

Inhibitory effects of crude alpha-mangostin, a xanthone derivative, on two different categories of colon preneoplastic lesions induced by 1, 2-dimethylhydrazine in the rat.

Nabandith V, Suzui M, Morioka T, Kaneshiro T, Kinjo T, Matsumoto K, Akao Y, Iinuma M, Yoshimi N.

Tumor Pathology Division, Faculty of Medicine, University of the Ryukyus, Okinawa 903-0215, Japan.

The purpose of this study was to examine whether crude alpha-mangostin (a major xanthone derivative in mangosteen pericarp (*Garcinia mangostana*)) has short-term chemopreventive effects on putative preneoplastic lesions involved in rat colon carcinogenesis. The crude preparation was obtained by simple recrystallization of an ethylacetate extract of mangosteen pericarps. A total of 33 five-week-old male F344 rats were randomly divided into 5 experimental groups. Rats in groups 1-3 were given a subcutaneous injection of 1,2-dimethylhydrazine (DMH)(40 mg/kg body weight) once a week for 2 weeks. Starting one week before the first injection of DMH, rats in groups 2 and 3 were fed a diet containing 0.02% and 0.05% crude alpha-mangostin, respectively, for 5 weeks. Rats in group 4 also received the diet containing 0.05% crude alpha-mangostin, while rats in group 5 served as untreated controls. The experiment was terminated 5 weeks after the start. Dietary administration of crude alpha-mangostin at both doses significantly inhibited the induction and/or development of aberrant crypt foci (ACF) ($P < 0.05$ for 0.02% crude alpha-mangostin, $P < 0.01$ for 0.05% crude alpha-mangostin), when compared to the DMH-treated group (group 1). Moreover, treatment of rats with 0.05% crude alpha-mangostin significantly decreased dysplastic foci (DF) ($P < 0.05$) and beta-catenin accumulated crypts (BCAC) ($P < 0.05$), to below the group 1 values. The proliferating cell nuclear antigen (PCNA) labeling indices of colon epithelium and focal lesions in groups 2 and 3 were also significantly lower than in group 1 and this effect occurred in a dose dependent manner of the crude alpha-mangostin. **This finding that crude alpha-mangostin has potent chemopreventive effects in our short-term colon carcinogenesis bioassay system suggests that longer exposure might result in suppression of tumor development.**

PMID: 15546251 [PubMed - indexed for MEDLINE]

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, Bangkok 10400, Thailand. typmk@mahidol.ac.th

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 microg/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 ED(50) of 9.25+/-0.64 microg/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 - indexed for MEDLINE]

A geranylated biphenyl derivative from *Garcinia malvostana*.

[Dharmaratne HR](#), [Piyasena KG](#), [Tennakoon SB](#).

Natural Products Programme, Institute of Fundamental Studies, Kandy 20000, Sri Lanka. hrwd@ifs.ac.lk

Extracts of root bark, stem bark and the latex collected from the green fruits of *Garcinia mangostana* gave alpha-mangostin, beta-mangostin, gamma-mangostin, garcinone-E, methoxy-beta-mangostin and a new geranylated biphenyl derivative 3-hydroxy-4-geranyl-5-methoxybiphenyl. The latex of *G. mangostana* consists of more than 75% of xanthenes which have strong antibacterial (anti-MRSA and -VRE), anti-inflammatory, antifungal and a number of other biological activities. Hence the presence of the above highly bioactive compounds in large quantities should be the causative factor for *G. mangostana*'s medicinal value in indigenous medicine.

PMID: 15702637 [PubMed - indexed for MEDLINE]

Preferential target is mitochondria in alpha-mangostin-induced apoptosis in human leukemia HL60 cells.

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

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

Our previous study has shown that alpha-mangostin, a xanthone from the pericarps of mangosteen, induces caspase-3-dependent apoptosis in HL60 cells. In the current study, we investigated the mechanism of apoptosis induced by alpha-mangostin in HL60 cells. Alpha-mangostin-treated HL60 cells demonstrated caspase-9 and -3 activation but not -8, which leads us to assume that alpha-mangostin may mediate the mitochondrial pathway in the apoptosis. Parameters of mitochondrial dysfunction including swelling, loss of membrane potential (deltapsim), decrease in intracellular ATP, ROS accumulation, and cytochrome c/AIF release, were observed within 1 or 2 h after the treatment. On the other hand, alpha-mangostin-treatment did not affect expression of bcl-2 family proteins and activation of MAP kinases. These findings indicate that alpha-mangostin preferentially targets mitochondria in the early phase, resulting in indication of apoptosis in HL60 cells. Furthermore, we examined the structure-activity relationship between xanthone derivatives including alpha-mangostin and the potency of deltapsim-loss in HL60 cells. Interestingly, replacement of hydroxyl group by methoxy group remarkably decreased its potency. It was also shown that the cytotoxicity substantially correlated with deltapsim decrease. These results indicate that alpha-mangostin and its analogs would be candidates for preventive and therapeutic application for cancer treatment.

PMID: 15498656 [PubMed - indexed for MEDLINE]

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.

Gifu International Institute of Biotechnology, 1-1 Naka-Fudogaoka, Kakamigahara, 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 - indexed for MEDLINE]

Fitoterapia. 2004 Jun;75(3-4):375-7.

[Related Articles, Links](#)

Antiproliferative activity of Thai medicinal plant extracts on human breast adenocarcinoma cell line.

Moongkarndi P, Kosem N, Luanratana O, Jongsomboonkusol S, Pongpan N.

Department of Microbiology, Faculty of Pharmacy, Mahidol University, Rajdhevee, Sri Ayudthaya Rd, Bangkok 10400, Thailand.
pypmk@mahidol.ac.th

Ethanollic extracts of selected nine Thai medicinal plants were tested for antiproliferative activity against SKBR3 human breast adenocarcinoma cell line using MTT assay. *Garcinia mangostana* showed the most potent activity. However, all plant extracts showed activity in potential range for further investigation on cancer cells. Copyright 2004 Elsevier B.V.

PMID: 15158999 [PubMed - indexed for MEDLINE]

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

[Related Articles, Links](#)

Antimycobacterial activity of prenylated xanthenes 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 xanthenes, 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 xanthenes 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 - indexed for MEDLINE]

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

[Related Articles, Links](#)

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]

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]

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]

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]

[J Ethnopharmacol.](#) 2005 Oct 3;101(1-3):330-3. [Links](#)

Antimicrobial effects of Thai medicinal plants against acne-inducing bacteria.

[Chomnawang MT](#), [Surassmo S](#), [Nukoolkarn VS](#), [Gritsanapan W](#).

Department of Microbiology, Faculty of Pharmacy, Mahidol University, 447 Sri Ayudthaya Road, Rachathevi, Bangkok 10400, Thailand. scmt@mahidol.ac.th

Propionibacterium acnes and *Staphylococcus epidermidis* have been recognized as pus-forming bacteria triggering an inflammation in acne. The present study was conducted to evaluate antimicrobial activities of Thai medicinal plants against these etiologic agents of acne vulgaris. Crude extracts were tested for antimicrobial activities by disc diffusion and broth dilution methods. The results from the disc diffusion method showed that 13 medicinal plants could inhibit the growth of *Propionibacterium acnes*. Among those, *Senna alata*, *Eupatorium odoratum*, *Garcinia mangostana*, and *Barleria lupulina* had strong inhibitory effects. Based on a broth dilution method, the *Garcinia mangostana* extract had the greatest antimicrobial effect. The MIC values were the same (0.039 mg/ml) for both bacterial species and the MBC values were 0.039 and 0.156 mg/ml against *Propionibacterium acnes* and *Staphylococcus epidermidis*, respectively. In bioautography assay, the *Garcinia mangostana* extract produced strong inhibition zones against *Propionibacterium acnes*. Antimicrobial activity from fractions of column chromatography revealed one of the active compounds in *Garcinia mangostana* could be mangostin, a xanthone derivative. **Taken together, our data indicated that *Garcinia mangostana* had a strong inhibitory effect on *Propionibacterium acnes* and *Staphylococcus epidermidis*. Therefore, this plant would be an interesting topic for further study and possibly for an alternative treatment for acne.**

PMID: 16009519 [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* var. *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]

Activity of medicinal plant extracts against hospital isolates of methicillin-resistant *Staphylococcus aureus*.

[Voravuthikunchai SP](#), [Kitpipit L](#).

Department of Microbiology, Faculty of Science, Prince of Songkla University, Hatyai, Songkla, Thailand. supayang.v@psu.ac.th

Aqueous and ethanolic extracts of ten traditional Thai medicinal plants were investigated for their ability to inhibit 35 hospital isolates of methicillin-resistant *Staphylococcus aureus* (MRSA). Nine medicinal plants displayed activity against all isolates tested. Ethanolic extracts of *Garcinia mangostana*, *Punica granatum* and *Quercus infectoria* were most effective, with MICs for MRSA isolates of 0.05-0.4, 0.2-0.4 and 0.2-0.4 mg/mL, respectively, and for *S. aureus* ATCC 25923 of 0.1, 0.2 and 0.1 mg/mL, respectively. MBCs for MRSA isolates were 0.1-0.4, 1.6-3.2 and 0.4-1.6 mg/mL, and for *S. aureus* ATCC 25923 were 0.4, 3.2 and 1.6 mg/mL, respectively.

PMID: 15882206 [PubMed - in process]

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

Chairungrilerd 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.

PMID: 8923814 [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.

Department of Chemistry, La Trobe University, Bundoora, Victoria, Australia.

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.

PMID: 1368866 [PubMed - indexed for MEDLINE]

gamma-Mangostin inhibits inhibitor-kappaB kinase activity and decreases lipopolysaccharide-induced cyclooxygenase-2 gene expression in C6 rat glioma cells.

[Nakatani K](#), [Yamakuni T](#), [Kondo N](#), [Arakawa T](#), [Oosawa K](#), [Shimura S](#), [Inoue H](#), [Ohizumi Y](#).

Department of Pharmaceutical Molecular Biology, Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan.

We investigated the effect of gamma-mangostin purified from the fruit hull of the medicinal plant *Garcinia mangostana* on spontaneous prostaglandin E(2) (PGE(2)) release and inducible cyclooxygenase-2 (COX-2) gene expression in C6 rat glioma cells. An 18-h treatment with gamma-mangostin potently inhibited spontaneous PGE(2) release in a concentration-dependent manner with the IC(50) value of approximately 2 microM, without affecting the cell viability even at 30 microM. By immunoblotting and reverse-transcription polymerase chain reaction, we showed that gamma-mangostin concentration-dependently inhibited lipopolysaccharide (LPS)-induced expression of COX-2 protein and its mRNA, but not those of constitutive COX-1 cyclooxygenase. Because LPS is known to stimulate inhibitor kappaB (IkappaB) kinase (IKK)-mediated phosphorylation of IkappaB followed by its degradation, which in turn induces nuclear factor (NF)-kappaB nuclear translocation leading to transcriptional activation of COX-2 gene, the effect of gamma-mangostin on the IKK/IkappaB cascade controlling the NF-kappaB activation was examined. An in vitro IKK assay using IKK protein immunoprecipitated from C6 cell extract showed that this compound inhibited IKK activity in a concentration-dependent manner, with the IC(50) value of approximately 10 microM. Consistently gamma-mangostin was also observed to decrease the LPS-induced IkappaB degradation and phosphorylation in a concentration-dependent manner, as assayed by immunoblotting. Furthermore, luciferase reporter assays showed that gamma-mangostin reduced the LPS-inducible activation of NF-kappaB and human COX-2 gene promoter region-dependent transcription. gamma-Mangostin also inhibited rat carrageenan-induced paw edema. These results suggest that gamma-mangostin directly inhibits IKK activity and thereby prevents COX-2 gene transcription, an NF-kappaB target gene, probably to decrease the inflammatory agent-stimulated PGE(2) production in vivo, and is a new useful lead compound for anti-inflammatory drug development.

PMID: 15322259 [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]

Alpha-mangostin induces Ca²⁺-ATPase-dependent apoptosis via mitochondrial pathway in PC12 cells.

[Sato A](#), [Fujiwara H](#), [Oku H](#), [Ishiguro K](#), [Ohizumi Y](#).

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

We investigated the cell death effects of eight xanthenes on PC12 rat pheochromocytoma cells. Among these compounds, alpha-mangostin, from the fruit hull of *Garcinia mangostana* L., had the most potent effect with the EC(50) value of 4 microM. Alpha-mangostin-treated PC12 cells demonstrated typical apoptotic DNA fragmentation and caspase-3 cleavage (equivalent to activation). The flow cytometric analysis indicated that this compound induced apoptosis in time- and concentration-dependent manners. Alpha-mangostin showed the features of the mitochondrial apoptotic pathway such as mitochondrial membrane depolarization and cytochrome c release. Furthermore, alpha-mangostin inhibited the sarco(endo)plasmic reticulum Ca(2+)-ATPase markedly. There was a correlation between the Ca(2+)-ATPase inhibitory effects and the apoptotic effects of the xanthone derivatives. On the other hand, c-Jun NH(2)-terminal kinase (JNK/SAPK), one of the signaling molecules of endoplasmic reticulum (ER) stress, was activated with alpha-mangostin treatment. These results suggest that alpha-mangostin inhibits Ca(2+)-ATPase to cause apoptosis through the mitochondrial pathway.

PMID: 15153648 [PubMed - indexed for MEDLINE]

Antibacterial activity of alpha-mangostin against vancomycin resistant Enterococci (VRE) and synergism with antibiotics.

[Sakagami Y](#), [Iinuma M](#), [Piyasena KG](#), [Dharmaratne HR](#).

Osaka Prefectural Institute of Public Health, Osaka, Japan. sakagami@iph.pref.osaka.jp

alpha-Mangostin, isolated from the stem bark of *Garcinia mangostana* L., was found to be active against vancomycin resistant Enterococci (VRE) and methicillin resistant *Staphylococcus aureus* (MRSA), with MIC values of 6.25 and 6.25 to 12.5 microg/ml, respectively. Our studies showed synergism between alpha-mangostin and gentamicin (GM) against VRE, and alpha-mangostin and vancomycin hydrochloride (VCM) against MRSA. Further studies showed partial synergism between alpha-mangostin and commercially available antibiotics such as ampicillin and minocycline. These findings suggested that alpha-mangostin alone or in combination with GM against VRE and in combination with VCM against MRSA might be useful in controlling VRE and MRSA infections.

PMID: 15830842 [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.

Publication Types:
Letter

PMID: 8792678 [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](#), [Chairungrilerd 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]

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

[Chairungsrierd 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]

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

[Article in Japanese]

[Furukawa K](#), [Chairungsrierd 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]

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

[Chairungrilerd 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 ($pA_2 = 8.2$) without affecting the contractile responses to KCl, phenylephrine (α_1) or histamine (H1). The perfusion pressure response of rat coronary artery to 5-HT (5-HT_{2A}) was reduced concentration dependently by gamma-mangostin ($IC_{50} = 0.32 \mu M$). 5-HT amplified, ADP-induced aggregation of rabbit platelets (5-HT_{2A}) was inhibited by gamma-mangostin ($IC_{50} = 0.29 \mu M$), 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 μM). Gamma-mangostin inhibited [³H]spiperone binding to cultured rat aortic myocytes ($IC_{50} = 3.5 \text{ nM}$). 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]

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 (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.**

PMID: 7581813 [PubMed - indexed for MEDLINE]

Antimicrobial activities of *Garcinia mangostana*.

[Sundaram BM](#), [Gopalakrishnan C](#), [Subramanian S](#), [Shankaranarayanan D](#), [Kameswaran L](#).

PMID: 6611746 [PubMed - indexed for MEDLINE]

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

[Gopalakrishnan C](#), [Shankaranarayanan D](#), [Kameswaran L](#), [Nazimudeen SK](#).

PMID: 7461736 [PubMed - indexed for MEDLINE]

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

[Related Articles](#), [Links](#)

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-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. 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 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.

PMID: 314790 [PubMed - indexed for MEDLINE]

[Chem Pharm Bull \(Tokyo\)](#). 2006 Mar;54(3):301-5.

[Related Articles](#), [Links](#)

Cytotoxic Prenylated Xanthenes from the Young Fruit of *Garcinia mangostana*.

[Suksamrarn S](#), [Komutiban O](#), [Ratananukul P](#), [Chimnoi N](#), [Lartpornmatulee N](#), [Suksamrarn A](#).

Department of Chemistry, Faculty of Science, Srinakharinwirot University.

Three new prenylated xanthenes, mangostenones C (1), D (2), and E (3), together with 16 known xanthenes 4-19, were isolated from the young fruit (7-week maturity stage) of *Garcinia mangostana*. The structural elucidation of the new compounds was mainly established on the basis of 1D and 2D NMR and HR-MS spectroscopic analysis. Compound 1 showed cytotoxic properties against three human cancer cell lines, epidermoid carcinoma of the mouth (KB), breast cancer (BC-1), and small cell lung cancer (NCI-H187), with IC(50) values of 2.8, 3.53, and 3.72 µg/ml, respectively. **Among the isolates, alpha-mangostin (12), the major metabolite, exhibited the most potent effects against the BC-1 cells with an IC(50) value of 0.92 µg/ml, an activity greater than that of the standard drug ellipticine (IC(50)=1.46 µg/ml). Compound 12 also showed the highest activity against KB cells, while gartanin (10) displayed the strongest activity against the NCI-H187 cells at the respective IC(50) values of 2.08 µg/ml and 1.08 µg/ml.**

PMID: 16508181 [PubMed - in process]

Effects of herbal mouthwash containing the pericarp extract of *Garcinia mangostana* L on halitosis, plaque and papillary bleeding index.

[Rassameemasmaung S](#), [Sirikulsathean A](#), [Amornchat C](#), [Hirunrat K](#), [Rojanapanthu P](#), [Gritsanapan W](#).

Department of Oral Medicine, Faculty of Dentistry, Mahidol University, Bangkok, Thailand. dtsrs@mahidol.ac.th

OBJECTIVES: To determine the effects of herbal mouthwash containing the pericarp extract of *Garcinia mangostana* L on volatile sulfur compound (VSC) levels, plaque index (PI) and papillary bleeding index (PBI) in gingivitis subjects and the recurrence of these parameters after periodontal treatment. **METHODS:** Sixty subjects who were diagnosed as having mild or moderate chronic gingivitis were randomly distributed into herbal or placebo mouthwash groups. On day 1, all parameters were recorded. Subjects rinsed with the assigned mouthwash and VSC was measured at 30 min and 3 h post-rinsing. For the following 2 weeks, subjects practiced their usual oral hygiene and rinsed with the assigned mouthwash twice daily after tooth brushing. On day 15, parameters were recorded. In the 4-week washout period that followed, subjects received scaling and polishing. After another baseline examination, they were re-randomized into the herbal or placebo group and rinsed with mouthwash for 2 weeks. All parameters were re-evaluated on day 15. **RESULTS:** All parameters were significantly different compared to baseline in both groups at 30 min, 3 h and day 15 ($p < 0.05$). When compared between groups, VSC was significantly different at day 15 ($p < 0.05$). After scaling, polishing and rinsing with mouthwash for 2 weeks, PI and PBI were significantly different compared to baseline ($p < 0.05$) while VSC was not ($p > 0.05$). When compared between groups, VSC was significantly different ($p < 0.05$).

CONCLUSION: Herbal mouthwash containing the pericarp extract of *G. mangostana* may be used as an adjunct in treating oral malodor.

PMID: 17274236 [PubMed - indexed for MEDLINE]

Characterized mechanism of alpha-mangostin-induced cell death: caspase-independent apoptosis with release of endonuclease-G from mitochondria and increased miR-143 expression in human colorectal cancer DLD-1 cells.

[Nakagawa Y](#), [Iinuma M](#), [Naoe T](#), [Nozawa Y](#), [Akao Y](#).

Gifu International Institute of Biotechnology, 1-1 Naka-Fudogaoka, Kakamigahara, Gifu 504-0838, Japan.

alpha-Mangostin, a xanthone from the pericarps of mangosteen (*Garcinia mangostana* Linn.), was evaluated for in vitro cytotoxicity against human colon cancer DLD-1 cells. The number of viable cells was consistently decreased by the treatment with alpha-mangostin at more than 20 microM. The cytotoxic effect of 20 microM alpha-mangostin was found to be mainly due to apoptosis, as indicated by morphological findings. Western blotting, the results of an apoptosis inhibition assay using caspase inhibitors, and the examination of caspase activity did not demonstrate the activation of any of the caspases tested. However, endonuclease-G released from mitochondria with the decreased mitochondrial membrane potential was shown. The levels of phospho-Erk1/2 were increased in the early phase until 1h after the start of treatment and thereafter decreased, and increased again in the late phase. On the other hand, the level of phospho-Akt was sharply reduced with the process of apoptosis after 6h of treatment. Interestingly, the level of microRNA-143, which negatively regulates Erk5 at translation, gradually increased until 24h following the start of treatment. We also examined the synergistic growth suppression in DLD-1 cells by the combined treatment of the cells with alpha-mangostin and 5-FU which is one of the most effective chemotherapeutic agents for colorectal adenocarcinoma. The co-treatment with alpha-mangostin and 5-FU, both at 2.5 microM, augmented growth inhibition compared with the treatment with 5 microM of alpha-mangostin or 5 microM 5-FU alone. These findings indicate unique mechanisms of alpha-mangostin-induced apoptosis and its action as an effective chemosensitizer.

PMID: 17553685 [PubMed - indexed for MEDLINE]

Antimicrobial activity in cultures of endophytic fungi isolated from *Garcinia* species.

[Phongpaichit S](#), [Rungjindamai N](#), [Rukachaisirikul V](#), [Sakayaroj J](#).

Natural Products Research Unit and Department of Microbiology, Faculty of Science, Prince of Songkla University, Hat Yai, Songkla, Thailand. souwalak.p@psu.ac.th

The aim of the present study was to screen for antimicrobial activity in endophytic fungi isolated from surface sterilized leaves and branches of five *Garcinia* plants, *G. atroviridis*, *G. dulcis*, *G. mangostana*, *G. nigrolineata* and *G. scortechinii*, found in southern Thailand. Fermentation broths from 377 isolated fungi were tested for antimicrobial activity by the agar diffusion method. Minimum inhibitory concentrations (MICs) were obtained for crude ethyl acetate extracts. Seventy isolates (18.6%) displayed antimicrobial activity against at least one pathogenic microorganism, such as *Staphylococcus aureus*, a clinical isolate of methicillin-resistant *S. aureus*, *Candida albicans* and *Cryptococcus neoformans*. The results revealed that 6-10%, 1-2% and 18% of the crude ethyl acetate extracts inhibited both strains of *S. aureus* (MIC 32-512 microg mL(-1)), *Ca. albicans* and *Cr. neoformans* (MIC 64-200 microg mL(-1)), and *Microsporium gypseum* (MIC 2-64 microg mL(-1)), respectively. Isolates D15 and M76 displayed the strongest antibacterial activity against both strains of *S. aureus*. Isolates M76 and N24 displayed strong antifungal activity against *M. gypseum*. Fungal molecular identification based on internal transcribed spacer rRNA gene sequence analysis demonstrated that isolates D15 (DQ480353), M76 (DQ480360) and N24 (DQ480361) represented *Phomopsis* sp., *Botryosphaeria* sp. and an unidentified fungal endophyte, respectively. **These results indicate that some endophytic fungi from *Garcinia* plants are a potential source of antimicrobial agents.**

PMID: 17052267 [PubMed - indexed for MEDLINE]

Effect of *Garcinia mangostana* on inflammation caused by *Propionibacterium acnes*.

[Chomnawang MT](#), [Surassmo S](#), [Nukoolkarn VS](#), [Gritsanapan W](#).

Department of Microbiology, Faculty of Pharmacy, Mahidol University, 447 Sri Ayudthaya Road, Rachathevi, Bangkok, 10400, Thailand.

The present study was aimed to investigate the activity of Thai medicinal plants on inflammation caused by *Propionibacterium acnes* in terms of free radical scavenging and cytokine reducing properties. *P. acnes* have been recognized as pus-forming bacteria triggering an inflammation in acne. Antioxidant activity was determined by DPPH scavenging and NBT reduction assay. **The result showed that *Garcinia mangostana* possessed the most significant antioxidant activity and reduced reactive oxygen species production.** *Houttuynia cordata*, *Eupatorium odoratum*, and *Senna alata* had a moderate antioxidant effect. In addition, *Garcinia mangostana* extracts could reduce the TNF-alpha production as determined by ELISA. ***Garcinia mangostana* was highly effective in scavenging free radicals and was able to suppress the production of pro-inflammatory cytokines. This study has identified the promising source of anti-inflammatory agent which could be useful in treatment of acne vulgaris.**

PMID: 17644272 [PubMed - in process]

Antioxidant xanthenes from the pericarp of *Garcinia mangostana* (Mangosteen).

[Jung HA](#), [Su BN](#), [Keller WJ](#), [Mehta RG](#), [Kinghorn AD](#).

Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, Ohio 43210, USA.

As part of ongoing research on cancer chemopreventive agents from botanical dietary supplements, *Garcinia mangostana* L. (commonly known as mangosteen) was selected for detailed study. Repeated chromatography of a CH₂Cl₂-soluble extract of the pericarp led to the isolation of two new highly oxygenated prenylated xanthenes, 8-hydroxycudraxanthone G (1) and mangostingone [7-methoxy-2-(3-methyl-2-butenyl)-8-(3-methyl-2-oxo-3-butenyl)-1,3,6-trihydroxyxanthone, 2], together with 12 known xanthenes, cudraxanthone G (3), 8-deoxygartanin (4), garcimangosone B (5), garcinone D (6), garcinone E (7), gartanin (8), 1-isomangostin (9), alpha-mangostin (10), gamma-mangostin (11), mangostinone (12), smeathxanthone A (13), and tovophyllin A (14). The structures of compounds 1 and 2 were elucidated by spectroscopic data analysis. Except for compound 2, which was isolated as a minor component, the antioxidant activities of all isolates were determined using authentic and morpholinopyridone-derived peroxyxanthone methods, and compounds 1, 8, 10, 11, and 13 were the most active. Alpha-mangostin (10) inhibited 7,12-dimethylbenz[alpha]anthracene-induced preneoplastic lesions in a mouse mammary organ culture assay with an IC₅₀ of 1.0 microg/mL (2.44 microM).

PMID: 16536578 [PubMed - indexed for MEDLINE]

Antioxidative and neuroprotective activities of extracts from the fruit hull of mangosteen (*Garcinia mangostana* Linn.).

[Weecharangsan W](#), [Opanasopit P](#), [Sukma M](#), [Ngawhirunpat T](#), [Sotanaphun U](#), [Siripong P](#).

Faculty of Pharmacy, Silpakorn University, Nakhonpathom, Thailand.

OBJECTIVE: The aim of this study was to investigate the antioxidative and neuroprotective activities of various extracts from the fruit hull of mangosteen (*Garcinia mangostana* Linn., GM). **MATERIALS AND METHODS:** Four extracts: water, 50% ethanol, 95% ethanol and ethyl acetate, were used. The antioxidative activity was evaluated using 2,2-diphenyl-1-picrylhydrazyl free-radical scavenging assay at extract concentrations of 1, 10, 50 and 100 microg/ml. Based on the free radical scavenging activity of the extracts, two (water and 50% ethanol) were selected for their protective activity in NG108-15 neuroblastoma cells against H₂O₂-induced oxidative stress and for cell viability using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay. **RESULTS:** All extracts exhibited antioxidative activity. The water and 50% ethanol extracts showed high free-radical scavenging activity with IC₅₀ values of 34.98 +/- 2.24 and 30.76 +/- 1.66 microg/ml, respectively. Both water and 50% ethanol extracts exhibited neuroprotective activity on NG108-15 cells. The highest activity was observed at the concentration of 50 microg/ml for both the water and 50% ethanol extracts. For cytotoxicity test, none of the extracts was toxic to the cells except at the high concentration of 100 microg/ml. **CONCLUSIONS:** These results suggest that the water and 50% ethanol extracts from the fruit hull of GM may be potent neuroprotectants.

PMID: 16763395 [PubMed - indexed for MEDLINE]

[Planta Med.](#) 2006 Aug;72(10):912-6. Epub 2006 Aug 10. [Links](#)

Prenylated xanthenes as potential antiplasmodial substances.

[Mahabusarakam W](#), [Kuaha K](#), [Wilairat P](#), [Taylor WC](#).

Department of Chemistry, Prince of Songkla University, Hat Yai, Songkhla, Thailand. wilawan.m@psu.ac.th

Mangostin, the major xanthone of *Garcinia mangostana*, and a series of synthetic derivatives were investigated for their in vitro antiplasmodial activity against *Plasmodium falciparum*. Mangostin itself showed moderate activity, but prenylated xanthenes containing alkylamino functional groups exhibited quite potent antiplasmodial activity. Some structure-activity relationships are proposed.

PMID: 16902859 [PubMed - indexed for MEDLINE]

[J Agric Food Chem.](#) 2007 Nov 28;55(24):9805-10. Epub 2007 Oct 26.

Assay-guided Fractionation Study of alpha-Amylase Inhibitors from *Garcinia mangostana* Pericarp.

[Eng Kiat Loo A](#), [Huang D](#).

chmhdj@nus.edu.sg.

alpha-Amylase inhibitor (alpha-AI) activity of *Garcinia mangostana*, commonly known as mangosteen, pericarp extracts was studied by assay guided fractionations from lipophilic to hydrophilic using combined solvent extraction and Amberlite XAD2 adsorption chromatography. Neither the lipophilic, xanthone containing fraction, nor the highly polar fraction, which has no affinity on Amberlite XAD2, showed any alpha-AI. The fraction that shows very high inhibitory activity contains primarily polyphenols and can be adsorbed on Amberlite XAD2. The IC₅₀ of 5.4 microg/mL of this fraction is comparable to that of acarbose, a prescribed alpha-AI used in the control of type II diabetes, at 5.2 microg/mL. Total phenolic content (TPC) of each fraction was measured and the TPC has no correlation with the alpha-AI activity. The lipophilic fraction contains mainly xanthenes as revealed by HPLC-MS analysis. Colorimetric analysis coupled with UV-vis and IR spectroscopic analysis demonstrated that the fractions with high alpha-AI activity are primarily oligomeric proanthocyanidins (OPCs) with little gallate moiety. There is also evidence to show that the alpha-AI by these OPCs is not purely by nonspecific protein complexation. Both tannic acid and *G. mangostana* OPCs precipitate BSA equally well but *G. mangostana* OPCs are 56 times more effective in inhibiting alpha-amylase.

PMID: 17960880 [PubMed - as supplied by publisher]

[Bioorg Med Chem.](#) 2008 Apr 15;16(8):4500-8. Epub 2008 Feb 21.

Inhibitory effect of xanthenes isolated from the pericarp of *Garcinia mangostana* L. on rat basophilic leukemia RBL-2H3 cell degranulation.

[Itoh T](#), [Ohguchi K](#), [Inuma M](#), [Nozawa Y](#), [Akao Y](#).

Gifu International Institute of Biotechnology, Bio-active Substances Research, 1-1 Naka-Fudogaoka, Kakamigahara, Gifu 504-0838, Japan.

Mangostin, *Garcinia mangostana* L. is used as a traditional medicine in southeast Asia for inflammatory and septic ailments. Hitherto we indicated the anticancer activity induced by xanthenes such as alpha-, beta-, and gamma-mangostin which were major constituents of the pericarp of mangosteen fruits. In this study, we examined the effect of xanthenes on cell degranulation in rat basophilic leukemia RBL-2H3 cells. Antigen (Ag)-mediated stimulation of high affinity IgE receptor (FcεRI) activates intracellular signal transductions resulting in the release of biologically active mediators such as histamine. The release of histamine and other inflammatory mediators from mast cell or basophils is the primary event in several allergic responses. These xanthenes suppressed the release of histamine from IgE-sensitized RBL-2H3 cells. In order to reveal the inhibitory mechanism of degranulation by xanthenes, we examined the activation of intracellular signaling molecules such as Lyn, Syk, and PLCγ. All the xanthenes tested significantly suppressed the signaling involving Syk and PLCγ. In Ag-mediated activation of FcεRI on mast cells, three major subfamilies of mitogen-activated protein kinases were activated. The xanthenes decreased the level of phospho-ERKs. Furthermore, the levels of phospho-ERKs were observed to be regulated by Syk/LAT/Ras/ERK pathway rather than PKC/Raf/ERK pathway, suggesting that the inhibitory mechanism of xanthenes was mainly due to suppression of the Syk/PLCγ/PKC pathway. Although intracellular free Ca²⁺ concentration ([Ca²⁺]_i) was elevated by FcεRI activation, it was found that alpha- or gamma-mangostin treatment was reduced the [Ca²⁺]_i elevation by suppressed Ca²⁺ influx.

PMID: 18328716 [PubMed - as supplied by publisher]

[Food Chem Toxicol.](#) 2008 Feb;46(2):688-93. Epub 2007 Sep 26. [Links](#)

Anti-inflammatory activity of mangostins from *Garcinia mangostana*.

[Chen LG](#), [Yang LL](#), [Wang CC](#).

Graduate Institute of Biomedical and Biopharmaceutical Sciences, College of Life Sciences, National Chiayi University, 300 University Road, Chiayi 600, Taiwan, ROC.

The fruit hull of *Garcinia mangostana* Linn (Guttiferae) is used as an anti-inflammatory drug in Southeast Asia. Two xanthenes, alpha- and gamma-mangostins, were isolated from the fruit hull of *G. mangostana*, and both significantly inhibited nitric oxide (NO) and PGE₂ production from lipopolysaccharide (LPS)-stimulated RAW 264.7 cells. The IC₅₀ values for the inhibition of NO production by alpha- and gamma-mangostins were 12.4 and 10.1 microM, respectively. After iNOS enzyme activity was stimulated by LPS for 12 h, treatment with either alpha- or gamma-mangostin at 5 microg/ml (12.2 and 12.6 microM, respectively) for 24 h did not significantly inhibit NO production. The data show that the inhibitory activities of alpha- and gamma-mangostins are not due to direct inhibition of iNOS enzyme activity. On the other hand, expression of iNOS was inhibited by alpha- and gamma-mangostins in LPS-stimulated RAW 264.7 cells, but not by COX-2. However, the level of PGE₂ production was reduced by the two xanthenes. In an in vivo study, alpha-mangostin significantly inhibited mice carrageenan-induced paw edema. In conclusion, alpha- and gamma-mangostins from *G. mangostana* are bioactive substances with anti-inflammatory effects.

PMID: 18029076 [PubMed - in process]

[Exp Toxicol Pathol.](#) 2008 Aug;60(4-5):357-64. Epub 2008 Apr 18.

Ameliorative prospective of alpha-mangostin, a xanthone derivative from *Garcinia mangostana* against beta-adrenergic catecholamine-induced myocardial toxicity and anomalous cardiac TNF-alpha and COX-2 expressions in rats.

[Sampath PD, Vijayaragavan K.](#)

Centre for Advanced Studies in Botany, University of Madras, Guindy Campus, Chennai, India.

Altered membrane integrity and inflammation play a key role in cardiovascular damage. We investigated the salubrious effect of exogenously administered alpha-mangostin against beta-adrenergic catecholamine-induced cardiovascular toxicity with special reference to membrane ATPases, lysosomal hydrolases and inflammatory mediators TNF-alpha and Cyclooxygenase-2 (COX-2) expressions in albino rats. Induction of rats with isoproterenol (150mg/kg body wt, i.p.) for 2 days resulted in a significant increase in the activities of serum and cardiac lysosomal hydrolases (beta-d-glucuronidase, beta-d-galactosidase, beta-d-N-acetylglucosaminidase, acid phosphatase and cathepsin-D). A significant increase in cardiac levels of sodium, calcium with a decrease in the level of potassium paralleled by abnormal activities of membrane-bound phosphatases (Na(+)-K(+) ATPase, Ca(2+) ATPase and Mg(2+) ATPase) were observed in the heart of ISO-administered rats. Cardiac TNF-alpha and COX-2 expressions were assessed by Western blotting. Cardiac TNF-alpha and COX-2 expressions were significantly elevated in ISO-intoxicated rats. Pre-co-treatment with alpha-mangostin (200mg/kg body wt.) orally for 8 days significantly attenuated these abnormalities and restored the levels to near normalcy when compared to ISO intoxicated group of rats. **In conclusion, alpha-mangostin preserves the myocardial membrane integrity and extenuates anomalous TNF-alpha and COX-2 expressions by mitigating ISO-induced oxidative stress and cellular damage effectively. Restoration of cellular normalcy accredits the cytoprotective role of alpha-mangostin.**

PMID: 18424012 [PubMed - as supplied by publisher]

[J Asian Nat Prod Res.](#) 2008 May;10(5):481-5.

***Garcinia mangostana*: a source of potential anti-cancer lead compounds against CEM-SS cell line.**

[Ee GC, Daud S, Izzaddin SA, Rahmani M.](#)

Chemistry Department, Faculty of Science, Universiti Putra Malaysia, Serdang, Selangor, Malaysia.

Our current interest in searching for natural anti-cancer lead compounds from plants has led us to the discovery that the stem and roots of *Garcinia mangostana* can be a source of such compounds. The stem furnished 2,8-dihydroxy-6-methoxy-5-(3-methylbut-2-enyl)-xanthone (1), which is a new xanthone. Meanwhile, the root bark of the plant furnished six xanthones, namely alpha-mangostin (2), beta-mangostin (3), gamma-mangostin (4), garcinone D (5), mangostanol (6), and gartanin (7). The hexane and chloroform extracts of the root bark of *G. mangostana* as well as the hexane extract of the stem bark were found to be active against the CEM-SS cell line. **gamma-Mangostin (4) showed good activity** with a very low IC(50) value of 4.7 mug/ml, while **alpha-mangostin (2), mangostanol (6), and garcinone D (5) showed significant activities** with IC(50) values of 5.5, 9.6, and 3.2 mug/ml, respectively. This is the first report on the cytotoxicity of the extracts of the stem and root bark of *G. mangostana* and of alpha-mangostin, mangostanol, and garcinone D against the CEM-SS cell line.

PMID: 18464091 [PubMed - in process]

Cardioprotective effect of alpha-mangostin, a xanthone derivative from mangosteen on tissue defense system against isoproterenol-induced myocardial infarction in rats.

[Devi Sampath P](#), [Vijayaraghavan K](#).

Centre for Advanced Studies in Botany, University of Madras, Guindy Campus, Chennai, India.

Increased oxidative stress and antioxidant deficit have been suggested to play a major role in isoproterenol-induced myocardial infarction. The present study was designed to evaluate the effect of alpha-mangostin on the antioxidant defense system and lipid peroxidation against isoproterenol-induced myocardial infarction in rats. Induction of rats with ISO (150 mg/kg body weight, ip) for 2 days resulted in a marked elevation in lipid peroxidation, serum marker enzymes (LDH, CPK, GOT, and GPT) and a significant decrease in the activities of endogenous antioxidants (SOD, CAT, GPx, GST, and GSH). Pre-treatment with alpha-mangostin (200 mg/kg of body weight per day) orally for 6 days prior to the ISO administration and 2 days along with ISO administration significantly attenuated these changes when compared to the individual treatment groups. These findings indicate the protective effect of alpha-mangostin on lipid peroxidation and antioxidant tissue defense system during ISO-induced myocardial infarction in rats.

PMID: 17994576 [PubMed - indexed for MEDLINE]

Effects of compounds from *Garcinia mangostana* on inflammatory mediators in RAW264.7 macrophage cells.

[Tewtrakul S](#), [Wattanapiromsakul C](#), [Mahabusarakam W](#).

Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand.

ETHNOPHARMACOLOGICAL RELEVANCE: The fruit hull of *Garcinia mangostana* Linn. has been used in Thai traditional medicine for treatment of abscess and skin infection. **AIM OF THE STUDY:** The mangosteen fruit hull and its compounds were carried out to investigate for anti-inflammatory activity. **MATERIAL AND METHODS:** The extract of *Garcinia mangostana* together with alpha- and gamma-mangostins were tested for anti-inflammatory effect against lipopolysaccharide (LPS)-induced nitric oxide (NO), prostaglandin E(2) (PGE(2)), tumor necrosis factor alpha (TNF-alpha) and interleukin-4 (IL-4) releases as well as their mechanisms in transcriptional levels using RAW264.7 macrophage cells. **RESULTS:** Mangosteen extract possessed potent NO inhibitory effect with an IC(50) value of 1.0µg/ml. The isolated compounds from the extract including alpha-mangostin and gamma-mangostin, possessed marked inhibitory effect against NO release with IC(50) values of 3.1 and 6.0µM, respectively. The extract exhibited potent inhibitory effect on PGE(2) release (IC(50)=6.0µg/ml), whereas those of alpha- and gamma-mangostins were 13.9 and 13.5µM, respectively. However, mangostins possessed only moderate effects towards TNF-alpha and IL-4 releases with IC(50) values ranging from 31.8 to 64.8µM. Both extract and alpha-mangostin suppressed transcription of gene encoding inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in dose-dependent manners, whereas gamma-mangostin had only an inhibitory effect on transcription of iNOS. **CONCLUSION:** The present study may support the Thai traditional use of *Garcinia mangostana* fruit hull for treatment of inflammatory-related diseases through the inhibition of NO and PGE(2) releases, but moderate effect through TNF-alpha and IL-4.

PMID: 19056479 [PubMed - as supplied by publisher]

[J Nat Prod.](#) 2008 Jul;71(7):1161-6. Epub 2008 Jun 18.

Xanthenes from the Botanical Dietary Supplement Mangosteen (*Garcinia mangostana*) with Aromatase Inhibitory Activity.

[Balunas MJ](#), [Su B](#), [Brueggemeier RW](#), [Kinghorn AD](#).

kinghorn.4@osu.edu.

Twelve xanthone constituents of the botanical dietary supplement mangosteen (the pericarp of *Garcinia mangostana*) were screened using a noncellular, enzyme-based microsomal aromatase inhibition assay. Of these compounds, garcinone D (3), garcinone E (5), alpha-mangostin (8), and gamma-mangostin (9) exhibited dose-dependent inhibitory activity. In a follow-up cell-based assay using SK-BR-3 breast cancer cells that express high levels of aromatase, the most potent of these four xanthenes was gamma-mangostin (9). **Because xanthenes may be consumed in substantial amounts from commercially available mangosteen products, the consequences of frequent intake of mangosteen botanical dietary supplements require further investigation to determine their possible role in breast cancer chemoprevention.**

PMID: 18558747 [PubMed - as supplied by publisher]

[Phytochemistry.](#) 2008 Feb;69(3):754-8. Epub 2007 Nov 7.

Xanthenes with quinone reductase-inducing activity from the fruits of *Garcinia mangostana* (Mangosteen).

[Chin YW](#), [Jung HA](#), [Chai H](#), [Keller WJ](#), [Kinghorn AD](#).

Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH 43210, USA.

Bioactivity-guided fractionation of a dichloromethane-soluble extract of *Garcinia mangostana* fruits has led to the isolation and identification of five compounds, including two xanthenes, 1,2-dihydro-1,8,10-trihydroxy-2-(2-hydroxypropan-2-yl)-9-(3-methylbut-2-enyl)furo[3,2-a]xanthen-11-one (1) and 6-deoxy-7-demethylmangostanin (2), along with three known compounds, 1,3,7-trihydroxy-2,8-di-(3-methylbut-2-enyl)xanthone (3), mangostanin (4), and alpha-mangostin (5). The structures of compounds 1 and 2 were determined from analysis of their spectroscopic data. **All isolated compounds in the present study together with eleven other compounds previously isolated from the pericarp of mangosteen, were tested in an in vitro quinone reductase-induction assay using murine hepatoma cells (Hepa 1c1c7) and an in vitro hydroxyl radical antioxidant assay. Of these, compounds 1-4 induced quinone reductase (concentration to double enzyme induction, 0.68-2.2microg/mL) in Hepa 1c1c7 cells and gamma-mangostin (6) exhibited hydroxyl radical-scavenging activity (IC50, 0.20microg/mL).**

PMID: 17991497 [PubMed - indexed for MEDLINE]

[Fitoterapia](#). 2008 Nov 5. [Epub ahead of print]

Antibacterial Activity of Thai Medicinal Plants against Methicillin-resistant *Staphylococcus aureus*.

[Chomnawang MT](#), [Surassmo S](#), [Wongsariya K](#), [Bunvaphratsara N](#).

Department of Microbiology, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major nosocomial pathogen which causes severe morbidity and mortality worldwide. Seventeen Thai medicinal plants were investigated for their activity against MRSA. *Garcinia mangostana* was identified as the most potent plant, and its activity was traced to the prenylated xanthone, alpha-mangostin (MIC and MBC values of 1.95 and 3.91 microg/ml, respectively).

PMID: 19022354 [PubMed - as supplied by publisher]

[Food Chem Toxicol](#). 2008 Oct;46(10):3227-39. Epub 2008 Aug 6.

Medicinal properties of mangosteen (*Garcinia mangostana*).

[Pedraza-Chaverri J](#), [Cárdenas-Rodríguez N](#), [Orozco-Ibarra M](#), [Pérez-Rojas JM](#).

Facultad de Química, Departamento de Biología, Universidad Nacional Autónoma de México, Ciudad Universitaria, 04510 Mexico, DF, Mexico. pedraza@servidor.unam.mx

Many tropical plants have interesting biological activities with potential therapeutic applications. *Garcinia mangostana* Linn. (GML) belongs to the family of Guttiferae and is named "the queen of fruits". It is cultivated in the tropical rainforest of some Southeast Asian nations like Indonesia, Malaysia, Sri Lanka, Philippines, and Thailand. People in these countries have used the pericarp (peel, rind, hull or ripe) of GML as a traditional medicine for the treatment of abdominal pain, diarrhea, dysentery, infected wound, suppuration, and chronic ulcer. Experimental studies have demonstrated that extracts of GML have antioxidant, antitumoral, anti-allergic, anti-inflammatory, antibacterial, and antiviral activities. The pericarp of GML is a source of xanthones and other bioactive substances. Prenylated xanthones isolated from GML have been extensively studied; some members of these compounds possess antioxidant, antitumoral, anti-allergic, anti-inflammatory, antibacterial, antifungal and antiviral properties. Xanthones have been isolated from pericarp, whole fruit, heartwood, and leaves. The most studied xanthones are alpha-, beta-, and gamma-mangostins, garcinone E, 8-deoxygartanin, and gartanin. The aim of this review is to summarize findings of beneficial properties of GML's extracts and xanthones isolated from this plant so far.

PMID: 18725264 [PubMed - indexed for MEDLINE]

Evaluating the efficacy in improving facial photodamage with a mixture of topical antioxidants.

[Hsu J](#), [Skover G](#), [Goldman MP](#).

University of California, San Diego, USA.

This study evaluates the efficacy and tolerability of an investigational study cream composed of 3 ingredients (green and white teas, mangosteen, and pomegranate extract), Vitaphenol Skin Cream (La Jolla Spa MD, La Jolla CA), as compared to a placebo cream in rejuvenating facial skin. Twenty healthy females between the ages of 35 and 65 with demonstrable facial wrinkling, achieving a Rao-Goldman wrinkle scale score of 2 or above, applied either Vitaphenol Skin Cream or placebo cream to a randomized half of their face twice daily for 60 days and returned for follow-up after 2 weeks. Twice as many subjects indicated an enhancement of skin texture (eg, reduction in pore size, roughness, and touch) with the usage of Vitaphenol versus placebo. In all, 41% of the study subjects preferred the half of their face that had been receiving Vitaphenol, while only 0.06% of the subjects favored the placebo side. PRIMOS images from periorbital skin treated with Vitaphenol demonstrated an average improvement in skin smoothness of 1 mm³, whereas skin treated with placebo showed an average decrease in smoothness or an increase in skin roughness of 0.9 mm³. The addition of 3 antioxidants, green and white teas, mangosteen, and pomegranate, have an additive effect to enhance the improvement of age-related changes in the skin.

PMID: 18038502 [PubMed - indexed for MEDLINE]