

Hamada M, Iikubo K, Ishikawa Y, Ikeda A, Umezawa K, Nishiyama S. Biological activities of alpha-mangostin derivatives against acidic sphingomyelinase.

Bioorg Med Chem Lett. 2003 Oct 6;13(19):3151-3.
PMID: 12951083 [PubMed - in process]

Biological activities of alpha-mangostin derivatives against acidic sphingomyelinase.

Hamada M, Iikubo K, Ishikawa Y, Ikeda A, Umezawa K, Nishiyama S.

Department of Chemistry, Faculty of Science and Technology, Keio University,
Hiyoshi 3-14-1, Kohoku-ku, Yokohama 223-8522, Japan.

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]

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

Induction of apoptosis by xanthenes from mangosteen in human leukemia cell lines.
J Nat Prod. 2003 Aug;66(8):1124-7.

PMID: 12932141 [PubMed - in process]

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

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

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Gifu 504-0838, Japan. kmatsumoto@giib.or.jp

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

PMID: 12932141 [PubMed - in process]

Nakatani K, Nakahata N, Arakawa T, Yasuda H, Ohizumi Y.
Inhibition of cyclooxygenase and prostaglandin E2 synthesis
by gamma-mangostin, a xanthone derivative in mangosteen, in
C6 rat glioma cells.

Biochem Pharmacol. 2002 Jan 1;63(1):73-9.
PMID: 11754876 [PubMed - indexed for MEDLINE]

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]

Mahabusarakam W, Proudfoot J, Taylor W, Croft K.

Inhibition of lipoprotein oxidation by prenylated xanthenes derived from mangostin. *Free Radic Res.* 2000 Nov;33(5):643-59.

PMID: 11200095 [PubMed - indexed for MEDLINE]

Inhibition of lipoprotein oxidation by prenylated xanthenes derived from mangostin.

Mahabusarakam W, Proudfoot J, Taylor W, Croft K.

Chemistry Department, Prince of Songkla University, Hat Yai, Thailand.

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 xanthenes. 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]

Okudaira C, Ikeda Y, Kondo S, Furuya S, Hirabayashi Y, Koyano T, Saito Y, Umezawa K.

Inhibition of acidic sphingomyelinase by xanthone compounds isolated from *Garcinia speciosa*.
J Enzyme Inhib. 2000;15(2):129-38.

PMID: 10938539 [PubMed - indexed for MEDLINE]

Inhibition of acidic sphingomyelinase by xanthone compounds isolated from *Garcinia speciosa*.

Okudaira C, Ikeda Y, Kondo S, Furuya S, Hirabayashi Y, Koyano T, Saito Y, Umezawa K.

Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1
Hiyoshi, Kohoku-ku, Yokohama 223-0061, Japan.

Sphingomyelinase is considered to be involved in the regulation of apoptosis (cell death) and cell growth. In the course of our screening for acidic sphingomyelinase inhibitors we isolated three xanthone compounds, alpha-mangostin, cowanin, and cowanol, from the bark of *Garcinia speciosa*. These compounds competitively inhibited bovine brain-derived acidic sphingomyelinase with IC(50) values of 14.1, 19.2, and 10.9 microM, respectively and inhibited the acidic sphingomyelinase more effectively than the neutral sphingomyelinase of bovine brain. alpha-Mangostin inhibited the acidic sphingomyelinase in the most selective manner. alpha-Mangostin was chemically modified and its structure-activity relationships are discussed.

PMID: 10938539 [PubMed - indexed for MEDLINE]

Lu ZX, Hasmeda M, Mahabusarakam W, Ternai B, Ternai PC, Polya GM.

Inhibition of eukaryote protein kinases and of a cyclic nucleotide-binding phosphatase by prenylated xanthenes.

Chem Biol Interact. 1998 Jul 3;114(1-2):121-40.

PMID: 9744560 [PubMed - indexed for MEDLINE]

Inhibition of eukaryote protein kinases and of a cyclic nucleotide-binding phosphatase by prenylated xanthenes.

Lu ZX, Hasmeda M, Mahabusarakam W, Ternai B, Ternai PC, Polya GM.
School of Biochemistry, La Trobe University, Bundoora, Victoria, Australia.

A series of prenylated xanthenes are variously potent inhibitors of the catalytic subunit (cAK) of rat liver cyclic AMP-dependent protein kinase (PKA), rat brain Ca²⁺ and phospholipid-dependent protein kinase C (PKC), chicken gizzard myosin light chain kinase (MLCK), wheat embryo Ca²⁺-dependent protein kinase (CDPK) and potato tuber cyclic nucleotide-binding phosphatase (Pase). The prenylated xanthenes examined are mostly derivatives of alpha-mangostin in which the 3-hydroxyl and 6-hydroxyl are variously substituted with groups R or R', respectively, or derivatives of 3-isomangostin (mangostanol) in which the 9-hydroxyl is substituted with groups R' or the prenyl side chain is modified. The most potent inhibitors of cAK have non-protonatable and relatively small R' and R groups. Conversely, the most potent inhibitors of PKC and MLCK have bulkier and basic R' groups. Some prenylated xanthenes are also potent inhibitors of CDPK. PKC and cAK are competitively inhibited by particular prenylated xanthenes whereas the compounds that are the most potent inhibitors of MLCK and CDPK are non-competitive inhibitors. Prenylated xanthenes having relatively small and non-protonatable R' and R groups inhibit a high-affinity

cyclic nucleotide binding Pase in a non-competitive fashion.

(Protein kinases make up a veritable treasure trove of targets for a variety of indications, including diabetes, inflammatory disorders, and especially cancer.)

PMID: 9744560 [PubMed - indexed for MEDLINE]

Hopert AC, Beyer A, Frank K, Strunck E, Wunsche W, Vollmer G.

Characterization of estrogenicity of phytoestrogens in an endometrial-derived experimental model.

Environ Health Perspect. 1998 Sep;106(9):581-6.

PMID: 9721258 [PubMed - indexed for MEDLINE]

Characterization of estrogenicity of phytoestrogens in an endometrial-derived experimental model.

Hopert AC, Beyer A, Frank K, Strunck E, Wunsche W, Vollmer G.

Institut fur Molekulare Medizin, Medizinische Universitat zu Lubeck, Lubeck, Germany.

Severe developmental and reproductive disorders in wild animals have been linked to high exposure to persistent environmental chemicals with hormonal activity. These adverse effects of environmental estrogens have raised considerable concern and have received increasing attention. Although numerous chemicals with the capacity to interfere with the estrogen receptor (ER) have been identified, information on their molecular mechanism of action and their relative potency is rather limited. For the endometrium, the lack of information is due to the lack of a suitable experimental model. We investigated the functions of phytoestrogens in an endometrial-derived model, RUCa-I rat endometrial adenocarcinoma cells. The cells were cultured on a reconstituted basement membrane to preserve their functional differentiation and estrogen responsiveness. We assessed the relative binding affinity to the estrogen receptor of the selected phytoestrogens coumestrol, genistein, daidzein, and the putative phytoestrogen mangostin compared to estradiol by a competitive Scatchard analysis. The following affinity ranking was measured: 17 β -estradiol >>> coumestrol > genistein > daidzein >>> mangostin. In addition, we investigated the capacity of these compounds to promote the increased production of complement C3, a well-known estradiol-regulated protein of the rat endometrium. All substances tested increased the production of complement C3, although different concentrations were necessary to achieve equivalent levels of induction compared to estradiol. Mechanistically we were able to demonstrate that the increase of complement C3 production was mediated by primarily increasing its steady-state mRNA level. These findings indicate that RUCa-I cells represent a sensitive model system to elucidate relative potencies and functions of environmental estrogens in an endometrium-derived model.

PMID: 9721258 [PubMed - indexed for MEDLINE]

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

Effect of gamma-mangostin through the inhibition of 5-hydroxy-tryptamine_{2A} receptors in 5-fluoro-alpha-methyltryptamine-induced head-twitch responses of mice.

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

PMID: 9535013 [PubMed - indexed for MEDLINE]

Effect of gamma-mangostin through the inhibition of 5-hydroxy-tryptamine_{2A} 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. Intracerebroventricular (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-HT_{1A}-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-HT_{2A} receptor antagonist, to mouse brain membranes. 6. Kinetic analysis of the [³H]-spiperone binding revealed that gamma-mangostin increased the K_d value without affecting the B_{max} 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-HT_{2A} receptors not by blocking the release of 5-HT from the central neurone. Gamma-mangostin is a promising 5-HT_{2A} receptor antagonist in the central nervous system.

PMID: 9535013 [PubMed - indexed for MEDLINE]

Vlietinck AJ, De Bruyne T, Apers S, Pieters LA.

Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection.

Planta Med. 1998 Mar;64(2):97-109. Review.

PMID: 9525100 [PubMed - indexed for MEDLINE]

Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection.

Vlietinck AJ, De Bruyne T, Apers S, Pieters LA.

Department of Pharmaceutical Sciences, University of Antwerp (UA), Belgium.

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Many compounds of plant origin have been identified that inhibit different stages in the replication cycle of human immunodeficiency virus (HIV): 1) virus adsorption: chromone alkaloids (schumannificine), isoquinoline alkaloids (michellamines), sulphated polysaccharides and polyphenolics, flavonoids, coumarins (glycocoumarin, licopyranocoumarin) phenolics (caffeic acid derivatives, galloyl acid derivatives, catechinic acid derivatives), tannins and triterpenes (glycyrrhizin and analogues, soyasaponin and analogues); 2) virus-cell fusion: lectins (mannose- and N-acetylglucosamine-specific) and triterpenes (betulinic acid and analogues); 3) reverse transcription; alkaloids (benzophenanthridines, protoberberines, isoquinolines, quinolines), coumarins (calanolides and analogues), flavonoids, phloroglucinols, lactones (protolichesterinic acid), tannins, iridoids (fulvoplumierin) and triterpenes; 4) integration: coumarins (3-substituted-4-

hydroxycoumarins), depsidones, O-caffeoyl derivatives, lignans (arctigenin and analogues) and phenolics (curcumin); 5) translation: single chain ribosome inactivating proteins (SCRIP's); 6) proteolytic cleavage (protease inhibition): saponins (ursolic and maslinic acids), xanthenes (mangostin and analogues) and coumarins; 7) glycosylation: alkaloids including indolizidines (castanospermine and analogues), piperidines (1-deoxynojirimicin and analogues) and pyrrolizidines (australine and analogues); 8) assembly/release: naphthodianthrones (hypericin and pseudohypericin), photosensitisers (terthiophenes and furoisocoumarins) and phospholipids. The target of action of several anti-HIV substances including alkaloids (O-demethyl-buchenavianine, papaverine), polysaccharides (acemannan), lignans (intheriotherins, schisantherin), phenolics (gossypol, lignins, catechol dimers such as peltatols, naphthoquinones such as conocurvone) and saponins (celasdin B, Gleditsia and Gymnocladus saponins), has not been elucidated or does not fit in the proposed scheme. Only a very few of these plant-derived anti-HIV products have been used in a limited number of patients suffering from AIDS viz. glycyrrhizin, papaverine, trichosanthin, castanospermine, N-butyl-1-deoxynojirimicin and acemannan.

Publication Types:

- Review
- Review, Academic

PMID: 9525100 [PubMed - indexed for MEDLINE]

Furukawa K, Chairungsrilerd N, Ohta T, Nozoe S, Ohizumi Y.
[Novel types of receptor antagonists from the medicinal plant *Garcinia mangostana*]

Nippon Yakurigaku Zasshi. 1997 Oct;110 Suppl 1:153P-158P. Japanese.
PMID: 9503424 [PubMed - indexed for MEDLINE]

[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-HT_{2A} 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]

Likhitwitayawuid K, Phadungcharoen T, Krungkrai J.
Antimalarial xanthenes from *Garcinia cowa*.
Planta Med. 1998 Feb;64(1):70-2.
PMID: 9491769 [PubMed - indexed for MEDLINE]

Antimalarial xanthenes from *Garcinia cowa*.

Likhitwitayawuid K, Phadungcharoen T, Krungkrai J.

Five xanthenes from the bark of *Garcinia cowa*, namely 7-O-methylgarcinone E (1), cowanin (2), cowanol (3), cowaxanthone (4), and beta-mangostin (5), were found to possess in vitro antimalarial activity against *Plasmodium falciparum* with IC₅₀ values ranging from 1.50 to 3.00 micrograms/ml. Complete ¹H- and ¹³C-NMR assignments of these compounds are also reported.

Publication Types:

· Letter

PMID: 9491769 [PubMed - indexed for MEDLINE]

Chairungsrilerd N, Furukawa KI, Ohta T, Nozoe S, Ohizumi Y.
Gamma-mangostin, a novel type of 5-hydroxytryptamine 2A receptor antagonist.
Naunyn Schmiedebergs Arch Pharmacol. 1998 Jan;357(1):25-31.
PMID: 9459569 [PubMed - indexed for MEDLINE]

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 (α₁) or histamine (H₁). The perfusion pressure response of rat coronary artery to 5-HT (5-HT_{2A}) was reduced concentration dependently by gamma-mangostin (IC₅₀ = 0.32 microM). 5-HT amplified, ADP-induced aggregation of rabbit platelets (5-HT_{2A}) 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-HT_{2B}) 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 K_d for [³H]spiperone binding was increased by gamma-mangostin (3 nM) from 11.7 to 27.4 nM without affecting B_{max}. These results suggest that gamma-mangostin is a novel competitive antagonist, free from a nitrogen atom, for the 5-HT_{2A} receptors in vascular smooth muscles and platelets.

PMID: 9459569 [PubMed - indexed for MEDLINE]

Gopalakrishnan G, Banumathi B, Suresh G.

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

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

PMID: 9213587 [PubMed - indexed for MEDLINE]

Evaluation of the antifungal activity of natural xanthenes 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 xanthenes 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 xanthenes 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]

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

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

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

PMID: 8957258 [PubMed - indexed for MEDLINE]

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

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

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

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]

Chairungsrilerd N, Furukawa K, Ohta T, Nozoe S, Ohizumi Y.
Histaminergic and serotonergic receptor blocking substances from the medicinal plant *Garcinia mangostana*.

Planta Med. 1996 Oct;62(5):471-2.
PMID: 8923814 [PubMed - indexed for MEDLINE]

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]

Iinuma M, Tosa H, Tanaka T, Asai F, Kobayashi Y, Shimano R, Miyauchi K.
Antibacterial activity of xanthenes from guttiferaceous plants against methicillin-resistant *Staphylococcus aureus*.

J Pharm Pharmacol. 1996 Aug;48(8):861-5.
PMID: 8887739 [PubMed - indexed for MEDLINE]

Antibacterial activity of xanthenes from guttiferaceous 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 xanthenes 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]

Furukawa K, Shibusawa K, Chairungsrilerd N, Ohta T, Nozoe S, Ohizumi Y.
The mode of inhibitory action of alpha-mangostin, a novel inhibitor, on the sarcoplasmic reticulum Ca(2+)-pumping ATPase from rabbit skeletal muscle.

Jpn J Pharmacol. 1996 Aug;71(4):337-40.
PMID: 8886932 [PubMed - indexed for MEDLINE]

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]

Chen SX, Wan M, Loh BN.
Active constituents against HIV-1 protease from *Garcinia mangostana*.
Planta Med. 1996 Aug;62(4):381-2.
PMID: 8792678 [PubMed - indexed for MEDLINE]

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.

PMID: 8792678 [PubMed - indexed for MEDLINE]

Williams P, Ongsakul M, Proudfoot J, Croft K, Beilin L.
Mangostin inhibits the oxidative modification of human low density lipoprotein.
Free Radic Res. 1995 Aug;23(2):175-84.
PMID: 7581813 [PubMed - indexed for MEDLINE]

Mangostin inhibits the oxidative modification of human low density lipoprotein.

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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 (Cu^{2+}) and independent (aqueous peroxy 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 μM 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 μM Cu^{2+} in the presence or absence of 50 μM or 100 μM mangostin. We observed an inhibition of TBARS formation with 100 μM mangostin at 4 hours ($P = 0.027$) but not at 24 hours ($P = 0.163$). Similar results were observed in the presence of 50 μM mangostin. Mangostin, at 100 μM , retarded the relative electrophoretic mobility of LDL at both 4 and 24 hours after Cu^{2+} induced oxidation. Mangostin (100 μM) significantly inhibited the consumption of alpha-tocopherol in the LDL during Cu^{2+} 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.

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Jinsart W, Ternai B, Buddhasukh D, Polya GM.
Inhibition of wheat embryo calcium-dependent
protein kinase and other kinases by mangostin and gamma-mangostin.

Phytochemistry. 1992 Nov;31(11):3711-3.
PMID: 1368866 [PubMed - indexed for MEDLINE]

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

Jinsart W, Ternai B, Buddhasukh D, Polya GM.

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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 xanthenes 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 xanthenes 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 xanthenes.

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Sundaram BM, Gopalakrishnan C, Subramanian S, Shankaranarayanan D, Kameswaran L.
Antimicrobial activities of *Garcinia mangostana*.
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Gopalakrishnan C, Shankaranarayanan D, Kameswaran L, Nazimudeen SK.
Effect of mangostin, a xanthone from *Garcinia mangostana* Linn. in immunopathological & inflammatory reactions.
Indian J Exp Biol. 1980 Aug;18(8):843-6. No abstract available.
PMID: 7461736 [PubMed - indexed for MEDLINE]

Effect of mangostin, a xanthone from *Garcinia mangostana* Linn. in immunopathological & inflammatory reactions.

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Shankaranarayanan D, Gopalakrishnan C, Kameswaran L.
Pharmacological profile of mangostin and its derivatives.
Arch Int Pharmacodyn Ther. 1979 Jun;239(2):257-69.
PMID: 314790 [PubMed - indexed for MEDLINE]

Pharmacological profile of mangostin and its derivatives.

Shankaranarayanan 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-O-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... M, IM and MT produced pronounced antiinflammatory activity both by intraperitoneal and oral routes in rats as tested by carrageenin-induced 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.

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

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Abstract

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 (0–50 g/ml) for 48 h 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 ED50 of 9.25 ± 0.64 g/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.

Antiproliferation = stops the cell from spreading

Antioxidation = stops free radical damage which can result in further mutation

Induction of apoptosis = This is a process of cell death - Apoptotic cells break into smaller pieces called apoptotic bodies that other body cells recognize and eat.