

The Mangosteen Fruit and Xanthones

Clinical Compendium

A compilation of current scientific evidence on
Xanthones and the Mangosteen Fruit

A Compilation of Current Scientific Evidence on the Health Benefits of Xanthenes and the Mangosteen Fruit

Introduction

This booklet is a collection of clinical research relative to the health benefits of xanthenes from the mangosteen fruit (*garcinia mangostana*), and the role these xanthenes play in general health and wellness.

Emerging evidence of the effects of xanthenes has sparked the scientific community to produce numerous studies and research relating to the health benefits provided by xanthenes. The abstracts contained in this book emphasize key studies about xanthenes that have had a significant impact on the interpretation of the health and the effects of xanthenes on the body.

Please use the information contained in this book to learn more regarding xanthenes from the mangosteen fruit, and their effects on the human body and on various conditions of health.

No information contained herein is meant to replace advice of a doctor or healthcare practitioner. Readers are encouraged to seek advice from qualified health professionals in the instance that they have a medical condition.

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XANTHONES

What are Xanthonenes? Xanthonenes are a family of phytonutrients loaded with potent health benefits and antioxidant properties. Xanthonenes even offer greater antioxidant properties than vitamins C and E.

Where are xanthonenes found? They are found in a select number of rain forest plants, but nowhere are they found in more abundance than in the pericarp, or rind of the mangosteen fruit. The mangosteen – not just the inner flesh, but the whole fruit – represents the single greatest supply of these beneficial xanthonenes. Research has revealed the mangosteen is the source of more than 40 distinct xanthonenes, and ongoing science is finding new benefits of these xanthonenes every day.

The mangosteen fruit is the single greatest supply of xanthonenes.

This research has revealed xanthonenes' importance in such areas as support for microbiological balance, maintenance of immune system health, promotion of joint flexibility, and help with positive mental support.

According to these professional journals, such as the Indian Journal of Experimental Biology, Journal of Pharmacology, and Free Radical Research, these xanthonenes have a remarkable effect on overall health; and are some of the most powerful antioxidants to be found in nature.

The two most beneficial xanthonenes found in the mangosteen have been named Alpha-Mangostin and Gamma Mangostin. When isolated and thoroughly tested by researchers, such as in the studies profiled in this booklet, these two xanthonenes have been found to carry a host of potent health benefits.

INFLAMMATION

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

ABSTRACT: 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.

AUTHOR(S): Nakatani K, Yamakuni T, Kondo N, Arakawa T, Oosawa K, Shimura S, Inoue H, Ohizumi Y.

JOURNAL: Mol Pharmacol. 2004 Sep;66(3):667-74.

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

ABSTRACT: 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.

AUTHOR(S): Nakatani K, Nakahata N, Arakawa T, Yasuda H, Ohizumi Y.

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

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

Comments: The fruit hull of mangosteen fruit, *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, the investigators studied the effect of gamma-mangostin, a xanthone contained in the mangosteen fruit, and showed it had a potent inhibitory activity of prostaglandin E2 (PGE2) release.

CANCER

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

ABSTRACT: Ethanolic 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.

AUTHOR(S): Moongkarndi P, Kosem N, Luanratana O, Jongsomboonkusol S, Pongpan N.

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

Alpha-mangostin induces Ca(2+)-ATPase-dependent apoptosis via mitochondrial pathway in PC12 cells. *J Pharmacol Sci*. 2004 May;95(1):33-40. Sato A, Fujiwara H, Oku H, Ishiguro K, Ohizumi Y. Department of Pharmaceutical Molecular Biology, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Japan.

Comments: The researchers investigated the cell death effects of eight xanthones on pheochromocytoma (cancer) cells. Among these compounds, alpha-mangostin, from the fruit hull of *Garcinia mangostana* L. (mangosteen fruit), had the most potent effect with apoptosis (death) of these cells.

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.

ABSTRACT: 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.

AUTHOR(S): Nabandith V, Suzui M, Morioka T, Kaneshiro T, Kinjo T, Matsumoto K, Akao Y, Iinuma M, Yoshimi N.

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

.JOURNAL: Asian Pac J Cancer Prev. 2004 Oct-Dec;5(4):433-8.

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

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 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.

AUTHOR(S): Moongkarndi P, Kosem N, Kaslungka S, Luanratana O, Pongpan N, Neungton N.

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

Comments: These investigators found that an extract from the pericarp of the mangosteen fruit (major component in XanGo) inhibited the growth of breast cancer cells. They also showed that the extract had potent antioxidant and cancer cell death properties. They concluded that the extract from the pericarp of the mangosteen fruit has potential for chemoprevention.

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

ABSTRACT: 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.

AUTHOR(S): Matsumoto K, Akao Y, Kobayashi E, Ohguchi K, Ito T, Tanaka T, Iinuma M, Nozawa Y.

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

Comments: These authors examined the effects of six xanthenes extracted from the pericarps of the mangosteen fruit, *Garcinia mangostana*, on the cell growth inhibition of human leukemia cell line HL60. All xanthenes displayed growth inhibitory effects. Among them, alpha-mangostin (a xanthone) showed the most potent ability to cause the cancer cells death.

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

ABSTRACT: 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.

AUTHOR(S): Matsumoto K, Akao Y, Yi H, Ohguchi K, Ito T, Tanaka T, Kobayashi E, Iinuma M, Nozawa Y.

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

.JOURNAL: Bioorg Med Chem. 2004 Nov 15;12(22):5799-806.

Comments: These investigators found that an extract from the pericarp of the mangosteen fruit (major component in XanGo) inhibited the growth of breast cancer cells. They also showed that the extract had potent antioxidant and cancer cell death properties. They concluded that the extract from the pericarp of the mangosteen fruit has potential for chemoprevention.

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

ABSTRACT: 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.

AUTHOR(S): Ho CK, Huang YL, Chen CC.

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

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

Comments: Treatment of hepatocellular carcinomas (liver cancer) with chemotherapy has generally been disappointing and it is most desirable to have more effective new drugs. The investigators extracted and purified 6 xanthone compounds from the rinds (peel) of the fruit of *Garcinia mangostana*, mangosteen fruit. The investigators tested this extract on 14 different human liver cancer cell lines. Several chemotherapeutic agents (drugs) were included in the study for comparison. The results showed that one of the xanthone derivatives which could be identified as garcinone E has potent cytotoxic effect (kill cells) on all liver cancer cell lines as well as on the other gastric and lung cancer cell lines included in the screen. The investigators suggested that garcinone E may be potentially useful for the treatment of certain types of cancer

ANTI-BACTERIAL

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

ABSTRACT: 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.

AUTHOR(S): Sakagami Y, Iinuma M, Piyasena KG, Dharmaratne HR.

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JOURNAL: Phytomedicine. 2005 Mar;12(3):203-8.

Antibacterial activity of xanthenes from guttiferaceous plants against methicillin-resistant *Staphylococcus aureus*.

ABSTRACT: 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.

AUTHOR(S): Iinuma M, Tosa H, Tanaka T, Asai F, Kobayashi Y, Shimano R, Miyauchi K.

FACILITY: Department of Pharmacognosy, Gifu Pharmaceutical University, Japan.

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

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

ABSTRACT: Abstract 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.

AUTHOR(S): Voravuthikunchai SP, Kitpipit L.

FACILITY: Department of Microbiology, Faculty of Science, Prince of Songkla University, Hatyai, Songkla, Thailand.

.JOURNAL: Clin Microbiol Infect. 2005 Jun;11(6):510-2.

Antimycobacterial activity of prenylated xanthenes from the fruits of *Garcinia mangostana*.

ABSTRACT: 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.

AUTHOR(S): Suksamrarn S, Suwannapoch N, Phakhodee W, Thanuhiranlert J, Ratananukul P, Chimnoi N, Suksamrarn A.

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

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

Comments: Xanthenes, isolated from the fruit hulls and the edible arils and seeds of *Garcinia mangostana*, mangosteen fruit, were tested for their antituberculosis potential. The investigators found alpha- and beta-mangostins and garcinone B exhibited strong inhibitory effect against *Mycobacterium tuberculosis* (TB)

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

ABSTRACT: 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 \pm SD) of NBT test of 100 polymorphonuclear phagocytic cells were 145 \pm 78, 338 \pm 58, 222 \pm 73, 209 \pm 77, 211 \pm 63, 372 \pm 19, 369 \pm 20, 355 \pm 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*).

AUTHOR(S): Chanarat P, Chanarat N, Fujihara M, Nagumo T.

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

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

Comments: Polysaccharides from the pericarps of mangosteen, *Garcinia mangostana* Linn., mangosteen fruit, were extracted from the dried ground pericarps of the mangosteen fruit. The results showed that the number of *S. enteritidis* (bacteria) in cultured monocyte with extract of the pericarp of the mangosteen fruit was killed. This paper showed that polysaccharides in the extract can stimulate phagocytic cells to kill intracellular bacteria (*S. enteritidis*).

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.

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 (0.039mg/ml) for both bacterial species and the MBC values were 0.039 and 0.156mg/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.

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JOURNAL J Ethnopharmacol. 2005 Jul 8;

ANTI-HISTAMINE

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

ABSTRACT: 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.

AUTHOR(S): Chairungsrilerd N, Furukawa K, Ohta T, Nozoe S, Ohizumi Y.

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

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

ABSTRACT: 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.

AUTHOR(S): Nakatani K, Atsumi M, Arakawa T, Oosawa K, Shimura S, Nakahata N, Ohizumi Y

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

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

Comments: The fruit hull of mangosteen, *Garcinia mangostana* L., mangosteen fruit, 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 fruit extracts on histamine release and prostaglandin E2 synthesis. The investigators found the mangosteen fruit extract strongly inhibited histamine release and prostaglandin E2 synthesis. This has great importance in preventing allergies.

ANTI-OXIDANT

Mangostin inhibits the oxidative modification of human low density lipoprotein.

ABSTRACT: 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.

AUTHOR(S): Williams P, Ongsakul M, Proudfoot J, Croft K, Beilin L.

FACILITY: University of Western Australia, Department of Medicine, Royal Perth Hospital, Australia.

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

Comments: The oxidation of low density lipoprotein (LDL) may play an important role in atherosclerosis. The researchers investigated the possible antioxidant effects of mangostin, isolated from *Garcinia mangostana* (found in mangosteen fruit), on the oxidation of human LDL (bad cholesterol). From these results, they concluded that mangostin is acting as a free radical scavenger ("mop up" sponge) to protect the LDL from oxidative damage in this in vitro system. In other words, it a potent antioxidant.

Inhibition of lipoprotein oxidation by prenylated xanthenes derived from mangostin. Free Radic Res. 2000 Nov;33(5):643-59. Mahabusarakam W, Proudfoot J, Taylor W, Croft K. Chemistry Department, Prince of Songkla University, Hat Yai, Thailand.

Comments: 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. The researchers have previously shown that the xanthone, mangostin (found in mangosteen fruit), can inhibit the oxidation of LDL, low density lipoprotein (bad cholesterol). Researchers studied more xanthone derived compounds and found enhanced antioxidant activities. Note: If the oxidation of LDL cholesterol can be prevented or inhibited, then the LDL-cholesterol cannot exert its "bad" effect and cause heart disease.

ANTI-FUNGAL

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

ABSTRACT: 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.

AUTHOR(S): Gopalakrishnan G, Banumathi B, Suresh G.

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

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

ANTI-VIRAL

Active constituents against HIV-1 protease from *Garcinia mangostana*.

ABSTRACT: 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.

AUTHOR(S): Chen SX, Wan M, Loh BN.

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

Comments: The investigators found that an extract of *Garcinia mangostana* L., mangosteen fruit, showed potent inhibitory activity against HIV-1 protease which affects the replication of HIV.

Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection. *Planta Med.* 1998 Mar;64(2):97-109. Vlietinck AJ, De Bruyne T, Apers S, Pieters LA. Department of Pharmaceutical Sciences, University of Antwerp (UA), Belgium.

Comments: The investigators showed many compounds of plant origin have been identified that inhibit different stages in the replication cycle of human immunodeficiency virus (HIV). Among these compounds, the xanthone mangostin, derived from mangosteen fruit, was shown to inhibit the replication cycle of HIV.

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