
AA1011	
AA1012	
AA1013	
AA1014	
AA1015	
AA1017	
AA1018	
AA1019	
AA1020	
AA1021	

Clinical Abstrasts

J Nat Prod 2002 Apr;65(4):470-5
New cytotoxic monotetrahydrofuran annonaceous acetogenins from Annona muricata.
Liaw, C. C., et al.
Three new monotetrahydrofuran annonaceous acetogenins, muricin H (1), muricin I (2), and cis-annomontacin (3), along with five known acetogenins, annonacin, annonacinone, annomontacin, murisolin, and xylomaticin, were isolated from the seeds of Annona muricata. Additionally, two new monotetrahydrofuran annonaceous acetogenins, cis-corossolone (4) and annocatalin (5), together with four known ones, annonacin, annonacinone, solamin, and corossolone, were isolated from the leaves of this species. The structures of all new isolates were elucidated and characterized by spectral and chemical methods. These new acetogenins exhibited significant activity in in vitro cytotoxic assays against two human hepatoma cell lines, Hep G(2) and 2,2,15. Compound 5 showed a high selectivity toward the Hep 2,2,15 cell line.

J Nat Prod 2001 Jul;64(7):925-31
Novel cytotoxic annonaceous acetogenins from Annona muricata.
Chang, F. R., et al.
Seven new annonaceous acetogenins, muricins A-G (1-7), as well as five known compounds, a mixture of muricatetrocin A (8) and muricatetrocin B (9), longifolicin (10), corossolin (11), and corossolone (12), were isolated from the seeds of Annona muricata. The structures of all isolates were elucidated and characterized by spectral and chemical methods. These acetogenins showed significantly selective in vitro cytotoxicities toward the human hepatoma cell lines Hep G(2) and 2,2,15.

J Asian Nat Prod Res 2001;3(4):267-76
Annonaceous acetogenins of the seeds from Annona muricata.
Li, D. Y., et al.
Muricatenol (1) is a new C37 non-THF ring acetogenin with four hydroxyls and one isolated double bond in the long aliphatic chain. 2,4-cis-Gigantetrocinone (2) and 2,4-trans-gigantetrocinone (3) have been isolated as their acetates by preparative TLC. 2,4-trans-Isoannonacin-10-one (4) and 2,4-trans-isoannonacin (5) have been isolated as only 2,4-trans-form for the first time (no cis-form). Also four known acetogenins, gigantetrocin-A (6), gigantetrocin-B (7), annomontacin (8), gigantetronenin (9) and a mixture of N-fatty acyl tryptamines have been isolated (10). Their structures have been established on the basis of spectral analyses. The CHCl3 fraction of the seeds showed strong antitumor activities.

J Med Chem 2000 Dec 14;43(25):4793-800
Semisynthesis of antitumoral acetogenins: SAR of functionalized alkyl-chain bis-tetrahydrofuranic acetogenins, specific inhibitors of mitochondrial complex I.
Gallardo, T., et al.
The acetogenins of Annonaceae are known by their potent cytotoxic activity. In fact, they are promising candidates as a new future generation of antitumoral drugs to fight against the current chemio-therapic resistant tumors. The main target enzyme of these compounds is complex I (NADH:ubiquinone oxidoreductase) of the mitochondrial respiratory chain, a key enzymatic complex of energy metabolism. In an attempt to characterize the relevant structural factor of the acetogenins that determines the inhibitory potency against this enzyme, we have
prepared a series of bis-tetrahydrofuranic acetogenins with different functional groups along the alkyl chain.

Fitoterapia 2000 Apr;71(2):183-6
Cytotoxicity and antileishmanial activity of Annona muricata pericarp.
Jaramillo, M. C., et al.
Hexane, ethyl acetate and methanol extracts of Annona muricata pericarp were tested in vitro against Leishmania braziliensis and L. panamensis promastigotes, and against cell line U-937. The ethyl acetate extract was more active than the other extracts and even of Glucantime used as reference substance. Its fractionation led to the isolation of three acetogenins--annonacin, annonacin A and annomuricin A.

Me Arch Pharm Res 1999 Oct;22(5):524-8

cis-Annonacin and (2,4)-cis-and trans-isoannonacins: cytotoxic monotetrahydrofuran annonaceous acetogenins from the seeds of Annona cherimolia.

Woo, M. H., et al.

Department of Pharmacy, College of Pharmacy, Catholic University of Taegu-Hyosung, Kyongsan, Korea.

cis-Annonacin (1) and the mixture of (2,4)-cis-and trans-isoannonacins (2 and 3), three known mono-tetrahydrofuran annonaceous acetogenins, have been isolated from the seeds of Annona cherimolia by the use of the brine shrimp lethality test (BST) for bioactivity directed fractionation. Their structures were elucidated based on spectroscopic and chemical methods. 1 showed potent cytotoxicities in the brine shrimp lethality test (BST) and among six human solid tumor cell lines with notable selectivity for the pancreatic cell line (PaCa-2) at about 1,000 times the potency of adriamycin. The mixture of 2 and 3 is over 10,000 times cytotoxic as adriamycin in the pancreatic cell line (PaCa-2). All of the compounds are about 10 to 100 times as cytotoxic as adriamycin in the prostate cell line (PC-3).

Inst Oswaldo Cruz 1999 Jul-Aug;94(4):531-5

Antitumor and antiviral activity of Colombian medicinal plant extracts.

Betancur-Galvis, L., et al

Extracts of nine species of plants traditionally used in Colombia for the treatment of a variety of diseases were tested in vitro for their potential antitumor (cytotoxicity) and antiherpetic activity. MTT (Tetrazolium blue) and Neutral Red colorimetric assays were used to evaluate the re-duction of viability of cell cultures in presence and absence of the extracts. MTT was also used to evaluate the effects of the extracts on the lytic activity of herpes simplex virus type 2 (HSV-2). The 50% cytotoxic concentration (CC50) and the 50% inhibitory concentration of the viral effect (EC50) for each extract were calculated by linear re-gression analysis. Extracts from Annona muricata, A. cherimolia and Rollinia membranacea, known for their cytotoxicity were used as pos-itive controls. Likewise, acyclovir and heparin were used as positive controls of antiherpetic activity. Methanolic extract from Annona sp. on Hep-2 cells presented a CC50 value at 72 hr of 49.6x10(3)mg/ml. Neither of the other extracts examined showed a significant cytotoxicity. The aqueous extract from Beta vulgaris, the ethanol extract from Callisia grasilis and the methanol extract Annona sp. showed some antiherpetic activity with acceptable therapeutic indexes (the ratio of CC50 to EC50). These species are good candidates for further activity-monitored fractionation to identify active principles.

Chem Biol Interact 1999 Nov 1;122(3):171-83

Specific interactions of monotetrahydrofuranic Annonaceous acetogenins as inhibitors of mitochondrial complex I.

Tormo, J. R., et al.

Annonaceous acetogenins (ACG) are a wide group of cytotoxic compounds isolated from plants of the Annonaceae family. Some of them are promising candidates to be a future new generation of antitumor drugs due to the ability to inhibit the NADH:ubiquinone oxidoreductase of the respiratory chain (mitochondrial complex I), main gate of the energy production in the cell. ACG are currently being tested on standard antitumor trials although little is known about the structure activity relationship at the molecular level. On recent studies, the relevance of several parts of the molecule for the inhibitory potency has been evaluated.

Phytochemistry 1998 Sep;49(2):565-71

Muricoreacin and murihexocin C, mono-tetrahydrofuran aceto-genins, from the leaves of Annona muricata.

Kim, G. S., et al.

Bioactivity-directed fractionation of the leaves of Annona muricata L.(Annonaceae) resulted in the isolation of two new Annonaceous acetogenins, muricoreacin (1) and murihexocin C (2). Compounds 1 and 2 showed significant cytotoxicities among six human tumor cell lines with selectivities to the prostate adenocarinoma (PC-3) and pancreatic carcinoma (PACA-2) cell lines.

J Nat Prod 1999 Mar;62(3):504-40
Annonaceous acetogenins: recent progress.
Alali, F. Q., et al.
The Annonaceous acetogenins are promising new antitumor and pesticidal agents that are found only in the plant family Annonaceae. Chemically, they are derivatives of long-chain fatty acids. Biologically, they exhibit their potent bioactivities through depletion of ATP levels via inhibiting complex I of mitochondria and inhibiting the NADH oxidase of plasma membranes of tumor cells. Thus, they thwart ATP-driven resistance mechanisms. This review presents the progress made in the chemistry, biology, and development of these compounds since December 1995.

J Nat Prod 1998 Apr;61(4):432-6
Two new mono-tetrahydrofuran ring acetogenins, annomuricin E and muricapentocin, from the leaves of Annona muricata.
Kim, G.S., et al.
Bioactivity-directed fractionation of the leaf extract of Annona muricata L. (Annonaceae) has resulted in the isolation of two new Annonaceous acetogenins, annomuricine (1) and muricapentocin (2). Compounds 1 and 2 are monotetrahydrofuran ring acetogenins bearing two flanking hydroxyl groups; however, each has three additional hydroxyl groups. Compound 1 has an erythro 1,2-diol, and 2 has a 1,5,9-triol moiety. Both 1 and 2 showed significant cytotoxicities against six types of human tumors, with selectivities to the pancreatic carcinoma (PACA-2) and colon adenocarcinoma (HT-29) cell lines.

Ethnopharmacol 1998 May;61(1):81-3
Effect of the extract of Annona muricata and Petunia nyctaginiflora on Herpes simplex virus.
Padma, P., et al.
Annona muricata (Annonaceae) and Petunia nyctaginiflora (Solana-ceae) were screened for their activity against Herpes simplex virus-1 (HSV-1) and clinical isolate (obtained from the human keratitis lesion). We have looked at the ability of extract(s) to inhibit the cytopathic effect of HSV-1 on vero cells as indicative of anti-HSV-1 potential. The minimum inhibitory concentration of ethanolic extract of A. muricata and aqueous extract of P. nyctaginiflora was found to be 1 mg/ml.

J Med Chem 1997 Jun 20;40(13):2102-6
Structure-activity relationships of diverse Annonaceous acetogenins against multidrug resistant human mammary adenocarcinoma (MCF-7/Adr) cells.
Oberlies, N.H., et al.
Fourteen structurally diverse Annonaceous acetogenins, representing the three main classes of bis-adjacent, bis-nonadjacent, and single-THF ring(s), were tested for their ability to inhibit the growth of adriamycin resistant human mammary adenocarcinoma (MCF-7/Adr) cells. This cell line is resistant to treatment with adriamycin, vincristine, and vinblastine and is, thus, multidrug resistant (MDR). Among a series of bis-adjacent THF ring acetogenins, those with the stereochemistry of threo-trans-threo-trans-erythro (from C-15 to C-24) were the most potent with as much as 250 times the potency of adriamycin. A spacing of 13 carbons between the flanking hydroxyl of the THF ring system and the gamma-unsaturated lactone seems to be optimum with a spacing of 11 and 9 carbons being significantly less active. Several single-THF ring compounds were also quite potent with gigantetrocin A (11) being the most potent compound tested. The acetogenins may, thus, have chemotherapeutic potential, especially with regard to MDR tumors.

J Nat Prod 1996 Feb;59(2):100-8
Five novel mono-tetrahydrofuran ring acetogenins from the seeds of Annona muricata.
Rieser, M. J., et al.
Bioactivity-directed fractionation of the seeds of Annona muricata L.
(Annonaceae) resulted in the isolation of five new compounds: cis-annonacin (1), cis-annonacin-10-one (2), cis-goniothalamicin (3), arianacin (4), and javoricin (5). Three of these (1-3) are among the first cis mono-tetrahydrofuran ring acetogenins to be reported. NMR analyses of published model synthetic compounds, prepared cyclized formal acetals, and prepared Mosher ester derivatives permitted the determinations of absolute stereochemistries. Bioassays of the pure compounds, in the brine shrimp test, for the inhibition of crown gall tumors, and in a panel of human solid tumor cell lines for cytotoxicity,

evaluated relative potencies. Compound 1 was selectively cytotoxic to colon adenocarcinoma cells (HT-29) in which it was 10,000 times the potency of adriamycin.

J Nat Prod 1996 Nov;59(11):1035-42

Five new monotetrahydrofuran ring acetogenins from the leaves of Annona muricata.

Zeng, L., et al.

Bioactivity-directed fractionation of the leaves of Annona muricata resulted in the isolation of annopentocins A (1), B (2), and C(3), and cis- and trans-annomuricin-D-ones (4, 5). Compounds 1-3 are the first acetogenins reported bearing a mono-tetrahydrofuran (THF) ring with one flanking hydroxyl, on the hydrocarbon side, and another hydroxyl, on the lactone side, that is one carbon away from the THF ring. Compounds 4 and 5 were obtained in a mixture and are new mono-THF ring acetogenins bearing two flanking hydroxyls and an erythro-diol located between the THF and the ketolactone rings. Compound 1 was selectively cytotoxic to pancreatic carcinoma cells (PACA-2), and 2 and 3 were selectively cytotoxic to lung carcinoma cells (A-549); the mixture of 4 and 5 was selectively cytotoxic for the lung (A-549), colon (HT-29), and pancreatic (PACA-2) cell lines with potencies equal to or exceeding those of Adriamycin.

J Nat Prod 1995 Sep;58(9):1430-7

Additional bioactive acetogenins, annomutacin and (2,4-trans and cis)-10R-annonacin-A-ones, from the leaves of Annona muricata.

Wu, F. E., et al.

In a continuation of our research on bioactive components from the leaves of Annona muricata, three novel monotetrahydrofuran Annonaceous acetogenins, namely, annomutacin [1], (2,4-trans)- 10R-annonacin-A-one [2], and (2,4-cis)-10R-annonacin-A-one [3], have been identified. Their structures were deduced by ms, nmr, ir, and uv spectral and chemical methods, and the absolute configurations were determined by Mosher ester methodology. A known bioactive amide,
N-p-coumaroyl tyramine, was also found. Compound 1 and the mixture of compounds 2 and 3 showed selective cytotoxicities against the human A-549 lung tumor cell line.

Cancer Lett 1995 Sep 4;96(1):55-62

Tumor cell growth inhibition by several Annonaceous acetogenins in an in vitro disk diffusion assay.

Oberlies, N. H., et al.

The cell inhibition activities of several Annonaceous acetogenins, covering the three major structural classes of bis-adjacent, bis-non-adjacent, and single tetrahydrofuran (THF) ring compounds and their respective ketolactone rearrangement products, were tested in an in vitro disk diffusion assay against three murine (P388, PO3, and M17/Adr) and two human (H8 and H125) cancerous cell lines as well as a non-cancerous immortalized rat GI epithelial cell line (I18). The results demonstrate a dose-dependent inhibition of cancerous cell growth, while non-cancerous cell growth is not inhibited by the same dosages. All of the acetogenins, irrespective of their various structural types, inhibit the growth of adriamycin resistant tumor cells and non-resistant tumor cells at the same levels of potency. These results show that the Annon-aceous acetogenins are an extremely potent class of compounds, and their inhibition of cell growth can be selective for cancerous cells and also effective for drug resistant cancer cells, while exhibiting only minimal toxicity to 'normal' non-cancerous cells.

J Nat Prod 1995 Jun;58(6):909-15

New bioactive monotetrahydrofuran Annonaceous acetogenins, annomuricin C and muricatocin C, from the leaves of Annona muricata.

Wu, F. E., et al.

The leaves of Annona muricata have yielded two additional monotetrahydrofuran Annonaceous acetogenins, annomuricin C [1] and muricatocin C [2]. Compounds 1 and 2 each possess five hydroxyl groups; two hydroxyl groups are at the C-10/C-11 and C-10/C-12 positions in 1 and 2, respectively. The absolute configurations of 1 and 2, except for positions C-10 and C-11 or C-12, were determined by Mosher ester methodology. The C-10/C-11 and C-10/C-12 acetonides
(1c, 2c) suggested relative stereochemistry and significantly enhanced the cytotoxicities against the A-549 human lung and the MCF-7 human beast solid tumor cell lines. One known monotetrahydrofuran acetogenin, gigantetronenin, not described previously from this plant, was also found.

J Nat Prod 1995 Jun;58(6):902-8

Muricatocins A and B, two new bioactive monotetrahydrofuran Annonaceous acetogenins from the leaves of Annona muricata.

Wu, F. E., et. al.

The leaves of Annona muricata have yielded the novel monotetra-hydrofuran Annonaceous acetogenins, muricatocins A [1] and B [2]. Each compound possesses five hydroxyl groups, with two hydroxyl groups at the C-10 and C-12 positions. The absolute configurations of 1 and 2 (except for positions C-10 and C-12) were determined by Mosher ester methodology. The C-10, C-12 acetonides (1c, 2c) suggested relative stereochemistry and significantly enhanced cytotoxicity against the A-549 human lung tumor cell line. Three known monotetra-hydrofuran acetogenins, annonacin A, (2,4-trans)-isoannonacin, and (2,4-cis)-isoannonacin, were also found.

Chem Biol Interact 1995 Oct 20;98(1):1-13

Determination of structure-activity relationships of Annonaceous acetogenins by inhibition of oxygen uptake in rat liver mitochondria.

Landolt, J.L., et al.

A new group of natural compounds, the Annonaceous acetogenins, have recently been determined to inhibit ATP production at a similar site of action and higher levels of potency as rotenone, i.e., at NADH- ubiquinone oxido-reductase, complex I of the mitochondrial electron-transport chain. The acetogenins had earlier been determined to be pesticidal, antimalarial, antimicrobial, anti-parasitic, cytotoxic, and in vivo active as potentially new antitumor agents. In order to determine structural activity relationships (SARs) among these compounds, at the subcellular level, several available acetogenins have been tested. Data obtained, from the inhibition of oxygen consumption by rat liver mitochondria, demonstrated that all of the twenty acetogenins tested are active with IC50 values in the range of 15-800 nM/mg protein. The IC50 value of rotenone was 17 nM/mg protein.

J Nat Prod 1991 Jul-Aug;54(4):967-71

[Annomonysvin: a new cytotoxic gamma-lactone- monotetrahydrofuranyl acetogenin from Annona montana]

Jossang, A., et al.

The structure of annomontacin [I], a novel monotetrayhydrofuran fatty acid gamma-lactone (acetogenin) isolated from the seeds of Amnona montana, was determined by spectral analysis. The cytotoxicities in vitro of annomontacin [I], annonacinone [2], and annonacin were measured against murine leukemia L1210, human breast adenocarcinoma MDA-MB231, and human breast carcinoma MCF7 cell lines and compared with adriamycin.

J Nat Prod 1990 Mar-Apr;53(2):237-78

Annonaceous acetogenins: a review.

Rupprecht, J. K., et al.

The Annonaceous acetogenins are a series of apparently polyketide- derived fatty acid derivatives that possess tetrahydrofuran rings and a methylated gamma-lactone (sometimes rearranged to a methyl ketolactone) with various hydroxyl, acetoxyl, and/or ketoxyl groups along the hydrocarbon chain. They exhibit a broad range of potent biological activities (cytotoxicity, antitumor, antimalarial, antimicrobial, immunosuppressant, antifeedant, and pesticidal). The sources, isolation, chemistry, biogenesis, and biological actions of these compounds, published to date, are tabulated and discussed. Strategies for structural elucidation are reviewed, and structural revisions and refinements are suggested for some of the previously published compounds.