ADVANCED

GRAVIOLA

support your immune system

Product Overview:

In the last couple of decades numerous investigations have substantiated the activities of Graviola extracts, including anticancer, anticonvulsant, anti-arthritic, antiparasitic, antimalarial, hepatoprotective and antidiabetic, analgesic, hypotensive, anti-inflammatory, and immune enhancing effects. Phytochemical studies reveal that annonaceous acetogenins are the major constituents of Graviola. More than 100 annonaceous acetogenins have been isolated from leaves, barks, seeds, roots and fruits of Graviola extracts (A review on a miracle fruits of Annona muricata, Journal of pharmacognsy and phytochemistry).

Graviola traditional uses:

Graviola extracts were used but not limited to according to different countries and cultures for several indications (Table 1). (1),(2)

Table 1: Worldwide Ethnomedical uses of *Annona muricata*

Worldwide Ethnomedical Uses	
Brazil	For abscesses, bronchitis, chest problems, cough, diabetes, diarrhoea,dysentry, edma, fever, intestinal parasites, liver propblems, neuralgia, nervousness, pain, parasites, rhematism,spasm , wolrms
Caribbean	for chills, fever, flu, indigestion, nervousness, palpitation, rash, spasm, skin disease, and as a sedative
Curacao	for childbirth, gallblader problems, nervousness, and as a sedative and tranquilizer
Haiti	for digestive sluggishness, coughs, diarrhoea, fever, flu, heart conditions, lactation aid, lice, nerves, parasites, pain, pellagra, sores, spasms, weakness, wounds, and as a sedative
Jamaica	for asthma, fevers, heart conditions, hypertension, lactation aid, nervousness, parasites, spasms, water retention, weakness, worms, and as a sedative
Malaysia	for boils, coughs, diarrhoea, dermatosis, hypertension, rheumatism, and to reduce bleeding
Mexico	for diarrhoea, dysentery, fever, chest colds, ringworm, scurvy, and to reduce bleeding
Panama	for diarrhoea, dyspepsia, kidney, stomach ulcers, worms
Peru	for diabetes, diarrhoea, dysentery, fever, hypertension, indigestion, inflammation, lice, liver disorders, parasites, spasms, tumours, ulcers (internal), and as a sedative
Trinidad	for blood cleansing, fainting, flu, high blood pressure, insomnia, lactation aid, palpitations, ringworms
U.S.A	for cancer, depression, fungal infections, hypertension, intestinal parasites, tumours
West Indies	for asthma, childbirth, diarrhoea, hypertension, lactation aid, parasites, worms
Elsewhere	for arthritis, asthma, bile insufficiency, childbirth, cancer, diarrhoea, dysentery, fever, heart problems, kidney problems, lactation aid, lice, liver disorders, malaria, pain, ringworm, scurvy, stomach problems, and as a sedative

Lots of uses have been identified and studied for Graviola extracts:

1- Anti-Diabetic and Anti-Hyperlipedimic:

Due to the traditional application of Graviola against diabetes, several studies have investigated this potential in vivo. One of the studies reported that daily intraperitoneal injection of streptozotocin-induced diabetic Wistar rats with the methanol extract of A. Graviola extract (100 mg/kg) for two weeks significantly reduced their blood glucose concentration from 21.64 to 4.22 mmol/L .In addition, the extract at the same dose significantly decreased the serum total cholesterol, low-density lipoprotein, triglyceride and very low-density lipoprotein cholesterol . (1),(2)

2- Hepatoprotective:

Graviola is traditionally employed to treat jaundice in some countries. The hepatoprotective effect was reported for the extract of the leaves against carbon tetrachloride and acetaminophen-induced liver damage. A study conducted pre-treatment with different concentrations of the extract (50, 100, 200, and 400 mg/kg) for 7 days prior to liver damage restored liver function toward normal haemostasis, which was shown by biochemical and histological analyses [120]. Therefore, these findings substantiated the traditional use of Graviola against jaundice and showed the potential hepatoprotective activity. (1),(2)

3- Antioxidant Activity:

Immoderate generation of intracellular reactive oxygen species is a precursor of oxidative stress which subsequently catalyses metabolic deficiency and cellular death through biochemical and physiological lesions. The seeds and leaves of the plant are reported to possess enzymatic antioxidants, including catalase and superoxide dismutase, and non-enzymatic antioxidants, including vitamin C and E. A study showed that the ethanolic extract of the Graviola stem bark caused a reduction in lipid peroxidation induced by cold immobilization stress in the brain and liver of rats, indicating the adaptogenic potential of this plant. The DPPH test showed the antioxidant activity of the Graviola Extract. These findings strongly suggest the potential use of Graviola as a natural source of antioxidants. (1),(2)

Anticancer Characteristics:

It has been previously reported that the Graviola extracts have significant anti-cancer effects in a number of cancer cell lines both in vitro and in vivo. [39] Studies revealed the Graviola extracts as having selective inhibition of breast cancer cells via EGFR downregulation. The epidermal growth factor receptor (EGFR) is an oncogene frequently overexpressed in breast cancer (BC), and its overexpression has been associated with poor prognosis and drug resistance. EGFR is therefore a rational target for BC therapy development. In addition, experiments showed that Graviola fruit extract (GFE) inhibit the growth of BC cells using xenografts mouse model studies. Moreover, GFE selectively inhibited the growth of EGFR-overexpressing human BC (MDA-MB-468) cells but not in non-tumorigenic human breast epithelial cells (MCF-10A). [39] These studies strengthen the evidence that Graviola has selective anti-growth effects between cancer and non-cancer cells. (3)

Another study on breast cancer cells supported that Graviola promotes apoptosis in ER-related pathways. Moreover, Graviola decreased MCF-7 tumor growth while inhibiting ER cyclin D1 and Bcl-2 protein expressions in nude mice. [40] In colon cancer cells, Graviola leaves also has significant effects on cell survival potential via mitochondrial-mediated apoptosis associated with the G1 cell cycle arrest. Graviola induces apoptosis by generating reactive oxygen species ROS and down-regulating the anti-apoptotic Bcl-2 protein, while up regulating pro-apoptotic Bax protein. These processes subsequently lead to attenuation of mitochondrial membrane potential (MMP) and cytochrome c release. Release of cytochrome c activates apotosome and the intrinsic caspase cascade that triggers execution of apoptosis through DNA fragmentation. [41] Graviola has also been reported to have anti-proliferative effects of HL-60 cells via loss of cell viability, loss of MMP, G0/G1 phase cell arrest and Morphological apoptotic changes. These results substantiate and confirm that Graviola does indeed have anti-proliferative and cytostatic activity in HL-60 cells [42].(3)

according to recent study Graviola extracts and their constituents identified as promising sources for new chemo preventive and therapeutic agent(s) to be further developed for the control of Non melanoma skin cancer.(Graviola (Annona muricata) Exerts Anti-Proliferative, Anti-Clonogenic and Pro-Apoptotic Effects in Human Non-Melanoma Skin Cancer UW-BCC1 and A431 Cells In Vitro: Involvement of Hedgehog Signalling)

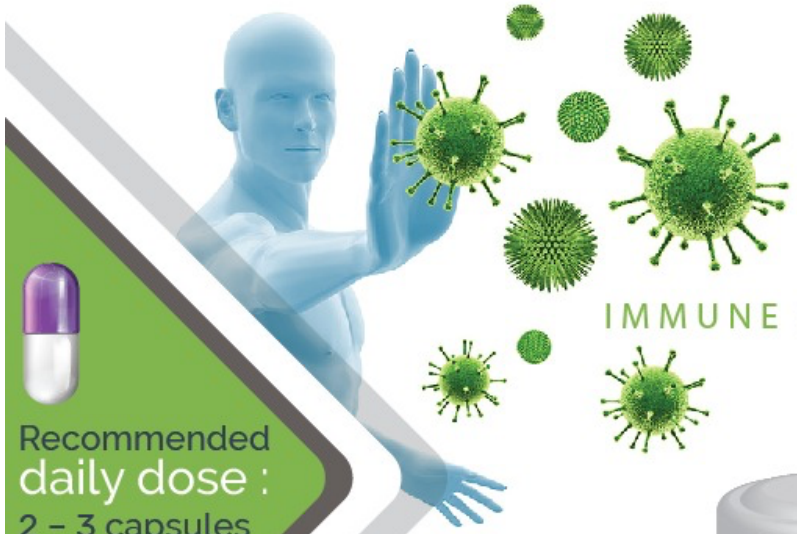
(3) Table 1. Scientific findings of previously published work on Graviola.

Trial type	Findings	Randomized	References
In Vivo	Graviola decreased MCF-7 tumor growth in nude mice.	No	Yu-Min Koa etal.(2011) [40]
In Vivo	Graviola has antitumor activity in lung cancer cells.	No	Wang, L. Q., et al (2002) [44] Woo, M. H., et al (1999) [45]
In Vivo	Graviola could act as a cancer prevention agent.	No	J.B. Minari *, U. Okeke (2014) [52]
In Vivo	Graviola selectively inhibited the growth of EGFR-overexpressing human breast cancer cells.	*N/A	Dai Y, Hogan Set al. (2011) [39]
In Vivo	Graviola induces apoptosis in colon cancer cells.	N/A	Soheil Zorofchian Moghadamtousi et al.(2014) [41]
In Vivo	Graviola promotes necrosis in PC-3 cells.	N/A	Torres, M. P et al. (2012) [26] Yang C et al. (2015) [43]
In Vivo	Graviola has antitumor activity in Lung cancer.	N/A	Kim, G. S., et al. (1998) [46] Zhao, G. X., et al. (1993) [47]

*N/A Not Applicable.

Who shall take Graviola:

1- Anyone with family history of developing Breast or Colon Cancer
2- Anyone seeking healthy body
3- Patient with high risk of developing Hepatic diseases



IMMUNE SUPPORT

Recommended daily dose :
2 – 3 capsules per day.

References:

1- Patel, M. S., & Patel, J. K. (2016). A review on a miracle fruits of Annona muricata. Journal of Pharmacognosy and Phytochemistry, 5(1), 137.

2- Moghadamtousi, S. Z., Fadaeinasab, M., Nikzad, S., Mohan, G., Ali, H. M., & Kadir, H. A. (2015). Annona muricata (Annonaceae): a review of its traditional uses, isolated acetogenins and biological activities. International journal of molecular sciences, 16(7), 15625-15658.

3- Ioannis, P., Anastasis, S., & Andreas, Y. (2015). Graviola: A systematic review on its anticancer properties. Am. J. Cancer Prev, 3, 128-131.

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