The Mangosteen Fruit & Xanthones

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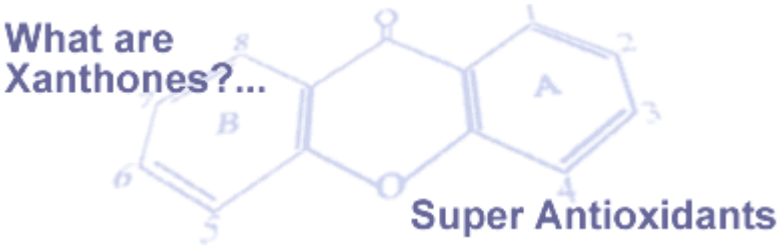


Creating a New Innovation with the
"The Queen of Fruits"

Disclaimer

The Mangosteen Fruit

The Mangosteen is tangerine-size and is deep purple in color on the outside, with a bright white pulp in the inside. Prized because of its excellent flavor, in Asia it is called the "Queen of Fruits", and, in the French Caribbean, the "Food of the Gods".

Used for centuries throughout the lands in which it grows, recent studies have revealed an incredible scope of potent human health benefits leading many to believe the Mangosteen well may be the most important fruit on earth.

Because the Mangosteen fruit has been used as a folk remedy for several hundred years in Malaysia and Thailand, universities throughout the Pacific Rim have studies on the fruit, initially for the purpose of debunking the seemingly outrageous claims made about the wide variety of health and wellness benefits. On the contrary, not only did the universities not debunk the claims, rather they more than corroborated them. These studies are ubiquitous on various research oriented websites.

The following are just a few of the sources you can look to for third part independent studies about Mangosteen and Xanthones:

Xanthones

The pericarp is the outer rind of the Mangosteen fruit and has been used for generations by Asian health practitioners for a myriad of healthful properties.

The pericarp is a concentrated source of a powerful family of Phytonutrients known as Xanthones. These days, everybody knows about free radicals and antioxidants. Free radicals attack the cells in our bodies every second of every day, and antioxidants work to repair the damage. **Much has been made of the extensive antioxidant properties of vitamins, especially Vitamin C and Vitamin E. But did you know there exists an antioxidant that is even more powerful than any vitamin?** This powerful, life-enhancing substance is called a Xanthone. In fact, there is a whole family of Xanthones, and the most dynamic of these are found in the amazing Mangosteen fruit.

Introducing XanGo™

While science has been researching the benefits of Mangosteen for decades, no one has thought to bring these incredible benefits to the world in a flavorful, convenient form.

Until Now!

Now there's **XanGo™,** the only product available that carries all of the power and goodness of the WHOLE Mangosteen Fruit, delivered in naturally delicious liquid form. **XanGo™** is not simply the juice of the Mangosteen. Instead, it is whole fruit puree, utilizing every bit of this extraordinary tropical fruit. That means that **XanGo™** provides an abundance of Xanthones, natural antioxidants that have a host of beneficial properties.

Experience XanGo™

The first and only product in the world that features the whole fruit puree of the exotic Mangosteen.

- Prized for Centuries
- Validated by modern Science
- Astonishingly Delicious
- No Added Sweetners
- No Artificial Flavors
- No Artificial Colors
- Rich in Antioxidant Xanthones

Research

The two most beneficial Xanthones found in the Mangosteen have been named Alpha Mangostin and Gamma Mangostin. When isolated and thoroughly tested by researchers, these two Xanthones have been found to carry a host of benefits. According to professional journals these Xanthones have a remarkable effect on cardiovascular health; are naturally antibiotic, antiviral, and anti-inflammatory; and are some of the most powerful antioxidants to be found in nature. According to professional exhaustive research journals such as:

Biochemical Pharmacology, Free Radical Research, Journal of Pharmacology, Journal of Enzyme Inhibitors, Environmental Health Perspectives, Planta Medica, Journal of Natural Products, European Journal of Pharmacology, Phytochemistry, and Much More…

“The Queen of Fruits”

1: J Ethnopharmacol. 2004 Jan; 90(1): 161-6.

Antiproliferation, antioxidation and induction of apoptosis by Garcinia mangostana (mangosteen) on SKBR3 human breast cancer cell line.

Moongkarndi P, Kosem N, Kaslungka S, Luanratana O, Pongpan N, Neungton N.

Department of Microbiology, Faculty of Pharmacy, Mahidol University, Sri Ayudthaya Road, Rajdhevee, 10400, Bangkok, Thailand

This study was designed to determine the antiproliferative, apoptotic and antioxidative properties of crude methanolic extract (CME) from the pericarp of Garcinia mangostana (family Guttiferae) using human breast cancer (SKBR3) cell line as a model system. SKBR3 cells were cultured in the presence of CME at various concentrations (0-50microg/ml) for 48h and the percentage of cell viability was evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-di phenyl tetrazolium bromide (MTT) assay. CME showed a dose-dependent inhibition of cell proliferation with ED(50) of 9.25+/-0.64microg/ml. We found that antiproliferative effect of CME was associated with apoptosis on breast cancer cell line by determinations of morphological changes and oligonucleosomal DNA fragments. In addition, CME at various concentrations and incubation times were also found to inhibit ROS production. These investigations suggested that the methanolic extract from the pericarp of Garcinia mangostana had strong antiproliferation, potent antioxidation and induction of apoptosis. Thus, it indicates that this substance can show different activities and has potential for cancer chemoprevention which were dose dependent as well as exposure time dependent.

PMID: 14698525 [PubMed - in process]

2: J Nat Prod. 2003 Aug; 66(8): 1124-7.

Induction of apoptosis by xanthones from mangosteen in human leukemia cell lines.

Matsumoto K, Akao Y, Kobayashi E, Ohguchi K, Ito T, Tanaka T, Iinuma M, Nozawa Y.

Gifu International Institute of Biotechnology, 1-1 Naka-Fudogaoka, Kakamigahara, Gifu 504-0838, Japan. kmatsumoto@giib.or.jp

We examined the effects of six xanthones from the pericarps of mangosteen, Garcinia mangostana, on the cell growth inhibition of human leukemia cell line HL60. All xanthones displayed growth inhibitory effects. Among them, alpha-mangostin showed complete inhibition at 10 microM through the induction of apoptosis.

PMID: 12932141 [PubMed - indexed for MEDLINE]

3: Chem Pharm Bull (Tokyo). 2003 Jul; 51(7): 857-9.

Antimycobacterial activity of prenylated xanthones from the fruits of Garcinia mangostana.

Suksamrarn S, Suwannapoch N, Phakhodee W, Thanuhiranlert J, Ratananukul P, Chimnoi N, Suksamrarn A.

Department of Chemistry, Faculty of Science, Srinakharinwirot University, Bangkok, Thailand. sunit@swu.ac.th

Prenylated xanthones, isolated from the fruit hulls and the edible arils and seeds of Garcinia mangostana, were tested for their antituberculosis potential. Alpha- and beta-mangostins and garcinone B exhibited strong inhibitory effect against Mycobacterium tuberculosis with the minimum inhibitory concentration (MIC) value of 6.25 microg/ml. Tri- and tetra-oxygenated xanthones with di-C5 units or with a C5 and a modified C5 groups are essential for high activities. Substitution in the A and C rings has been shown to modify the bioactivity of the compounds.

PMID: 12843596 [PubMed - in process]

4: Planta Med. 2002 Nov; 68(11): 975-9.

Thieme connect

Garcinone E, a xanthone derivative, has potent cytotoxic effect against hepatocellular carcinoma cell lines.

Ho CK, Huang YL, Chen CC.

Department of Medical Research & Education, Veterans General Hospital, Taipei, ROC.

Treatment of hepatocellular carcinomas (HCCs) with chemotherapy has generally been disappointing and it is most desirable to have more effective new drugs. We extracted and purified 6 xanthone compounds from the rinds (peel) of the fruits of Garcinia mangostana L., using partitioned chromatography and then tested the cytotoxic effects of these compounds on a panel of 14 different human cancer cell lines including 6 hepatoma cell lines, based on the MTT method. Several commonly used chemotherapeutic agents were included in the assay to determine the relative potency of the potential new drugs. Our results have shown that one of the xanthone derivatives which could be identified as garcinone E has potent cytotoxic effect on all HCC cell lines as well as on the other gastric and lung cancer cell lines included in the screen. We suggest that garcinone E may be potentially useful for the treatment of certain types of cancer.

PMID: 12451486 [PubMed - indexed for MEDLINE]

5: Biol Pharm Bull. 2002 Sep; 25(9): 1137-41.

J-STAGE

Inhibitions of histamine release and prostaglandin E2 synthesis by mangosteen, a Thai medicinal plant.

Nakatani K, Atsumi M, Arakawa T, Oosawa K, Shimura S, Nakahata N, Ohizumi Y.

Department of Pharmaceutical Molecular Biology, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Japan.

The fruit hull of mangosteen, Garcinia mangostana L. has been used as a Thai indigenous medicine for many years. However, its mechanism of action as a medicine has not been elucidated. The present study was undertaken to examine the effects of mangosteen extracts (100% ethanol, 70% ethanol, 40% ethanol and water) on histamine release and prostaglandin E2 synthesis. We found that the 40% ethanol extract of mangosteen inhibited IgE-mediated histamine release from RBL-2H3 cells with greater potency than the water extract of Rubus suavissimus that has been used as an anti-allergy crude drug in Japan. All extracts of mangosteen potently inhibited A23187-induced prostaglandin E2 synthesis in C6 rat glioma cells, while the water extract of Rubus suavissimus had no effect. The 40% ethanol extract of mangosteen inhibited the prostaglandin E2 synthesis in a concentration-dependent manner with relatively lower concentrations than the histamine release. In addition, passive cutaneous anaphylaxis (PCA) reactions in rats were significantly inhibited by this ethanol extract as well as by the water extract of Rubus suavissimus. These results suggest that the 40% ethanol extract of mangosteen has potent inhibitory activities of both histamine release and prostaglandin E2 synthesis.

PMID: 12230104 [PubMed - indexed for MEDLINE]

6: Phytochemistry. 2002 Jul; 60(5): 541-8.

ELSEVIER FULL-TEXT ARTICLE

Xanthones from the heartwood of Garcinia mangostana.

Nilar, Harrison LJ.

Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543, Singapore.

Twelve xanthones were isolated from the hexane extract of the heartwood of Garcinia mangostana from Myanmar. Their structures were determined using 1D and 2D NMR techniques

PMID: 12052521 [PubMed - indexed for MEDLINE]

7: J Nat Prod. 2002 May; 65(5): 761-3.

Xanthones from the green fruit hulls of Garcinia mangostana.

Suksamrarn S, Suwannapoch N, Ratananukul P, Aroonlerk N, Suksamrarn A.

Department of Chemistry, Faculty of Science, Srinakharinwirot University, Bangkok 10110, Thailand. sunit@psm.swu.ac.th

Three new xanthones, mangostenol (1), mangostenone A (2), and mangostenone B (3), were isolated from the green fruit hulls of Garcinia mangostana, along with the known xanthones, trapezifolixanthone, tovophyllin B (4), alpha- and beta-mangostins, garcinone B, mangostinone, mangostanol, and the flavonoid epicatechin. The structures of the new xanthones were elucidated by analysis of their spectroscopic data.

PMID: 12027762 [PubMed - indexed for MEDLINE]

8: Biochem Pharmacol. 2002 Jan 1; 63(1): 73-9.

Inhibition of cyclooxygenase and prostaglandin E2 synthesis by gamma-mangostin, a xanthone derivative in mangosteen, in C6 rat glioma cells.

Nakatani K, Nakahata N, Arakawa T, Yasuda H, Ohizumi Y.

Department of Pharmaceutical Molecular Biology, Graduate School of

Pharmaceutical Sciences, Tohoku University, Aoba, Aramaki, Aoba-ku, 980-8578, Sendai, Japan.

The fruit hull of mangosteen, Garcinia mangostana L., has been used for many years as a medicine for treatment of skin infection, wounds, and diarrhea in Southeast Asia. In the present study, we examined the effect of gamma-mangostin, a tetraoxygenated diprenylated xanthone contained in mangosteen, on arachidonic acid (AA) cascade in C6 rat glioma cells. gamma-Mangostin had a potent inhibitory activity of prostaglandin E2 (PGE2) release induced by A23187, a Ca2+ ionophore. The inhibition was concentration-dependent, with the IC50 value of about 5 microM. gamma-Mangostin had no inhibitory effect on A23187-induced phosphorylation of p42/p44 extracellular signal regulated kinase/mitogen-activated protein kinase or on the liberation of [14C]-AA from the cells labeled with [14C]-AA. However, gamma-mangostin concentration-dependently inhibited the conversion of AA to PGE2 in microsomal preparations, showing its possible inhibition of cyclooxygenase (COX). In enzyme assay in vitro, gamma-mangostin inhibited the activities of both constitutive COX (COX-1) and inducible COX (COX-2) in a concentration-dependent manner, with the IC50 values of about 0.8 and 2 microM, respectively. Lineweaver-Burk plot analysis indicated that gamma-mangostin competitively inhibited the activities of both COX-1 and -2. This study is a first demonstration that gamma-mangostin, a xanthone derivative, directly inhibits COX activity.

PMID: 11754876 [PubMed - indexed for MEDLINE]

9: J Nat Prod. 2001 Jul; 64(7): 903-6.

Three xanthones and a benzophenone from Garcinia mangostana.

Huang YL, Chen CC, Chen YJ, Huang RL, Shieh BJ.

National Research Institute of Chinese Medicine, No. 155-1, Sec. 2, Li Nung Street Peitou, Taipei, Taiwan, Republic of China.

Investigation of the constituents of Garcinia mangostana has led to the isolation of four new compounds: three minor xanthones, garcimangosone A (1), garcimangosone B (2), and garcimangosone C (3), and a benzophenone glucoside, garcimangosone D (4). The structures of these four compounds were established by spectral (NMR and MS) and chemical methods.

PMID: 11473420 [PubMed - indexed for MEDLINE]

10: Fitoterapia. 2000 Sep; 71(5): 607-9.

Two novel xanthones from Garcinia mangostana.

Gopalakrishnan G, Balaganesan B.

Centre for Natural Products SPIC Science Foundation 111, Mount Road, Chennai 600 032, India. geethagopal@hotmail.com

The isolation of two novel xanthones isolated from the fruit hulls of Garcinia mangostana is reported. The structures were elucidated by means of spectroscopic analysis.

PMID: 11449524 [PubMed - indexed for MEDLINE]

11: Nat Biotechnol. 1999 Jun; 17(6): 593-7.

nature biotechnology

Improved stearate phenotype in transgenic canola expressing a modified acyl-acyl carrier protein thioesterase.

Facciotti MT, Bertain PB, Yuan L.

Calgene, LLC, Davis, CA 95616, USA.

The engineering of crops for selected fatty acid production is one of the major goals of plant biotechnology. The Garm FatA1, an acyl-acyl carrier protein (ACP) thioesterase isolated from Garcinia mangostana, generates an elevated stearate (18:0) phenotype in transgenic Brassica plants. By site-directed mutagenesis, we generated seven mutants that showed up to a 13-fold increase in specific enzyme activity toward 18:0-ACP in vitro. The seed-specific expression of mutant S111A/V193A in Brassica plants results in transgenic plants that accumulate 55-68% more stearate than plants expressing the wild-type enzyme. Our results demonstrate that a thioesterase can be engineered to increase specific activity and that its improved function demonstrated in vitro is retained in vivo.

PMID: 10385326 [PubMed - indexed for MEDLINE]

12: Plant J. 1998 Mar; 13(6): 743-52.

Full text blackwell-synergy.com

Characterization of acyl-ACP thioesterases of mangosteen (Garcinia mangostana) seed and high levels of stearate production in

transgenic canola.

Hawkins DJ, Kridl JC.

Calgene, Inc., Davis, CA 95616, USA.

Acyl-acyl-carrier protein (ACP) thioesterases are, at least in part, responsible for the fatty acyl chain length composition of seed storage oils. Acyl-ACP thioesterases with specificity for each of the saturated acyl-ACP substrates from 8:0 through 16:0 have been cloned, with the exception of 18:0, and are members of the FatB class of thioesterases. The authors have determined that the tropical tree species mangosteen (Garcinia mangostana) stores 18:0 (stearate) in its seed oil in amounts of up to 56% by weight. Acyl-ACP thioesterase activity as measured in crude mangosteen seed extracts showed a preference for 18:1-ACP substrates, but had significant activity with 18:0 relative to that with 16:0-ACP, suggesting a thioesterase might be involved in the production of stearate. Three distinct acyl-ACP thioesterases were cloned from mangosteen seed cDNA; two representative of the FatA class and one representative of the FatB class. When expressed in vitro, the enzyme encoded by one of the FatAs (Garm FatA1) while preferring 18:1-ACP showed relatively low activity with 16:0-ACP as compared to 18:0-ACP, similar to the substrate preferences shown by the crude seed extract. Expression of Garm FatA1 in Brassica seeds led to the accumulation of stearate up to 22% in seed oil. These results suggest that Garm FatA1 is at least partially responsible for determining the high stearate composition of mangosteen seed oil and that FatA as well FatB thioesterases have evolved for specialized roles.

PMID: 9681015 [PubMed - indexed for MEDLINE]

13: Br J Pharmacol. 1998 Mar; 123(5): 855-62.

Effect of gamma-mangostin through the inhibition of 5-hydroxy-tryptamine2A receptors in 5-fluoro-alpha-methyltryptamine-induced head-twitch responses of mice.

Chairungsrilerd N, Furukawa K, Tadano T, Kisara K, Ohizumi Y.

Department of Molecular Biology, Faculty of Pharmaceutical Sciences, Tohoku University, Sendai, Japan.

1. Intracerebronventricular (i.c.v.) injection of gamma-mangostin (10-40 nmol/mouse), a major compound of the fruit hull of Garcinia mangostana Lin., like ketanserin (10, 20 nmol/mouse, i.c.v.) inhibited 5-fluoro-alpha-methyltryptamine (5-FMT) (45 mg kg(-1), i.p.)-induced head-twitch response in mice in the presence or absence of citalopram (a 5-hydroxytryptamine (5-HT)-uptake inhibitor). 2. Neither the 5-FMT- nor the 8-hydroxy-2-(di-n-propylamino)tetralin (5-HT1A-agonist)-induced 5-HT syndrome (head weaving and hindlimb abduction) was affected by gamma-mangostin or ketanserin. 3. The locomotor activity stimulated by 5-FMT through the activation of alpha1-

adrenoceptors did not alter in the presence of gamma-mangostin. 4. 5-HT-induced inositol phosphates accumulation in mouse brain slices was abolished by ketanserin. Gamma-mangostin caused a concentration-dependent inhibition of the inositol phosphates accumulation. 5. Gamma-mangostin caused a concentration-dependent inhibition of the binding of [3H]-spiperone, a specific 5-HT2A receptor antagonist, to mouse brain membranes. 6. Kinetic analysis of the [3H]-spiperone binding revealed that gamma-mangostin increased the Kd value without affecting the Bmax value, indicating the mode of the competitive nature of the inhibition by gamma-mangostin. 7. These results suggest that gamma-mangostin inhibits 5-FMT-induced head-twitch response in mice by blocking 5-HT2A receptors not by blocking the release of 5-HT from the central neurone. Gamma-mangostin is a promising 5-HT2A receptor antagonist in the central nervous system.

PMID: 9535013 [PubMed - indexed for MEDLINE]

14: Nippon Yakurigaku Zasshi. 1997 Oct; 110 Suppl 1: 153P-158P.

[Novel types of receptor antagonists from the medicinal plant Garcinia mangostana]

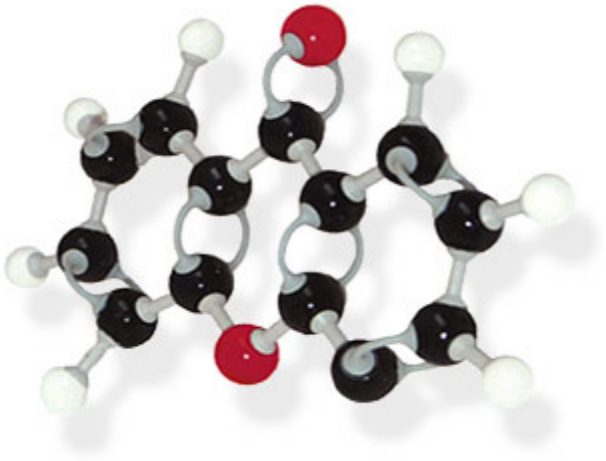
[Article in Japanese]

Furukawa K, Chairungsrilerd N, Ohta T, Nozoe S, Ohizumi Y.

Department of Pharmaceutical Molecular Biology, Faculty of Pharmaceutical Sciences, Tohoku University, Sendai, Japan.

A crude methanolic extract of the fruit hull of Garcinia mangostana L. inhibited the contraction of the isolated rabbit aorta induced by histamine and serotonin. The extract has been fractionated by silica gel chromatography, monitoring the pharmacological activity to give active compounds. On the basis of physicochemical data, the active substances were identified as alpha-mangostin and gamma-mangostin. To define the pharmacological properties of alpha-mangostin, the effect of alpha-mangostin on both histamine H1 and H2 receptors were examined by monitoring the mechanical responses of smooth muscles and measuring the radioligand binding to cultured vascular smooth muscle cells. The results suggest that alpha-mangostin acts as a selective and competitive histamine H1 receptor antagonist. The pharmacological actions of gamma-mangostin on 5-HT receptors were also investigated by using contractile response of vascular smooth muscle, platelet aggregation and radioligand binding studies. The results provide the evidence that gamma-mangostin is a selective and competitive 5-HT2A receptor antagonist. It is of great interest that the structures of alpha-mangostin and gamma-mangostin free from nitrogen atom are not resemble to the common structures of histamine and serotonin receptor antagonists. alpha-Mangostin and gamma-mangostin may become novel types of lead compounds for histamine and serotonin receptor antagonists.

PMID: 9503424 [PubMed - indexed for MEDLINE]



15: Naunyn Schmiedebergs Arch Pharmacol. 1998 Jan; 357(1): 25-31.

Gamma-mangostin, a novel type of 5-hydroxytryptamine 2A receptor antagonist.

Chairungsrilerd N, Furukawa KI, Ohta T, Nozoe S, Ohizumi Y.

Department of Pharmaceutical Molecular Biology, Faculty of Pharmaceutical Sciences, Tohoku University, Sendai, Japan.

Gamma-mangostin, purified from the fruit hull of the medicinal plant Garcinia mangostana caused a parallel rightwards shift of the concentration/response curve for the contraction elicited by 5-hydroxytryptamine (5-HT) in the rabbit aorta (pA2 = 8.2) without affecting the contractile responses to KCl, phenylephrine (alpha1) or histamine (H1). The perfusion pressure response of rat coronary artery to 5-HT (5-HT2A) was reduced concentration dependently by gamma-mangostin (IC50 = 0.32 microM). 5-HT amplified, ADP-induced aggregation of rabbit platelets (5-HT2A) was inhibited by gamma-mangostin (IC50 = 0.29 microM), whereas that induced by thrombin was not affected, nor did gamma-mangostin affect 5-HT-induced contraction of the guinea-pig ileum (5-HT3)in the presence of 5-HT1, 5-HT2 and 5-HT4 receptor antagonists. Furthermore, 5-HT-induced contraction of the rat fundus (5-HT2B) and 5-HT-induced relaxation of the rabbit aorta in the presence of ketanserin (5-HT1) and carbachol-induced contraction of the guinea-pig ileum (muscarinic M3) were not affected by gamma-mangostin (5 microM). Gamma-mangostin inhibited [3H]spiperone binding to cultured rat aortic myocytes (IC50 = 3.5 nM). The Kd for [3H]spiperone binding was increased by gamma-mangostin (3 nM) from 11.7 to 27.4 nM without affecting Bmax. These results suggest that gamma-mangostin is a novel competitive antagonist, free from a nitrogen atom, for the 5-HT2A receptors in vascular smooth muscles and platelets.

PMID: 9459569 [PubMed - indexed for MEDLINE]

16: J Med Assoc Thai. 1997 Sep; 80 Suppl 1: S149-54.

Immunopharmacological activity of polysaccharide from the pericarb of mangosteen garcinia: phagocytic intracellular killing activities.

Chanarat P, Chanarat N, Fujihara M, Nagumo T.

Department of Clinical Microscopy, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand.

Polysaccharides from the pericarbs of mangosteen, Garcinia mangostana Linn., was obtained by treating the dried ground pericarbs with hot water followed by ethanol precipitation (M fraction). The extract was fractionated by anion exchange chromatography on a DEAE-cellulose column as MDE1-5 fractions. The fractions of MDE3 and MDE4 composed of mainly D-galacturonic acid and a small amount of neutral sugar (L-arabinose as the major one and L-rhamnose and D-galactose as the minor ones) were studied for immunopharmacological activities by phagocytic test to intracellular bacteria (Salmonella enteritidis) and nitroblue tetrazolium (NBT) and superoxide generation tests. The results showed that the number of S. enteritidis in cultured monocyte with extract of pericarb of mangosteen (MDE3) was killed. Activating score (mean +/- SD) of NBT test of 100 polymorphonuclear phagocytic cells were 145 +/- 78, 338 +/- 58, 222 +/- 73, 209 +/- 77, 211 +/- 63, 372 +/- 19, 369 +/- 20, 355 +/- 34 in normal saline control, phorbol myristate acetate (PMA), MDE3, MDE4, indomethacin (I), PMA + MDE3, PMA + MDE4 and PMA + I, respectively. Superoxide generation test was also done by color reduction of cytochrome c. Both MDE3 and MDE4 stimulate superoxide production. The number of S. enteritidis in cultured monocyte with extract of pericarb of mangosteen was killed. This paper suggests that polysaccharides in the extract can stimulate phagocytic cells and kill intracellular bacteria (S. enteritidis).

PMID: 9347663 [PubMed - indexed for MEDLINE]

17: J Nat Prod. 1997 May; 60(5): 519-24.

Evaluation of the antifungal activity of natural xanthones from Garcinia mangostana and their synthetic derivatives.

Gopalakrishnan G, Banumathi B, Suresh G.

Centre for Agrochemical Research, SPIC Science Foundations, Madras, India.

The antifungal activity of several xanthones isolated from the fruit hulls of Garcinia mangostana and some derivatives of mangostin against three phytopathogenic fungi, Fusarium oxysporum vasinfectum, Alternaria tenuis, and Dreschlera oryzae, has been evaluated. The natural xanthones showed good

inhibitory activity against the three fungi. Substitution in the A and C rings has been shown to modify the bioactivities of the compounds.

PMID: 9213587 [PubMed - indexed for MEDLINE]

18: Planta Med. 1996 Oct; 62(5): 471-2.

Histaminergic and serotonergic receptor blocking substances from the medicinal plant Garcinia mangostana.

Chairungsrilerd N, Furukawa K, Ohta T, Nozoe S, Ohizumi Y.

A crude methanolic extract of the fruit hull of Mangosteen, Garcinia mangostana L. inhibited the contractions of isolated thoracic rabbit aorta induced by histamine and serotonin. The extract of the fruit hull has been fractionated by silica gel chromatography, monitoring the pharmacological activity to give alpha- and gamma-mangostin. On the basis of pharmacological data, it is suggested that alpha-mangostin and gamma-mangostin are a histaminergic and a serotonergic receptor blocking agent, respectively.

Publication Types:

- Letter

PMID: 8923814 [PubMed - indexed for MEDLINE]

19: J Pharm Pharmacol. 1996 Aug; 48(8): 861-5.

Antibacterial activity of xanthones from guttiferaeous plants against methicillin-resistant Staphylococcus aureus.

Iinuma M, Tosa H, Tanaka T, Asai F, Kobayashi Y, Shimano R, Miyauchi K.

Department of Pharmacognosy, Gifu Pharmaceutical University, Japan.

Extracts of Garcinia mangostana (Guttiferae) showing inhibitory effects against the growth of S. aureus NIHJ 209p were fractionated according to guidance obtained from bioassay and some of the components with activity against methicillin-resistant Staphylococcus aureus (MRSA) were characterized. One active isolate, alpha-mangostin, a xanthone derivative, had a minimum inhibitory concentration (MIC) of 1.57-12.5 micrograms mL-1. Other related xanthones were also examined to determine their anti-MRSA activity. Rubraxanthone, which was isolated from Garcinia dioica and has a structure similar to that of alpha-mangostin, had the highest activity against staphylococcal strains (MIC = 0.31-1.25 micrograms mL-1), an activity which was greater than that of the

antibiotic vancomycin (3.13-6.25 micrograms mL-1). The inhibitory effect against strains of MRSA of two of the compounds when used in conjunction with other antibiotics was also studied. The anti-MRSA activity of alpha-mangostin was clearly increased by the presence of vancomycin; this behaviour was not observed for rubraxanthone. The strong in-vitro antibacterial activity of xanthone derivatives against both methicillin-resistant and methicillin-sensitive Staphylococcus aureus suggests the compounds might find wide pharmaceutical use.

PMID: 8887739 [PubMed - indexed for MEDLINE]

20: Jpn J Pharmacol. 1996 Aug; 71(4): 337-40.

The mode of inhibitory action of alpha-mangostin, a novel inhibitor, on the sarcoplasmic reticulum Ca(2+)-pumping ATPase from rabbit skeletal muscle.

Furukawa K, Shibusawa K, Chairungsrilerd N, Ohta T, Nozoe S, Ohizumi Y.

Department of Pharmaceutical Molecular Biology, Faculty of Pharmaceutical Sciences, Tohoku University, Sendai, Japan.

alpha-Mangostin, the principal ingredient of the fruit hull of Garcinia mangostana, caused a concentration-dependent decrease in the activities of both Ca(2+)-ATPase and Ca(2+)-transport of the sarcoplasmic reticulum from rabbit skeletal muscle with an IC50 value of 5 microM. Neither Ca2+ release nor other enzyme activities were affected by alpha-mangostin. Kinetic analysis of the inhibitory effects of alpha-mangostin on Ca(2+)-ATPase suggests that the inhibition of the ATPase is a noncompetitive-type with respect to ATP or Ca2+. alpha-Mangostin may become a useful pharmacological tool for clarifying the physiological functions of Ca(2+)-pumping ATPase and sarcoplasmic reticulum.

PMID: 8886932 [PubMed - indexed for MEDLINE]

21: Planta Med. 1996 Aug; 62(4): 381-2.

Active constituents against HIV-1 protease from Garcinia mangostana.

Chen SX, Wan M, Loh BN.

The ethanol extract of Garcinia mangostana L. (Guttiferae) showed potent inhibitory activity against HIV-1 protease. The activity-guided purification of the extract resulted in the isolation of two active, known compounds. The chemical structures of the isolated compounds were established by spectroscopic analyses as mangostin (IC50 = 5.12 +/- 0.41 microM) and gamma-mangostin (IC50 = 4.81 +/- 0.32 microM). The type of inhibition by both compounds is noncompetitive.

Publication Types:

- Letter

PMID: 8792678 [PubMed - indexed for MEDLINE]

22 Free Radic Res. 1995 Aug; 23(2): 175-84.

Mangostin inhibits the oxidative modification of human low density lipoprotein.

Williams P, Ongsakul M, Proudfoot J, Croft K, Beilin L.
University of Western Australia, Department of Medicine, Royal Perth Hospital, Australia.

The oxidation of low density lipoprotein (LDL) may play an important role in atherosclerosis. We investigated the possible antioxidant effects of mangostin, isolated from Garcinia mangostana, on metal ion dependent (Cu2+) and independent (aqueous peroxyl radicals) oxidation of human LDL. Mangostin prolonged the lagtime to both metal ion dependent and independent oxidation of LDL in a dose dependent manner over 5 to 50 microM as monitored by the formation of conjugated dienes at 234 nm ($P < 0.001$). There was no significant effect of mangostin on the rate at which conjugated dienes were formed in the uninhibited phase of oxidation. Levels of thiobarbituric reactive substances (TBARS) generated in LDL were measured 4 and 24 hours after oxidation with 5

microM Cu2+ in the presence or absence of 50 microM or 100 microM mangostin. We observed an inhibition of TBARS formation with 100 microM mangostin at 4 hours (P = 0.027) but not at 24 hours (P = 0.163). Similar results were observed in the presence of 50 microM mangostin. Mangostin, at 100 microM, retarded the relative electrophoretic mobility of LDL at both 4 and 24 hours after Cu2+ induced oxidation. Mangostin (100 microM) significantly inhibited the consumption of alpha-tocopherol in the LDL during Cu2+ initiated oxidation over a 75 minute period (P < 0.001). From these results, we conclude that mangostin is acting as a free radical scavenger to protect the LDL from oxidative damage in this in vitro system.

PMID: 7581813 [PubMed - indexed for MEDLINE]

23: Phytochemistry. 1992 Nov; 31(11): 3711-3.

Inhibition of wheat embryo calcium-dependent protein kinase and other kinases by mangostin and gamma-mangostin.

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The hull of the fruit of the mangosteen tree (Garcinia mangostana) contains four inhibitors of plant Ca(2+)-dependent protein kinase. Two of these inhibitors have been purified and identified as the xanthones 1,3,6-trihydroxy-7-methoxy-2,8-bis(3-methyl-2-butenyl)-9H- xanthen-9-one (mangostin) and 1,3,6,7-tetrahydroxy-2,8-bis(3-methyl-2-butenyl)- 9H-xanthen-9-one (gamma-mangostin). Both xanthones also inhibit avian myosin light chain kinase and rat liver cyclic AMP-dependent protein kinase. This is the first report of inhibition of plant and animal second messenger-regulated protein kinases by plant-derived xanthones.

PMID: 1368866 [PubMed - indexed for MEDLINE]

24: Arch Int Pharmacodyn Ther. 1979 Jun; 239(2): 257-69.

Pharmacological profile of mangostin and its derivatives.

Shankaranarayan D, Gopalakrishnan C, Kameswaran L.

Mangostin (M), a naturally occurring xanthone in the rinds of the fruits of Garcinia mangostana Linn. (Guttiferae) and its derivatives such as 3-0-methyl mangostin (MM), 3,6-di-O-methyl mangostin (DM), 1-isomangostin (IM), mangostin triacetate (MT), mangostin 3,6-di-O-(tetra acetyl) glucoside (MTG) and mangostin-6,6-di-O-glucoside (MOG) were screened for various pharmacological effects in experimental animals. With the exception of DM all the test compounds produced CNS depression characterised by ptosis, sedation, decreased motor activity, potentiation of pentobarbital sleeping time and ether anaesthesia in mice and rats. None of the compounds exhibited analgesic, antipyretic and anticonvulsant effects. With the exception of MOG, none of the

test compounds produced significant effects on the cardiovascular system of frogs and dogs. MOG produced myocardial stimulation and a rise in blood pressure which was partially blocked by propranolol. M, IM and MT produced pronounced antiinflammatory activity both by intraperitoneal and oral routes in rats as tested by carrageenininduced hind paw oedema, cotton pellet implantation and granuloma pouch techniques. Antiinflammatory activity for M, IM and MT was observed even in bilaterally adrenalectomised rats. M, IM and MT did not produce any mast cell membrane stabilising effect and the degranulation effect of polymyxin B, diazoxide and Triton X-100 on rat peritoneal mast cells in vitro was not prevented. M, IM and MT did not alter the prothrombin time of albino rats. M alone produced significant antiulcer activity in rats.

PMID: 314790 [PubMed - indexed for MEDLINE]

25: Bioorg Med Chem Lett. 2003 Oct 6; 13(19): 3151-3.

ELSEVIER FULL-TEXT ARTICLE

Biological activities of alpha-mangostin derivatives against acidic sphingomyelinase.

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Deprenyl and benzofenone-type congeners of alpha-mangostin 1 have been synthesized to understand their role for the inhibitory activity against sphingomyelinase (SMase). While removal of the prenyl group of the right side (11 and 12) caused loss of the selectivity between ASMase (acidic sphingomyelinase) and NSMase (neutral sphingomyelinase), the prenyl group of the left side appeared to increase the inhibitory activities (16 and 17).

PMID: 12951083 [PubMed - in process]

26: Free Radic Res. 2000 Nov; 33(5): 643-59.

Inhibition of lipoprotein oxidation by prenylated xanthones derived from mangostin.

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Oxidative damage is thought to play a critical role in cardiovascular and other chronic diseases. This has led to considerable interest in the antioxidant activity of dietary compounds. Flavonoids have received the most attention and much is known about the structural requirements for antioxidant activity. However, little is

known about the antioxidant activity of other plant derived phenolic compounds such as the xanthones. We have previously shown that the prenylated xanthone, mangostin, can inhibit the oxidation of low density lipoprotein. In order to examine the effects of structure modification on antioxidant activity of this class of compound we have prepared a number of derivatives of mangostin and tested antioxidant activity in an isolated LDL and plasma assay. The results of this study show that structural modification of mangostin can have a profound effect on antioxidant activity. Derivatisation of the C-3 and C-6 hydroxyl groups with either methyl, acetate, propane diol or nitrile substantially reduces antioxidant activity. In contrast, derivatisation of C-3 and C-6 with aminoethyl derivatives enhanced antioxidant activity, which may be related to changes in solubility. Cyclisation of the prenyl chains had little influence on antioxidant activity.
PMID: 11200095 [PubMed - indexed for MEDLINE]

27: Eur J Pharmacol. 1996 Oct 31; 314(3): 351-6.

ELSEVIER FULL-TEXT ARTICLE

Pharmacological properties of alpha-mangostin, a novel histamine H1 receptor antagonist.

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In the isolated rabbit thoracic aorta and guinea-pig trachea, alpha-mangostin inhibited histamine-induced contractions in a concentration-dependent manner in the presence or absence of cimetidine, a histamine H2 receptor antagonist. But KCl-, phenylephrine- or carbachol-induced contractions were not affected by alpha-mangostin. The concentration-contractile response curve for histamine was shifted to the right in a parallel manner by alpha-mangostin. In the presence of chlorpheniramine, a histamine H1 receptor antagonist, alpha-mangostin did not affect the relaxation of the rabbit aorta induced by histamine. In the guinea-pig trachea, alpha-mangostin had no effect on the relaxation induced by dimaprit, a histamine H2 receptor agonist. alpha-Mangostin caused a concentration-dependent inhibition of the binding of [3H]mepyramine, a specific histamine H1 receptor antagonist to rat aortic smooth muscle cells. Kinetic analysis of [3H]mepyramine binding indicated the competitive inhibition by alpha-mangostin. These results suggest that alpha-mangostin is a novel competitive histamine H1 receptor antagonist in smooth muscle cells.

PMID: 8957258 [PubMed - indexed for MEDLINE]

28: Planta Med. 2002 Nov; 68(11): 975-9.

Thieme connect

Garcinone E, a xanthone derivative, has potent cytotoxic effect

against hepatocellular carcinoma cell lines.

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Treatment of hepatocellular carcinomas (HCCs) with chemotherapy has generally been disappointing and it is most desirable to have more effective new drugs. We extracted and purified 6 xanthone compounds from the rinds (peel) of the fruits of Garcinia mangostana L., using partitioned chromatography and then tested the cytotoxic effects of these compounds on a panel of 14 different human cancer cell lines including 6 hepatoma cell lines, based on the MTT method. Several commonly used chemotherapeutic agents were included in the assay to determine the relative potency of the potential new drugs. Our results have shown that one of the xanthone derivatives which could be identified as garcinone E has potent cytotoxic effect on all HCC cell lines as well as on the other gastric and lung cancer cell lines included in the screen. We suggest that garcinone E may be potentially useful for the treatment of certain types of cancer.

PMID: 12451486 [PubMed - indexed for MEDLINE]

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