Guanábana (Graviola)

Family: Annonaceae (Custard apple family)

Genus: Annona **Specie**: muricata L.

Common names: graviola, soursop, brazilian papaya, guanábana, guanábano, guanavana, guanaba, spiny corossol , huanaba, togebanreisi, durian benggala, nangka blanda

Part(s) used: Leaves (Folium annonae)

Description:

Graviola is a small, upright evergreen tree growing up to 5 - 6 m of height, with big, lustrous and smooth, dark green leaves. It gives big, heart-shaped, edible fruits, of 15 - 20 cm in diameter, of yellow-green colour with white flesh. Graviola is domestic in the hottest tropical regions of North and South America, including Amazonia. Its fruit is sold on local markets in the tropics where it is called guanabana in Spanish speaking countries and graviola in Brazil. Its flesh is excellent for production of drinks and sherbets and despite its slightly sour taste it can be eaten raw. All parts of the graviola tree are used in tropical native medicine - bark, leaves, roots, fruits and even seeds. To different parts of the tree different properties and potentials of use are attributed. Generally the fruit and its juice are used against earthworms and parasites, to reduce fever, to increase production of breast milk post partum and as an astringent for diarrhoea and dysentery. Crushed seeds are used against internal and external parasites as lice, etc. Bark, leaves and roots act as sedative, antispasmodic, hypotensive and nervous tranquillizer. The tea assists with diverse disorders caused by these phenomena.
The history of graviola use in herbal medicine is long and reach far into past. In Peruvian Andes the tea of leaves is used for catarrh (inflammation of the mucous membrane) and ground seeds are used against parasites. In Peruvian Amazonia the bark, roots and leaves are used for diabetes and as sedative and antispasmodic. Native tribes in Guiana drink tea of leaves and/or of bark as sedative and cardio tonic. In Brazilian Amazonia the tea of leaves is used for hepatic problems. The oil of leaves and the

unripe fruits are mixed with olive oil and used externally for neuralgia, rheumatism and arthritic pains. In Jamaica, Haiti and in the western India and around the fruits and/or juice of the fruits are used for fevers, parasites, diarrhoea and as lactagogue; the bark or the leaves then as spasmolytic, sedative and nervous tranquillizer, for heart rhythm moderation, against cough, influenza, difficult childbirth, asthma, asthenia, hypertension and parasites.
From the forties, when the research of graviola properties started, a lot of active substances and chemical compounds had been discovered in it. The research mainly concentrates on a new group of chemical substances which are called annonacenic acetogenines. Graviola produces these natural compounds in the leaves and the footstalk, the bark and the seeds. Three independent research teams confirmed in their eight clinical studies that these substances have considerable anti-oncogenous properties and selective toxicity against different types of cancerous cells (without harming sound cells). Many of acetogenines demonstrated selective toxicity against cancerous cells even at very small dosages - as small as one fraction to one million. In 1998 four studies, further specifying chemical components and acetogenines with the strongest anti-cancerous, anti-oncogenous and antivirus properties, were published. According to a study on animals of 1997, the alkaloids newly discovered in graviola fruits acted anti-depressively.
Annonacenic acetogenines appear only in the Annonaceae family. Anti-oncogenous, anti-parasitic, insecticidal and antimicrobial effects of these chemical compounds in general were documented. Studies on the way they act, carried recently out in three independent laboratories, found out that these acetogenines act as excellent inhibitors of enzymatic processes which only occur in membranes of the cells of the cancerous tumour. That is why they are toxic for cancer cells, but have no effect on sound cells. At Purdue University in West Lafayette, state Indiana, a lot of studies on acetogenines were produced, majority of which were financed by the National Institute for Research of Cancer and/or the National Institute of Health (NIH). In this way Purdue University or its research team had registered at least nine American or international patents to their work on anti-oncogenous and insecticidal properties and use of these acetogenines. In one of their papers called New Progress in the Field of Annonacenic acetogenines they state: We have recently announced that annonacenic acetogenines can selectively inhibit growth of cancerous cells as well as of those which are resistant to adriamycine. As more acetogenines were isolated and additional tests for cytotoxicity were carried out we noticed, though the majority of acetogenines have high effect on cellular lines of several serious tumours, that some of the derivates outside different structural types and positional isomers showed striking selectivity among certain cellular lines; e.g against prostate cancer. Now we finally understand primary effects of acetogenines. They are strong inhibitors of ubichinone (=coenzyme Q 10) of oxidoreductase NADH, which is a fundamental enzyme of a complex I leading to the oxidative phosphorylation in mitochondria. The research showed that it

acts directly on the spot of catalysis of coenzyme Q 10 inside the complex I and microbial glucosodehydrogenase. They also inhibit oxidase NADH connected with coenzyme Q 10, which is typical for plasmatic membranes of cancerous cells.
In 1997 Purdue University published a report with a promising news that several annonacenic acetogenines are … not only effective in struggle against tumours, which proved as resistant to anti-cancerous remedies, but it also seems that they have a special affection to such resistant cells. Chief research pharmacologist in Purdue University subsequently explained the principle of the action. According to his words, cancer cells, which survive chemotherapy, can further develop resistance to originally used remedies, as well as to other, even non-related pharmaceuticals. This phenomenon is called multiple resistance (multi-drug resistance, MDR). One of the main ways cancer cells develop resistance to chemotherapeutical remedies is that they generate intercellular pump, which is able to expel anti-cancerous remedies from the cell even before they can destruct it. It is called a P-glycoprotein pump. In average only 2 % of cancer cells in a given individual are able to develop this pump – however these 2 % can eventually grow and expand in multiple resistant tumours. The researchers from Purdue recorded that acetogenines in preference annihilated these very tumours by blocking the transfer of ATP – primary source of cellular energy – into them. The tumour cell needs energy to grow and reproduce and yet more to drive the pump and to expel the attacking remedies. By inhibition of cellular energy the pump cannot be driven. If the acetogenines block temporarily the supply of ATP into the tumour cell it will not have enough energy for the control of nutritive processes – and will die. Normal cells seldom develop such pump, that is why they do not require so much energy and generally do not behave adversely to inhibitors of ATP. The study further mentions that 14 different tested acetogenines show effective ATP blocking properties (including several found only in graviola). 13 of these 14 acetogenines were more effective against multiple resistant cells of breast cancer than all three standard pharmaceuticals (adriamycine, vincristine, vinblastine), which are used for comparison.
In a pilot biological programme of 1976 carried out in the National Institute for Research of Cancer, the leaves and the footstalk of graviola proved effective toxicity against cancer cells and since then the researchers keep adding pieces of knowlrdge to these discoveries. Specific acetogenines contained in graviola and/or its extracts documented in vitro selectively toxic properties to the following types of tumour cells: pulmonary carcinoma cells, serious mastocarcinoma cells, prostate adenocarcinoma cells, pancreatic carcinoma cells, colon adenocarcinoma cells; hepatic cancer cells, cells of human lymphoma, multiple resistant adenocarcinoma of human breast. In 2003 the researchers in Taiwan announced, that the main acetogenine, annonacine, acted with high toxicity on the cells of ovaryoncus, deciduom, mastocarcinoma, urinary bladder and skin cancer even in small dosages: …annonacine is a promising anti-cancerous remedy and is worthy of further studies on

animals and, hopefully, of clinical tests too.
An interesting study in vitro was published in March 2002 by researchers in Japan who examined many acetogenines found in different botanical species. They inoculated mice by Lewis pulmonary cancer cells. 1/3 got no treatment (control group), 1/3 got chemotherapeutic remedy adriamycine and 1/3 got annonacine (in dosage of 10 mg/kg). After two weeks 5 of 6 mice in the untreated control group were still alive. The size of pulmonary tumour was measured. The group with adriamycine showed tumour reduction by 54,6% - but 50% of the animals died of toxicity (3 of 6). Mice treated with annonacine were all still alive and the tumours were reduced by 57,6% - a little better than by adriamycine - and without toxicity. This led the scientists to the conclusion: „this proves that annonacine is less toxic for mice. Due to its anti-oncogenous activity and toxicity annonacine could be used as a clue to elaboration of potential anti-cancerous agent."
The research of cancer is still continuing on these important plants of genus Annona and on their chemical substances. Many pharmaceutical companies and universities continue in research, testing and patenting and attempting to synthesize these substances with new chemotherapeutics.
On top of it, the researchers reported that the inhibitors of NADH dehydrogenase can stop the infection HIV. This is a well known property of annonacenic acetogenines found in graviola and other plants of the genus Annona, which were included into a pilot programme of the National Institute of Health against AIDS at Purdue University.
Generally it seems that graviola will be next in a row as another well known remedy - Taxol. Since the researchers for the first time discovered the anti-oncogenous effect of the bark of Pacific yew and a taxane contained in it, it took 30 years of further research, before the first, FDA attested Taxol (based on natural taxane from the tree bark), started to sell. With graviola it took almost 10 years before the main anti-oncogenous component, annonacine, was successfully synthesized. These aceto-geninic compounds have a special paraffin nucleus and other unique properties of molecular energy which thwarted former experiments, till one prominent pharmaceutical company resigned during the elaboration process (though it was aware of the anti-oncogenous effects of natural chemical substances). At present the scientists are able to transform this substance and many other active acetogenines in laboratory, further step is to transform the substance sufficiently enough (without its losing any anti-oncogenous effects during the progress) to become a new compound which can be patented and converted into a new patented remedy. (The compounds existing in nature cannot be patented.) Thus is seems that the scientists stand again at bay - always when they transform a substance enough to be able to have it patented, a lot of anti-oncogenous properties disappear. Alike the elaboration of Taxol, the government authorities, as e.g . National Institute for Research of Cancer and National Institute of Health, should take appropriate steps to start the detailed research of cancer treatment on humans with synthesized unpatentable botanical

substances (which will allow all pharmaceutical companies to elaborate pharmaceuticals against cancer and to prioritize the research, as with Taxol). In this way this promising therapy could become available for the cancer patients at proper time.
Meanwhile, however, many patients and healers do not wait and file natural leaves and stem of graviola (over 40 recorded natural acetogenines including annonacine) as a supplementary treatment into their records on cancer. Besides, safe using of graviola has a long history in herbal medicine and the research proves that the anti-oncogenous acetogenines react in a selectively toxic way directly on the cancerous cells and not on the sound ones - and in tiny quantity. While the research confirms a high content of acetogenines in the seeds and roots of graviola, various alkaloid specimens from seeds and roots manifested before in vitro neurotoxic effects. The researchers presume that these alkaloids may be connected with atypical Parkinson disease in the countries, where the seeds are used as a common remedy against parasites. That is why the use of seeds and roots of graviola is not recommended now.
The recommended medical dosage of leaves of graviola is 2 - 3 grams 3 to 4 times a day. The products from graviola (capsules or tinctures) are getting more and more available on the American market. One of the effective mechanisms of graviola is that it deprives cancer cells of energy from ATP; in combination with other supplements and natural products, which increase cellular ATP, the effects of graviola can easily drop. The main supplement, which promotes the ATP growth, is a common antioxidant called Coenzyme Q 10 and on that account it should be avoided when using graviola.
Graviola is certainly a promising natural remedy and one of those, which will again stress the importance of protection and preservation of the ecosystem of rain forests. Perhaps – as enough people believe that a possible medical remedy against cancer really hides in the plant from the rain forest – necessary steps to protect the remains of the rain forests, before they are extinguished, will be taken. A certain researcher, who studies graviola, eloquently summarizes this idea: During the preparation of this up-to-date report out of 37 species over 350 kinds of annonacenic acetogenins were isolated. Our preliminary tests show that about 50% of more than 80 monitored kinds are significantly bio-active and suitable for fractional distillation; we can then expect, that this category of compounds will grow by the geometrical progression in future, but provided that similar experiments find financial support. Because of the decline of the world's virgin forests in tropical regions such work becomes urgent, before the big chemical diversity contained in these endangered species withers away.

Contraindications:

The tests on rats manifested stimulating influence of graviola on uterus,

so it should not be used during pregnancy. The study on rats, into whose stomachs the extract of stem bark (100 mg/kg) had been administered, evidenced growth of the activity of dopamine, norepinephrine and monominoxydase, as well as the inhibition of the secretion of serotonine by the rats subjected to stress. Taking this into account it is reasonable to conclude that the use of the herb can be contra-indicated in combination with inhibitors MAO and some of the usualy prescribed antidepressant drugs. Consult your physician. The alcoholic extracts from the leaves manifested non-toxicity nor adverse effects on mice in the dosage of 100 mg/kg; nevertheless, at the dosage of 300 mg/kg a lessening of exploratory behaviour and weak abdominal constrictions were observed. In case of weariness or sleepiness, adjust the quantity used. Interaction with other pharmaceuticals was not registered; even so graviola can amplify the effect of anti-hypertensives and cardiodepressant or antidepressant drugs and can interfere with MAO-inhibitors.

Side effects:

Tests on animals showed hypotensive, vasodilatal and cardiodepressive influence of graviola. The people using anti-hypertensives should consult their physician and monitor their blood pressure accordingly (as pharmaceuticals they should be adjusted). In one study on pigs emetic properties were manifested. Big dosages can cause nausea or vomiting. In such a case limit the use. Significant antimicrobial properties were documented in vitro. Chronic, long-term use of this herb can lead to the extinction of useful bacteria in alimentary tract. It is recommendable to substitute the diet with probiotic and digestion supporting enzymes, should graviola be used longer than 30 days.

Traditional enthomedicinal uses:

For above mentioned indications a medical dosage of 2 grams 3 times a day in capsules or tablets is recommended. At choice it can be replaced by a standard infusion (1 cup 3 times a day) or by standard tincture 4:1 (2-4 ml 3 times a day). If you want to know the definitions, see website Methods of preparation of traditional herbal remedies.

More information you can look on the site about ordinary preparation of the herbal remedies

Phytoterapeutic properties:

Anticancerous (cytostatic and cytotoxic), antitumorous, cardioactive and hypotensive, antispasmodic and muscle relaxant, antimicrobial and antiprotozoal, antiparasitic, antimalarial, antibacterial, antiviral, molluscicidal, insecticidal, antiulcerous, antioxidant, antihepatotoxic, neurological activities (antidepressant, sedative and tranquilizing)

Phytochemical composition:

Lactones, isoquinolines alkaloids and annonaceous acetogenins : annocatalin, annohexocin, annomonicin, annomontacin, annomuricatin A & B, annomuricin A thru E, annomutacin, annonacin, 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

source:

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