

Mangosteen info / research

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

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

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

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

PMID: 14698525 [PubMed - in process]

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

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

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

PMID: 12932141 [PubMed - indexed for MEDLINE]

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

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

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

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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 - in process]

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

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

Ho CK, Huang YL, Chen CC.

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Treatment of hepatocellular carcinomas (HCCs) with chemotherapy has generally been disappointing and it is most desirable to have more effective new drugs. We extracted and purified 6 xanthone compounds from the rinds (peel) of the fruits of *Garcinia mangostana* L., using partitioned chromatography and then tested the

cytotoxic effects of these compounds on a panel of 14 different human cancer cell lines including 6 hepatoma cell lines, based on the MTT method. Several commonly used chemotherapeutic agents were included in the assay to determine the relative potency of the potential new drugs. Our results have shown that one of the xanthone derivatives which could be identified as garcinone E has potent cytotoxic effect on all HCC cell lines as well as on the other gastric and lung cancer cell lines included in the screen. We suggest that garcinone E may be potentially useful for the treatment of certain types of cancer.

PMID: 12451486 [PubMed - indexed for MEDLINE]

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

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

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

PMID: 12230104 [PubMed - indexed for MEDLINE]

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

Xanthenes from the heartwood of *Garcinia mangostana*.

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Singapore 117543, Singapore.

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

PMID: 12052521 [PubMed - indexed for MEDLINE]

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

Xanthenes from the green fruit hulls of *Garcinia mangostana*.

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

PMID: 12027762 [PubMed - indexed for MEDLINE]

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

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

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

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

PMID: 11754876 [PubMed - indexed for MEDLINE]

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

Three xanthenes and a benzophenone from *Garcinia mangostana*.

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

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

PMID: 11473420 [PubMed - indexed for MEDLINE]

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

Two novel xanthenes from *Garcinia mangostana*.

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

PMID: 11449524 [PubMed - indexed for MEDLINE]

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

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

Facciotti MT, Bertain PB, Yuan L.

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

PMID: 10385326 [PubMed - indexed for MEDLINE]

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

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

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

PMID: 9681015 [PubMed - indexed for MEDLINE]

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

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

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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]

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

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

[Article in Japanese]

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

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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]

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

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

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

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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 ($IC_{50} = 0.32$ microM). 5-HT amplified, ADP-induced aggregation of rabbit platelets (5-HT_{2A}) was inhibited by gamma-mangostin ($IC_{50} = 0.29$ microM), whereas that induced by thrombin was not affected, nor did gamma-mangostin affect 5-HT-induced contraction of the guinea-pig ileum (5-HT₃) in the presence of 5-HT₁, 5-HT₂ and 5-HT₄ receptor antagonists. Furthermore, 5-HT-induced contraction of the rat fundus (5-HT_{2B}) and 5-HT-induced relaxation of the rabbit aorta in the presence of ketanserin (5-HT₁) and carbachol-induced contraction of the guinea-pig ileum (muscarinic M₃) were not affected by gamma-mangostin (5 microM). Gamma-mangostin inhibited [³H]spiperone binding to cultured rat aortic myocytes ($IC_{50} = 3.5$ nM). The K_d for [³H]spiperone binding was increased by gamma-mangostin (3 nM) from 11.7 to 27.4 nM without affecting B_{max} . These results suggest that gamma-mangostin is a novel competitive antagonist, free from a nitrogen atom, for the 5-HT_{2A} receptors in vascular smooth muscles and platelets.

PMID: 9459569 [PubMed - indexed for MEDLINE]

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

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

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

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

Polysaccharides from the pericarbs of mangosteen, *Garcinia mangostana* Linn., was obtained by treating the dried ground pericarbs with hot water followed by ethanol precipitation (M fraction). The extract was fractionated by anion exchange chromatography on a DEAE-cellulose column as MDE1-5 fractions. The fractions of MDE3 and MDE4 composed of mainly D-galacturonic acid and a small amount of neutral sugar (L-arabinose as the major one and L-rhamnose and D-galactose as the minor ones) were studied for immunopharmacological activities by phagocytic test to intracellular bacteria (*Salmonella enteritidis*) and nitroblue tetrazolium (NBT) and superoxide generation tests. The results showed that the number of *S. enteritidis* in cultured monocyte with extract of pericarb of mangosteen (MDE3) was killed. Activating score (mean \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*).

PMID: 9347663 [PubMed - indexed for MEDLINE]

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

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

Gopalakrishnan G, Banumathi B, Suresh G.

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

The antifungal activity of several xanthenes isolated from the fruit hulls of *Garcinia mangostana* and some derivatives of mangostin against three phytopathogenic fungi, *Fusarium oxysporum vasinfectum*, *Alternaria tenuis*, and *Dreschlera oryzae*, has been evaluated. The natural xanthenes showed good inhibitory activity against the three fungi. Substitution in the A and C rings has been shown to modify the bioactivities of the compounds.

PMID: 9213587 [PubMed - indexed for MEDLINE]

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

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.

Publication Types:

- Letter

PMID: 8923814 [PubMed - indexed for MEDLINE]

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

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]

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

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

Furukawa K, Shibusawa K, 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]

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

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

Chen SX, Wan M, Loh BN.

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

Publication Types:

- Letter

PMID: 8792678 [PubMed - indexed for MEDLINE]

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

Mangostin inhibits the oxidative modification of human low density lipoprotein.

Williams P, Ongsakul M, Proudfoot J, Croft K, Beilin L.

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The oxidation of low density lipoprotein (LDL) may play an important role in atherosclerosis. We investigated the possible antioxidant effects of mangostin, isolated from *Garcinia mangostana*, on metal ion dependent (Cu^{2+}) and independent (aqueous peroxy radicals) oxidation of human LDL. Mangostin prolonged the lagtime to both metal ion dependent and independent oxidation of LDL in a dose dependent manner over 5 to 50 μM as monitored by the formation of conjugated dienes at 234 nm ($P < 0.001$). There was no significant effect of mangostin on the rate at which conjugated dienes were formed in the uninhibited phase of oxidation. Levels of thiobarbituric reactive substances (TBARS) generated in LDL were measured 4 and 24 hours after oxidation with 5 μM Cu^{2+} in the presence or absence of 50 μM or 100 μM mangostin. We observed an inhibition of TBARS formation with 100 μM mangostin at 4 hours ($P = 0.027$) but not at 24 hours ($P = 0.163$). Similar results were observed in the presence of 50 μM mangostin. Mangostin, at 100 μM , retarded the relative electrophoretic mobility of LDL at both 4 and 24 hours after Cu^{2+} induced oxidation. Mangostin (100 μM) significantly inhibited the consumption of alpha-tocopherol in the LDL during Cu^{2+} initiated oxidation over a 75 minute period ($P < 0.001$). From these results, we conclude that mangostin is acting as a free radical scavenger to protect the LDL from oxidative damage in this in vitro system.

PMID: 7581813 [PubMed - indexed for MEDLINE]

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

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

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]

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

Pharmacological profile of mangostin and its derivatives.

Shankaranarayan D, Gopalakrishnan C, Kameswaran L.

Mangostin (M), a naturally occurring xanthone in the rinds of the fruits of *Garcinia mangostana* Linn. (Guttiferae) and its derivatives such as 3-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]

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

Biological activities of alpha-mangostin derivatives against acidic sphingomyelinase.

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

PMID: 12951083 [PubMed - in process]

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

Inhibition of lipoprotein oxidation by prenylated xanthenes derived from mangostin.

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

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Oxidative damage is thought to play a critical role in cardiovascular and other chronic diseases. This has led to considerable interest in the antioxidant activity of dietary compounds. Flavonoids have received the most attention and much is known about the structural requirements for antioxidant activity. However, little is known about the antioxidant activity of other plant derived phenolic compounds such as the xanthenes. We have previously shown that the prenylated xanthone, mangostin, can inhibit the oxidation of low density lipoprotein. In order to examine the effects of structure modification on antioxidant activity of this class of compound we have prepared a number of derivatives of mangostin and tested antioxidant activity in an isolated LDL and plasma assay. The results of this study show that structural modification of mangostin can have a profound effect on antioxidant activity. Derivatisation of the C-3 and C-6 hydroxyl groups with either methyl, acetate, propane diol or nitrile substantially reduces antioxidant activity. In contrast, derivatisation of C-3 and C-6 with aminoethyl derivatives enhanced antioxidant activity, which may be related to changes in solubility. Cyclisation of the prenyl chains had little influence on antioxidant activity.

PMID: 11200095 [PubMed - indexed for MEDLINE]

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

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

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

PMID: 8957258 [PubMed - indexed for MEDLINE]

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

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

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

PMID: 12451486 [PubMed - indexed for MEDLINE]

Oxidation - When those unstable free radicals “borrow” an electron from a normal cell in your body, the process is called oxidation. It’s the same process as when metal rusts...or a cut up apple turns brown. Yuck. Free radicals cause oxidation inside your body which is why you want plenty of antioxidants...or compounds that inhibit chemical reactions with oxygen.

Phytochemicals - Phytochemicals is simply a word that means “plant chemicals.” Once, researchers attributed the health promoting affects of plants to their numerous vitamins, minerals and fibers. More recently, however, researchers have discovered that the many other chemical compounds in plants also provide benefits to humans when consumed. Phytochemicals provide plants with protection from the environmental challenges they face, such as ultraviolet light. When we consume plants rich in phytochemicals, they seem to protect us as well. Some researchers estimate that up to 40,000 different phytochemicals will someday be fully catalogued and understood. Polyphenols are a class of phytochemicals that are particularly rich in antioxidants and plentiful in pomegranate Juice.

Plaque - Atherosclerosis occurs when fat, cholesterol and other substances accumulate in the walls of the arteries and form plaque. Eventually, plaque can erode the walls of the artery, diminish its elasticity and interfere with blood flow. Plaques can also rupture, causing debris to head downstream within the artery. What we’re talking about is a common cause for heart attack and stroke. Naturally, the less plaque, the better. And that’s where pomegranate juice comes in. A pilot study of 19 elderly patients with atherosclerosis showed that an 8 oz. glass a day can reduce plaque build-up in the arteries by up to 30%.

Polyphenols - Polyphenols are a class of phytochemicals found in plants and there may be at least 10,000 unique polyphenols in the world! Polyphenols literally means “many phenols.” A phenol is a kind of molecule, a carbon-based chemical structure, and many of them bound together form a polyphenol. Among the most potent of the antioxidants, polyphenols, like tannins, particularly punicalagin and anthocyanins, are really plentiful in pomegranate juice, which is why pomegranate is so good for you.

Punicalagin - A hydrolyzable tannin, punicalagin is found almost exclusively in pomegranates. This highly unique and potent polyphenol antioxidant breaks down to ellagic acid.

Systolic/Diastolic Blood Pressure - The systolic measurement is the first, or top number in a blood pressure reading. It’s the pressure of blood against your artery walls when the heart has just finished pumping or contracting. The diastolic measurement is the second, or bottom number in a blood pressure reading. It’s the pressure of blood against your artery walls when your heart is relaxed and filling with blood. When the numbers are at 140/90 or higher, you have high blood pressure. That means that your heart and arteries work harder and you’re in more danger of suffering from a stroke or heart attack.

Tannins - Tannins are plant polyphenols that add color and a slightly tart taste to pomegranates and many other vegetables and plants. The word tannin comes from the Celtic word for Oak and refers to the source of tannins used to convert animal skins into leather. In folk medicine, tannins were used to treat burns and as an astringent. While there are tannins in some teas and in red wine, tannins are truly abundant in pomegranate Juice, which account for the juice’s incredible antioxidant properties.

Pomegranate Juice May Slow Prostate Cancer Growth

Janet Raloff

Prostate cancer will claim the lives of an estimated 30,000 men in the United States this year. The second leading cause of cancer death in men, its incidence climbs with age. In Western countries, the disease is reaching nearly epidemic proportions among the elderly. However, the cancer can grow so slowly that many men with prostate cancer will die of something else first.

A mystery has always been what factors might improve a man's odds of having a slow-growing malignancy. A new study suggests that drinking pomegranate juice might be one of them.



granaatappel
pomegranate

Several studies have associated diets high in plant-derived polyphenols—principally, the deeply pigmented antioxidants in many fruits and vegetables—with lower risks of malignancies including prostate cancer. Because the blood-red juice of pomegranates is especially rich in such compounds, Allan J. Pantuck of the David Geffen School of Medicine at the University of California, Los Angeles and his colleagues decided to test it against metastatic prostate cancer. These are malignancies that have spread beyond the gland, which in these men had been removed or destroyed, along with tumors, by radiation.

Over time, the presence of these residual cancer cells was confirmed by rising concentrations of a protein in the men's blood: prostate-specific antigen (PSA). Because PSA is made by prostate cells—usually cancerous ones—and because these men no longer had intact prostates, the presence of the substance indicated that cancerous prostate cells continued to exist in the men's bodies, Pantuck explains.

The researchers calculated that the men's average doubling time in PSA concentrations—a rough gauge of cancer growth—was 15 months. After men drank a glass of juice a day, their average doubling time more than tripled. In nearly one-third of men, Pantuck notes, PSA values actually fell—in a few cases, dramatically.

Although this is just one study and the juice showed no sign of curing the disease, Pantuck says it shows that pomegranate juice might be a beneficial adjunct to other therapies in men with this potentially lethal disease.

A glass a day

Last fall, researchers at the University of Wisconsin–Madison reported related laboratory data. They incubated cells from an aggressive form of prostate cancer with pomegranate-fruit extract. The higher the concentration of the extract the greater the inhibition of the cancer cells' growth, notes team leader Hasan Mukhtar.

The team also injected human–prostate-cancer cells into lab mice. The cells grew into tumors, but the rate was reduced in animals fed pomegranate extract, his team reported in the Oct. 11 Proceedings of the National Academy of Sciences. The team confirmed the juice's effect by measuring PSA concentrations in the animals' blood.

The new study extends these trials into people. Pantuck's recruited 46 men who, despite having undergone prostate-cancer surgery, were exhibiting rising PSA values, as measured over a 6-month period. Concentrations of the protein at the start of the study ranged from 0.2 to 5 nanograms per liter of blood, indicative of small residues of cancer cells. These men had no medical sign of metastatic disease except for the PSA concentrations and were on no anticancer drugs or other therapies.

All recruits were then assigned to drink an 8-ounce bottle of pomegranate juice daily. PSA and other cancer indicators were measured every 3 months, and men were removed from the trial if they showed signs that their disease was advancing rapidly. By 33 months into the trial, PSA values had changed measurably in enough men to allow the researchers to calculate the concentration's new doubling time. On average, that figure was then about 54 months.

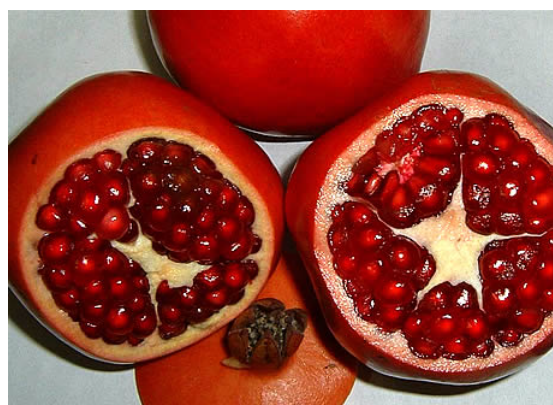
Overall, "more than 80 percent [of recruits] had a prolongation in their PSA doubling time," says Pantuck. "This means [that] for the majority of patients, their cancer's growth slowed."

PSA concentrations decreased in about a third of the study participants, the team reports in the July 1 Clinical Cancer Research. Most such decreases were small, but four men exhibited declines in the cancer indicator of more than 50 percent while taking the juice. One man's PSA concentration dropped a whopping 85 percent, Pantuck says. Once PSA becomes detectable, the urologist explains, it tends to rise inexorably—"you don't expect it to spontaneously decrease."

The researchers also conducted a few biochemical tests. For instance, they grew standard cultures of human-prostate cells in test tubes and fed the cells blood serum taken from the recruits at the beginning and end of the trial. The procedure was intended to reveal whether something changed in the men's blood that might affect cancer growth. Pantuck's group found that the cells' growth rate was 12 percent slower when the lab cultures were fed serum from the men after they had been drinking the juice.

The men's blood also tended to be less vulnerable to oxidation—a chemical reaction that can damage cells—once pomegranate-juice supplementation began.

granaatappel
pomegranate



Mangosteen fruit



Wat is Mangosteen ?

De mangosteen is een harde vrucht, met in de harde bolster zacht wit vruchtvlees. De vrucht komt voor over de gehele wereld in de tropische gebieden. De Boeddhistische monniken uit Zuidoost Azië hielden precies bij op welke ziektes deze vrucht een positieve invloed uitoefende. In alle gebieden waar mangosteen groeit, kent de bevolking de goede heilzame werking.

Maar vooral de huid (pericarp=schil) van de vrucht wordt gebruikt als ondersteuning van de gezondheid in Maleisië, Thailand, Indonesië, de Filippijnen, Australië, Centraal Amerika en Brazilië.

Mangosteen smaakt niet alleen erg lekker, het bevat vooral veel Xanthonen, natuurlijke anti-oxidanten. Xanthonen werken ontstekingsremmend. Er zijn 200 soorten Xanthonen bekend in de wetenschap en de mangosteen heeft er meer dan 40.

Ze helpen het lichaam om voedsel om te zetten in energie; ze helpen de darmen door een goede darmflora te bevorderen, waardoor het hele lichaam er profijt van heeft; en ze helpen om de aminozuren in het lichaam in evenwicht te houden. Dit alles maakt de mangosteen met zijn eeuwenoude bestaansgeschiedenis van heilzame werking tot een echte weldoener van het menselijk lichaam.

Mangosteen werkt mee als een antioxidant die de vrije radicalen probeert te onderscheppen voor deze hun verwoestende uitwerking op cellen kunnen krijgen.

De Mangosteen gebruiken als voedings supplement helpt het lichaam weer in balans te komen en samen met een gezonde voeding tot een gezonde stofwisseling te geraken, waarbij alle cellen gevoed en alle afvalstoffen uitgescheiden worden.

De vrucht bestaat uit de volgende segmenten:

De pericarp: een dikke donkerpaarse, zachte omhulsel dat de vruchtelementen omvat.

Het vruchtvlees: 4 tot 8 driehoekige elementen van wit, zacht vruchtvlees.

Vanwege haar fantastische smaak is de mangosteen verheven tot een van de besten onder de tropische vruchten.

Mangosteen, Xanthenes, and Mangostin

Research Abstracts -

Biological activities of alpha-mangostin derivatives against acidic sphingomyelinase.

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

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

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

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

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

PMID: 12932141 [PubMed - in process]

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

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

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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.

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

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

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

PMID: 11754876 [PubMed - indexed for MEDLINE]

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

Nakatani K, Nakahata N, Arakawa T, Yasuda H, Ohizumi Y. Department of Pharmaceutical Molecular Biology, Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba, Aramaki, Aoba-ku, 980-8578, Sendai, Japan.

The fruit hull of mangosteen, *Garcinia mangostana* L., has been used for many years as a medicine for treatment of skin infection, wounds, and diarrhea in Southeast Asia. In the present study, we examined the effect of gamma-mangostin, a tetraoxygenated diprenylated xanthone contained in mangosteen, on arachidonic acid (AA) cascade in C6 rat glioma cells. gamma-Mangostin had a potent inhibitory activity of prostaglandin E2 (PGE2) release induced by A23187, a Ca²⁺ ionophore. The inhibition was concentration-dependent, with the IC₅₀ value of about 5 microM. gamma-Mangostin had no inhibitory effect on A23187-induced phosphorylation of p42/p44 extracellular signal regulated kinase/mitogen-activated protein kinase or on the liberation of [¹⁴C]-AA from the cells labeled with [¹⁴C]-AA. However, gamma-mangostin concentration-dependently inhibited the conversion of AA to PGE2 in microsomal preparations, showing its possible inhibition of cyclooxygenase (COX).

In enzyme assay *in vitro*, gamma-mangostin inhibited the activities of both constitutive COX (COX-1) and inducible COX (COX-2) in a concentration-dependent manner, with the IC₅₀ values of about 0.8 and 2 microM, respectively. Lineweaver-Burk plot analysis indicated that gamma-mangostin competitively inhibited the activities of both COX-1 and -2. This study is a first demonstration that gamma-mangostin, a xanthone derivative, directly inhibits COX activity.

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

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

PMID: 11200095 [PubMed - indexed for MEDLINE]

Inhibition of lipoprotein oxidation by prenylated xanthenes derived from mangostin.

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

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

Oxidative damage is thought to play a critical role in cardiovascular and other chronic diseases. This has led to considerable interest in the antioxidant activity of dietary compounds. Flavonoids have received the most attention and much is known about the structural requirements for antioxidant activity. However, little is known about the antioxidant activity of other plant derived phenolic compounds such as the xanthenes. We have previously shown that the prenylated xanthone, mangostin, can inhibit the oxidation of low density lipoprotein. In order to examine the effects of structure modification on antioxidant activity of this class of compound we have prepared a number of derivatives of mangostin and tested antioxidant activity in an isolated LDL and plasma assay. The results of this study show that structural modification of mangostin can have a profound effect on antioxidant activity. Derivatisation of the C-3 and C-6 hydroxyl groups with either methyl, acetate, propane diol or nitrile substantially reduces antioxidant activity. In contrast, derivatisation of C-3 and C-6 with aminoethyl derivatives enhanced antioxidant activity, which may be related to changes in solubility. Cyclisation of the prenyl chains had little influence on antioxidant activity.

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

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

PMID: 10938539 [PubMed - indexed for MEDLINE]

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

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

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Sphingomyelinase is considered to be involved in the regulation of apoptosis (cell death) and cell growth. In the course of our screening for acidic sphingomyelinase inhibitors we isolated three xanthone compounds, alpha-mangostin, cowanin, and cowanol, from the bark of *Garcinia speciosa*. These compounds competitively inhibited bovine brain-derived acidic sphingomyelinase with IC₅₀ values of 14.1, 19.2, and 10.9 microM, respectively and inhibited the acidic sphingomyelinase more effectively than the neutral sphingomyelinase of bovine brain. alpha-Mangostin inhibited the acidic sphingomyelinase in the most selective manner. alpha-Mangostin was chemically modified and its structure-activity relationships are discussed

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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.

Key words mangosteen; histamine release; prostaglandin E2; passive cutaneous anaphylaxis.

Allergic inflammation is orchestrated by antigen-specific CD4⁺ T cells, eosinophils and mast cells, and is a characteristic feature of bronchial asthma, rhinitis and atopic dermatitis.^{1,2} Allergy is an immunological reaction to a foreign antigen (allergen) that causes tissue inflammation and organ dysfunction. Allergic reaction of types I, II and III is antibody mediated, and that of type IV is T-cell mediated.³ Inflammation is often accompanied by tissue injury and the pathogenesis of many chronic disease states, including those of an autoimmune nature.⁴ Regardless of etiology or localization, inflammation involves changes in vascular permeability, with concomitant recruitment of components of the immune system.⁵ Edema, redness, pain and heat are the four cardinal symptoms of inflammation. The early-phase mediators of inflammation are histamine and serotonin, and the late-phase mediators are prostaglandins, lymphokines and monokines.

Rat basophilic leukemia (RBL-2H3) cells display properties of mucosal-type mast cells. The RBL-2H3 cells contain several hundred thousand IgE receptors on the membrane surface, and after sensitization with mouse monoclonal IgE, the cells respond to antigen and release histamine. Therefore, we used RBL-2H3 cells as a model cell line for histamine release.

Prostanoids, arachidonic acid metabolites produced from a variety of inflammatory cells upon stimulation, are thought to be involved in the pathogenesis of diseases. Prostanoid synthesis is regulated by two successive metabolic steps, the release of arachidonic acid from membrane phospholipids by phospholipase A2 and its conversion to prostanoids by cyclooxygenase.^{6,7} Prostaglandin E2 is widely distributed in various organs and exerts an effect on various biological activities.⁸ In inflammation processes, prostaglandin E2 is believed to play crucial roles, since chemical mediators invoke prostaglandin E2 synthesis in fibroblasts,⁹ endothelial cells,¹⁰ monocytes,¹¹ and neutrophils¹² at inflammation sites. Cyclooxygenase-2, which is rapidly induced in inflammatory states, may produce the prostanoids involved in immune and/or inflammatory responses.

Mangosteen, *Garcinia mangostana* L. is a tree, which is fairly widespread in Thai, India, Sri Lanka and Myanmar. The fruit hull of mangosteen is used as a traditional medicine in Southeast Asia for anti-inflammatory, anti-diarrhoea, antiulcer and antiseptic purposes.^{13,14} In this study, we examined the effects of extracts of this fruit hull (100% ethanol, 70% ethanol, 40% ethanol and water) on histamine release and prostaglandin E2 synthesis. The results suggest that the 40% ethanol extract of the fruit hull has potent inhibitory activities on IgE-mediated histamine release and prostaglandin E2 synthesis. Furthermore, the extract is effective in cutaneous anaphylaxis in rats *in vivo*.

MATERIALS AND METHODS

Materials Fetal bovine serum was obtained from the Cell Culture Laboratory (Cleveland, OH, U.S.A.). Horse serum was purchased from Dainippon Pharmaceutical Co., Ltd. (Osaka, Japan). The fruit hull of mangosteen was extracted by maceration in ethanol, 70% ethanol, 40% ethanol and water, respectively. The leaf of *Rubus suavissimus* was extracted by maceration in water. Each extract was filtered, and the filtrate was evaporated to dryness at room temperature. Eagle's minimum essential medium (EMEM) was purchased from Nissui Pharmaceutical Co., Ltd. (Tokyo, Japan). F-10 (Nutrient Mixture: ham) was obtained from GIBCO BRL (Grand Island, NY, U.S.A.). Mouse monoclonal anti-DNP-BSA IgE was purchased from Seikagaku Corporation (Tokyo), and DNP-BSA was obtained from LSL Co., Ltd. (Tokyo). o-Phthalaldehyde (OPT) was purchased from Wako Pure Chemical Industries, Ltd. (Tokyo). Prostaglandin E2 was a generous gift from Ono Pharmaceuticals (Osaka).

Anti-prostaglandin E2 antibody was obtained from Chemicon International Inc (Temecula, CA, U.S.A.). [³H]-Prostaglandin E2 (200 Ci/mmol) was from NEN/DuPont (Boston, MA, U.S.A.). A final concentration of dimethyl sulfoxide, a solvent for mangosteen extract, was kept at less than 0.5%. Other chemicals and drugs were of reagent grade or of the highest quality available. Cell Culture RBL-2H3 cells were grown in EMEM containing 10% fetal bovine serum in a 37 °C humidified incubator in an atmosphere of 5% CO₂ in air. C6 rat glioma cells were grown in F-10 medium containing 15% horse serum and 2.5% fetal bovine serum in a 37 °C humidified incubator in an atmosphere of 5% CO₂ in air.

Assay of Histamine Release RBL-2H3 cells were seeded into 12 well plates at the density of 1.0 × 10⁵ cells per well. The experiment was performed two days after cell seeding. The cells were washed twice with PIPES buffer (10 mM PIPES, 140 mM NaCl, 5 mM KCl, 5.5 mM glucose, 0.6 mM MgCl₂, 1 mM CaCl₂, pH 7.4) and were preincubated with mouse monoclonal anti-DNP-BSA IgE antibody (0.5 mg/ml) at 37 °C for 60 min. After sensitization, the cells were again washed twice with PIPES buffer and were incubated with or without test extracts for 5 min. Then, the cells were incubated with phosphatidylserine (10 mg/ml) for 5 min, and were stimulated with 0.1 mg/ml of DNP-BSA as antigen for 30 min. The medium (0.5 ml) was transferred to a tube containing 1 ml of HClO₄ (0.8 N), and cells in each well were used to measure histamine remaining in the cells by adding 1.0 ml of HClO₄ (0.4 N). To 1 ml of sample, a mixture of 125 ml of NaOH (5 N), 0.4 g of NaCl and 2.5 ml of n-butanol was added. Then, the samples were centrifuged at 1000 rpm for 3 min. The upper organic phase was transferred to tubes containing 2 ml of NaOH (0.1 N) saturated with NaCl, and the sample was centrifuged to remove contaminated materials from the organic phase; the procedure was then repeated. Next, the upper organic phase was transferred to tubes containing 2 ml HCl (0.1 N) and 7.6 ml n-heptane. To the 1 ml of the lower aqueous phase, 0.1 ml of NaOH (10 N) was added. The histamine-OPT reaction was carried out by incubation with 0.1 ml of OPT (10 mg/ml methanol) for 4 min at room temperature, and terminated by addition of 0.6 ml HCl (3 N). The fluorescence of the conjugate was assessed at 450 nm emission activated at 360 nm. Histamine content in the cells per well was 20 ng/well to 45 ng/well.

Assay of Prostaglandin E2 C6 cells were seeded into 12well plates at the density of 1.0 × 10⁵ cells per well. The experiment was performed two days after cell seeding. The cells were washed twice with EMEM buffered with 20 mM 2-[4(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid (HEPES), pH 7.35 (EMEM-HEPES) and were preincubated with or without test extracts for 10 min, then further incubated with or without A23187 for an additional 10 min. The medium was acidified to pH 4.0 by addition of 1 N HCl, and prostaglandin E2 was extracted twice with ethyl acetate. After the ethyl acetate had been evaporated under a stream of N₂ gas, the sample was dissolved in 10 mM Tris-HCl (pH 7.6). Prostaglandin E2 was determined by radioimmunoassay, as described previously.¹⁵

Passive Cutaneous Anaphylaxis (PCA) Reaction An IgE-dependent skin reaction was generated in rats by sensitizing the shaved skin with an intradermal injection of anti DNP-BSA IgE antibody (0.1 mg/0.1 ml/rat) for 24 h and an intravenous injection of DNP-BSA (5 mg/0.5 ml/rat) from the tail vein. When antigen was injected, DNP-BSA containing 1% Evans blue was used to evaluate vascular permeability. Test extracts were administered intraperitoneally 30 min before antigen injection. The rats were sacrificed 30 min after the intravenous antigen challenge, and the dorsal skin was removed for measurement of the pigment area.

Data Analysis The statistical differences (p < 0.05) of values was determined by the analysis of variance (ANOVA).

Effects of Several Mangosteen Extracts on Histamine Release from RBL2H3 Cells Four kinds of extracts from mangosteen and water extract from *Rubus suavissimus* were examined for their inhibitory effects on histamine release from RBL-2H3 cells (Fig. 1). Histamine release from IgE sensitized RBL-2H3 cells was induced by DNP-BSA as antigen stimulation. The 40% ethanol extract from mangosteen was found to inhibit the histamine release potently, like the water extract from *Rubus suavissimus*. The 100% and 70% ethanol extracts and water extract from mangosteen had a tendency to inhibit this release. We examined the concentration-dependence of the 40% ethanol extract from mangosteen and the water extract from *Rubus suavissimus* in inhibiting the IgE-mediated histamine release (Fig. 2). The 40% ethanol mangosteen extract (100, 300 mg/ml) showed more than 80% inhibition of the histamine release. In contrast, the water extract from *Rubus suavissimus* significantly inhibited the histamine release only at the concentration of 300 mg/ml. Major constituents of mangosteen α - and γ -mangostin had no effect on IgE-mediated histamine release (Fig. 3).

Effect of Mangosteen Extracts on Prostaglandin E2 Synthesis Stimulated by A23187 in C6 Cells A23187, a Ca²⁺ ionophore, is known to stimulate prostaglandin synthesis mediated through the activation of PLA₂ followed by arachidonic acid liberation in glial cells.¹⁶

Four kinds of extracts from mangosteen and water extract from *Rubus suavissimus* were examined for their inhibitory effects on A23187-induced prostaglandin E2 release from C6 rat glioma cells.

Zoals ik in eerdere nieuwsbrieven heb aangetoond, is het voorkómen van ontstekingen een belangrijk onderdeel van een totaal preventieplan. Ontstekingen leiden nl. tot hart en vaat ziekten, kanker, reuma, dementie, Parkinson, MS etc. Bijna alle ouderen lijden aan een of andere vorm van ontsteking. Ouderen met lage ontstekingsactiviteit hebben een langere levensverwachting, zo blijkt uit onderzoek en de grote killers, nl hart en vaatziekten en kanker zijn gerelateerd aan ontstekingen.

Ontstekingen voorkómen is met een gezonde leefstijl deels mogelijk. Daarnaast is supplementengebruik aan te bevelen.

De vrucht mangosteent kan hierbij nuttig zijn als effectieve ontstekingsremmer, inzetbaar bij preventie en bij deskundige begeleiding bij behandeling.

Wat is mangosteent?

De vrucht mangosteent is niet hetzelfde en zelfs niet verwant aan de mango. Mangosteent behoort volgens de plantenleer tot de familie van de Guttiferae. Daar vallen honderden plantensoorten onder. Een van de bekendste is hypericum perforatum, ofwel St Jans Kruid.

In feite is mangosteent een heel grote bes. De grootte van de vrucht zit tussen een pruim en een sinaasappel.

De kleur van de schil is diep paars. De vrucht is wit als een lychee.

Mangosteent is nog grotendeels onbekend in het Westen.

De mangosteentboom groeit langzaam en kan tot 20 meter hoog worden. Door zijn langzame groei en grote hoogte is mangosteent niet een populaire teelt. Mogelijk is de vrucht daarom lang verborgen gebleven voor het Westen.

Xanthonen

De gezonde werking van mangosteent wordt toegeschreven aan de zgn. xanthonen. De hoeveelheid xanthonen die in de vrucht voorkomt is uniek, dit komt verder in de natuur niet voor. Het merendeel van de xanthonen zit in de schil. De schil is voor iedere vrucht een verdediging, barrière tegen de buitenwereld. De schil beschermt de vrucht. Door de dikte van de schil maar ook door de stoffen die de plant in de schil aanmaakt kan de vrucht zich verdedigen tegen infecties en andere bedreigingen. Deze stoffen die in de schil voorkomen zijn vaak heel 'bioactief'. Bioactief betekent dat het invloed uitoefent op onze biochemie. Zo blijkt de gezonde werking van een appel ook vooral in de schil te zitten. (Men doet er daarom verstandig aan de appel met schil te eten, maar wel wassen wegens de landbouwgiften). De xanthonen van de mangosteent zitten ook vnl. in de schil. Ze beschermen de vrucht. Ze beschermen ook uw gezondheid als u de mangosteent gebruikt. Xanthonen zijn dus biologisch actieve stoffen die in het plantenrijk weinig voorkomen.

Wetenschap en xanthonen

De traditionele volksgeneeskunde in Azië en Zuid Amerika dicht de mangosteent belangrijke eigenschappen toe. Uit onderzoek blijkt inmiddels dat dit naar alle waarschijnlijkheid te danken is aan de aanwezigheid van xanthonen. Er zijn door de wetenschap de laatste decennia 200 xanthonen vastgesteld. Daarvan komen er 40 voor in de mangosteent. Xanthonen komen verder niet of nauwelijks voor in het plantenrijk en dus ook niet in onze voeding. Tot nu lijkt de mangosteent de enige belangrijke leverancier van xanthonen.

Wat heeft de wetenschap aangetoond m.b.t. mangosteent en de xanthonen ?

De wetenschap heeft voor de mangosteent verschillende feiten aangetoond

mangosteent bevat een hoog gehalte aan xanthonen

xanthonen komen in de natuur verder nauwelijks voor

xanthonen werken doordat het een sterk positief effect heeft op de aanmaak van de gunstige zogenaamde prostaglandinen

in wetenschappelijke experimenten bleken de xanthonen sterk ontstekingsremmend

xanthonen beschermen het maagslijmvlies

xanthonen zijn sterke anti oxidanten

Het zijn zeer stabiele, hittebestendige moleculen

Door gebruik van mangosteent, met schil kunt u aanzienlijke hoeveelheden xanthonen binnen krijgen ! De schil is taai, u kunt er wel thee van zetten.

Waarom neigt ons lichaam tot ontsteking ?

Gedurende de evolutie was een heel actieve afweer tegen infecties, zoals bij verwondingen noodzakelijk. Het immuunsysteem is erg gericht op verweer tegen acute bedreigingen. Zonder zo'n actieve afweer was overleving als soort volstrekt uitgesloten. Het leven was vol gevaren en de hygiëne was slecht. De noodzaak tot zo'n actieve afweer is nu veel geringer, o.a. omdat de hygiëne enorm is toegenomen. Ons immuunsysteem past niet meer goed bij onze omstandigheden. Onze omstandigheden (behuizing, voeding, hygiëne) zijn zo snel veranderd (doordat wij onze omgeving zijn gaan aanpassen) dat de evolutie geen gelijke tred heeft kunnen houden. Ons immuunsysteem reageert nog alsof leven wij in de oertijd, alsof er voortdurend gevaar op de loer ligt! Overactiviteit van het immuunsysteem leidt in onze wereld tot een slechtere gezondheid en mindere vitaliteit. Het leidt tot ontstekingen, ziekte en aftakeling.

Een overactief immuunsysteem leidt o.a. tot overactiviteit van het zogenaamde cox 2 enzym. Hierdoor worden stoffen gevormd die leiden tot ontsteking en tot pijnklachten.

Zie voor de oorzaken van ontsteking: http://www.cbbr.nl/nieuws_11_febr2006_ontsteking.html en http://www.cbbr.nl/nieuws_12_mei2006_ontsteking.html

Anti ageing?

Aangezien ontstekingen ook bij verouderingsprocessen een belangrijke rol spelen, is de vrucht mangosteen ook goed bruikbaar bij preventie en anti ageing.

Info over goede mangosteen supplementen?

stuur een e mail naar info@cbbr.nl

Gebruik is nuttig bij ?

diverse situaties waarbij het nuttig is het cox enzym te remmen
bij preventie

Gezond oud worden ??

Over anti ageing en ontstekingspreventie in de volgende nieuwsbrief meer....

Bron : Henk de Valk, arts



De mangosteen vrucht kan een dikke schil hebben. In de schil zitten zoals bij meer vruchten, vele voor ons lichaam belangrijke ingrediënten.

Mouth

Cranberries Give Everyone Something To Smile About

We know what you're thinking, cranberries could help my teeth? Sounds crazy, but it's true. Your mouth is one place where the anti-stick power of cranberry may one day come in handy by helping to reduce the amount of bacteria in the mouth. Laboratory studies have suggested that cranberries may keep certain oral bacteria from attaching to teeth and gum surfaces(1-6). Less bacteria could potentially keep gums healthy and slow the development of plaque and cavities. We're not suggesting changing your mouthwash, but incorporating cranberry into oral care products may one day be a natural way to promote dental health. Also, keep in mind that cranberries are no substitute for regular dental care and check-ups. Always be sure to visit your dentist twice a year and brush and floss regularly.

Heart

Cranberry: A berry after your own heart.

Did you know 60 million Americans suffer from some sort of heart disease? That's about 1 in 4 adults. And there's more troubling news: cardiovascular diseases are the number one killer of both men and women in the U.S. Which is why it's so important for each of us to protect our hearts as best we can. The good news: preliminary research suggests that cranberries can help.



The antioxidants found in cranberries may help the body defend itself against free radical damage. In fact, laboratory studies show that cranberries can inhibit oxidation of low-density cholesterol, which is thought to be one way cholesterol becomes sticky, allowing it to attach to the blood vessel wall.(1-3) One small, preliminary study also found the same beneficial effect in humans after consumption of cranberry juice.(4) Organizations such as the Centers for Disease Control also recognize that diets high in fruits and vegetables, which are rich in fiber and natural antioxidants, are helpful in reducing the risk to chronic diseases, including heart disease.(5,6)

Isn't it amazing that such a little berry can have such big health benefits? And there's more. Emerging research suggests that cranberries may promote heart health in many ways.(7) One preliminary lab study suggests that a serving of cranberry juice cocktail may be as good for the heart as a glass of red wine.(3) And without the alcohol, so the whole family can enjoy the benefits. In test tube studies, scientists investigated cranberry juice cocktail, and 2 red wines, and found that serving for serving, cranberry juice cocktail was similarly effective to the red wines in modifying that activity of an enzyme that supports heart health. Studies also suggest that cranberry may promote heart health in other ways.(8) And, a clinical study reported that cranberry juice cocktail was beneficial to markers of heart health.(9) But remember, while cranberries can be a part of your overall heart health, they are no substitute for regular check-ups with your doctor.

Urinary Tract

Folklore, Wive's Tales & Other Truths

Turns out the old home remedy is true. Cranberries can help keep your urinary tract healthy. Naturally, too. Urinary tract health isn't something most women spend a lot of time thinking about. That is, until they experience the pain, discomfort and inconvenience first hand when the urinary tract is upset. It's not fun. Did you know half of all women will have at least one urinary tract infection (UTI) in her lifetime? In fact, an estimated 50 million cases are treated every year--with an estimated \$1 billion dollars in healthcare costs. It's also one of the leading causes of missed work for women. UTI's are just plain bad news. But thanks to the unique PACs in cranberries, you can minimize your chances of urinary tract problems.

Here's why the folklore is true: A urinary tract infection is caused when E. coli bacteria attach themselves to the walls of the bladder and multiply, causing redness, swelling and pain. Research suggests that the PACs in cranberries make it difficult for certain bacteria, even some nasty antibiotic resistant bacteria, from adhering to the bladder wall. The bacteria are harmlessly flushed out of the body(1,2,3).

Research shows drinking Cranberry Juice Cocktail daily can promote urinary tract health(4-11). The benefits of Cranberry Juice Cocktail start within two hours and can last up to ten hours(12). That means one serving (8 oz.) of Cranberry Juice Cocktail in the morning and one at night may better help keep certain harmful bacteria at bay all day. Bye, bye bacteria. Hello healthy urinary tract.

But remember, while Cranberry Juice Cocktail can be an effective part of a wellness routine it should not be used as a treatment for infection. If you suspect you have an infection, consult a healthcare professional.

Als we een stuk kaas blootstellen aan de lucht en zonlicht zal het bederven. Deze reactie noemen we een vrije radicaal reactie. De anti-oxidanten vertragen of voorkomen deze reactie en zitten daarom vaak in voedsel. Dezelfde gevreesde vrije radicalen proberen ook ons lichaam te 'bederven' en beschadigen daarbij lichaamscellen. De anti-oxidanten kunnen deze schade helpen beperken en daarom is het van belang om voeding te eten met veel anti-oxidanten. Deze zitten met name in groente en fruit. Tot nu toe hebben wetenschappers veel soorten groenten en fruit getest op hun anti-oxidatieve capaciteiten. De mate waarin het in staat is om vrije radicalen uit te schakelen wordt uitgedrukt in ORAC. Hoe hoger de ORAC waarde, des te beter.

Er zijn diverse factoren waar we rekening mee moeten houden bij het geven van gefundeerd voedingsadvies. We beginnen bij de essentiële micronutriënten. Dit zijn voedingscomponenten die ons lichaam absoluut nodig heeft om te functioneren, maar niet zelf aan kan maken. Het moet volledig uit voeding komen. Voorbeelden hiervan zijn vitamine C en de meervoudig onverzadigde vetzuren. De volgende groep bestaat uit de zogenaamde voorwaardelijk essentiële micronutriënten. Dit zijn voedingscomponenten die ons lichaam wel aan kan maken, maar niet in voldoende mate. Ook hier is goede voeding onontbeerlijk. Op latere leeftijd worden steeds meer micronutriënten voorwaardelijk essentieel. Voorbeelden van deze groep zijn bijvoorbeeld het verzadigde vetzuur, laurinezuur, co-enzym Q10 en het aminozuur, L-carnosine. De groep die overblijft is non-essentieel, maar dat betekent niet dat we ze niet hoeven te eten, want het kant- en klaar aanbieden scheelt het lichaam weer energie.

Een andere belangrijke factor is de glycemische belasting van voedsel. Dit is de mate en intensiteit waarin koolhydraten ons bloedsuikerspiegel niveau omhoog jaagt. Het continu moeten stabiliseren van de bloedsuikerspiegel put ons lichaam uit. Gebeurt dit vaak en intens dan heeft dat gevolgen voor onze gezondheid. Zodra het bloedsuikerspiegel niveau weer stabiel is zal ook ons hongergevoel terugkeren. De toename van koolhydraten die ons glycemisch belasten, zoals frisdranken, suikers en aardappelen is waarschijnlijk een van de oorzaken voor het toenemende overgewicht en de explosie van suikerziekte. Veel diëten maken een onderscheid tussen complexe en enkelvoudige koolhydraten. Dit blijkt in de praktijk weinig fysiologische waarde te hebben. De wereldgezondheidsorganisatie pleit dan ook voor afschaffing van dit onderscheid. We kunnen beter meteen leren welke producten goed en welke minder goed zijn voor onze bloedsuikerspiegel. Dit wordt uitgedrukt in een waarde genaamd, glycemische belasting. Een waarde van onder 10 wordt als laag beschouwd en dus gunstig, 11-19 middelhoog en producten met een waarde boven de 20 hoog. Sterke wetenschappelijke aanwijzingen pleiten voor een maximale belasting van 100 per dag.

Een belangrijk punt voor onze gezondheid is dat we van onze vetfobie af moeten. Nieuwe inzichten gebaseerd op sterke wetenschappelijke aanwijzingen, geven een veel genuanceerder beeld over vetten in relatie tot koolhydraten. Dit verklaart de verrassende verhouding in het gewenste dieet. Vetten zijn essentieel voor ons lichaam. Elke cel in ons lichaam heeft bijvoorbeeld een membraan van vet. Wij zouden, net als de eskimo's, zonder koolhydraten kunnen overleven. Dit is niet optimaal, want koolhydraten vormen een schonere brandstof, maar zonder vet zouden we heel snel omkomen. Door de vele berichten van de afgelopen tijd zou het idee kunnen ontstaan dat we alle verzadigde vetten links moeten laten liggen. Niets is minder waar, want er is overtuigend bewijs voor het wezenlijk belang voor onze gezondheid. Enkele verzadigde middellange-ketenvetzuren zoals laurinezuur dragen bij tot het natuurlijk vermogen van het lichaam om mogelijk schadelijke micro-organismen te bestrijden. Bovendien zijn verzadigde vetzuren nodig om het onverzadigd vetzuur alfa-linoleenzuur adequaat om te kunnen zetten in de verlengde omega-3-vetzuren EPA en DHA die we vooral in vette vis aantreffen. Laurinezuur, een verzadigd vetzuur, is voorwaardelijk essentieel voor lacterende vrouwen. Het lichaam maakt het aan, maar niet in voldoende mate. Moedermelk heeft sowieso een unieke samenstelling. Het vet is namelijk 45 to 50% verzadigd, 35% enkelvoudig onverzadigd en voor 15% meervoudig onverzadigd. De suggestie dat verzadigd vet de oorzaak van hartkwalen is, staat haaks op het feit dat de afzetting van vet op de aderen uit 74% onverzadigde vetzuren bestaat. Er is geen sterke relatie tussen verzadigde vetten en cardiovasculaire ziektebeelden. In tegenstelling tot de consumptie van transvetzuren en grote hoeveelheden onverzadigde omega 6 vetzuren. De eerder genoemde eskimo's met een hoog vetgehalte in hun voedingspatroon sterven zelden aan hart- en vaatziekten. Dit geeft ongetwijfeld een meer genuanceerd beeld over verzadigde vetten.

We vermoeden dat ongeveer 30% van onze energie uit vetten mag komen. De verhouding tussen verzadigde- en onverzadigde vetten 1 op 2 zou mogen zijn. Tot slot willen we ons nog richten op de productie en bereidingswijze van voeding. Regelmatig wordt om logistieke of marketingtechnische redenen ons voedsel 'mishandeld'. Voortschrijdende technologie heeft geleid tot nieuwe lichaamsvreemde stoffen of vreemde voedselverhoudingen. Ons lichaam kan hier slecht mee omgaan en zal door jarenlange consumptie hiervan, schade oplopen. Het betreft nieuwe voedingsstoffen zoals transvetzuren, vet- en zoetvervangers die onvoorspelbaar gedrag vertonen in ons lichaam. Het betreft ook bestaande voedingsstoffen die bijvoorbeeld door oververhitting veranderd zijn.

Grapes for taste and health

Do you want a healthy way to add flavor to your vegetable juice? Throw in some grapes, seeds and all. Adding a small amount of grapes tremendously improves the flavor of vegetable juice. I would limit the amount to about 5 grapes per every 8 ounces of juice, if you have evidence of high insulin levels, such as high blood pressure, high cholesterol, obesity or diabetes, and make sure you eat the pulp. I would also recommend you get the red seeded grapes.

You have probably heard of grape seed extract. Well you can get all the antioxidant and phytochemical benefits of grape seed extract when you juice the entire grape along with their seeds. It also tremendously improves the flavor of the juice. Grape seeds are known as a powerful antioxidant. Antioxidants help protect the body from premature aging, decay and disease. Antioxidants are needed to neutralize free radicals.

What is grape seed extract?

Grape seed extract is a nutrient derived from the seeds of grapes which belongs to the bioflavonoid family. The active ingredients contained in grape seed extract are called "proanthocyanidins". Proanthocyanidins are known to exhibit antioxidant properties. Proanthocyanidins are also called "procyanidolic oligomers", or PCOs for short - whew!

PCO bioflavonoids were first noticed in the laboratory because they have the remarkable ability to strengthen blood vessel walls within hours after taking them. The person responsible for the discovery of PCO bioflavonoids was a French scientist named Dr. Jacques Masquelier, who first tested bioflavonoid-containing peanuts on lab animals and discovered that their blood vessel walls would double in strength only hours after ingesting them. His discovery was made in 1948. In 1951, this same doctor extracted PCOs from pine bark.

Free radicals play a major role in the development of degenerative diseases, strokes, cardiovascular diseases and aging. Studies have shown that PCOs in grape seed extract are as much as 50 times more potent than those in Vitamin E and up to 20 times more potent than PCOs in Vitamin C.

The beneficial properties of flavonoids, including proanthocyanidins, have been extensively researched(2,7-9). In addition to their antioxidant and free radical scavenging activity, proanthocyanidins found in grape seed extract have been reported(1,8,10,11) to have antibacterial, anticarcinogenic, antiviral, anti-allergic, anti-inflammatory, and vasodilatory actions.(2,12)

Grape seed extract has also proven to be valuable in the treatment of inadequate blood flow in the capillaries and veins. Small studies have shown increased capillary strength using as little as 50 milligrams/day, and increased venous blood flow using 150 milligrams/day.

Flavonoids in general and proanthocyanidins in particular are free of side-effects. Since they are water-soluble, any excess proanthocyanidins are excreted via sweat or urine. There are no well-known drug interactions with grape seed extract or proanthocyanidins.

Resveratrol in the skin of grapes

But the seeds of the grape are not the only valuable part in a grape. There is a substance found in the skin (not flesh) of grapes, called "resveratrol".

Researchers reported in a study(13) that resveratrol is converted in the body to a known anti-cancer agent that can selectively target and destroy cancer cells.

Although previous studies have suggested that this phytoestrogen, resveratrol, might prevent cancer, the authors of this study said it was the first time that scientists had gained an insight into the underlying mechanism of the chemical's anti-cancer properties.

Fresh grape skin contains about 50 - 100 micrograms of resveratrol per gram, while red wine concentrations range from 1.5 to 3 milligrams per liter.

Bron : Marc Leduc , British Journal of Cancer 2002;5, Murray M, Pizzorno J. Procyanidolic oligomers. In: Murray M, Pizzorno J, eds. The Textbook of Natural Medicine. 2nd ed., Bravo L. Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. Nutr Rev 1998;56:317-333, Bagchi D, Garg A, Krohn R, et al. Protective effects of grape seed proanthocyanidins and selected antioxidants against TPA-induced hepatic and brain lipid peroxidation and DNA fragmentation, and peritoneal macrophage activation in mice. Gen Pharmacol 1998;30:771-776.



New Study Suggests **Concord Grape Juice May Provide Protection Against Breast Cancer**

Every three minutes, a woman in the United States is diagnosed with breast cancer⁽¹⁾. While factors like age and heredity contribute significantly to a woman's likelihood of contracting this disease, lifestyle and nutrition choices may also play a role. One dietary choice that may help provide protection against breast cancer is a glass of 100 percent grape juice made from deep purple Concord grapes.

According to a new study, published in the current issue of the *Journal of Medicinal Foods*, natural compounds in Concord grape juice protected healthy human breast cells from DNA damage. Healthy human breast cells were exposed in a test tube to an environmental carcinogen, benzo(a)pyrene, that is able to initiate a chain of events leading to breast cancer. However, the introduction of Concord grape juice compounds blocked the connection of the carcinogen to the DNA of the healthy cells.

"The purple grape compounds demonstrated the capacity to inhibit DNA adduct formation as well as to increase the activity of enzymes that metabolize and detoxify carcinogens, and suppress potentially cancer-causing oxidative stress," said Dr. Keith Singletary, nutrition professor and lead researcher at the University of Illinois. "These new data suggest that anthocyanins present in Concord grape juice, as well as some other fruits and juices, warrant further study for their breast cancer chemopreventive potential."

This research is the latest to suggest that Concord grape juice may be of value in maintaining breast health by suppressing oxidative stress and inhibiting DNA damage to cells that can lead to the initiation of cancer, or in helping to slow the progression of breast cancer by slowing the multiplication of cancer cells. Diets high in natural antioxidants have been associated with a reduced risk of some types of cancers, and Welch's 100% Grape Juice made from Concord grapes is particularly high in anthocyanins, potent natural antioxidants that give the juice its characteristic deep purple color.

At the same time, drinking Concord grape juice can be good for the heart -- much like red wine. And so, with the link between alcohol consumption and breast cancer causing concern for some women, drinking 100 percent grape juice made from Concord grapes can help your heart and perhaps your breast health.

Welch Foods Inc. is committed to supporting independent research exploring the role of Concord grape juice in a healthy lifestyle and provided the Concord grape juice compounds for this study.

(1) American Cancer Society, "Detailed Guide: Breast Cancer," 2006

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Drinking Concord Grape Juice May Reduce Blood Pressure In Hypertensive Men

-- One of first juice studies to feature randomized, double-blind, placebo-controlled design yields significant blood pressure data --

San Diego, CA (April 14, 2003)-Men with elevated blood pressure who drank Concord grape juice for twelve weeks experienced a significant drop in both their systolic and diastolic blood pressures, according to results from a preliminary study presented at Experimental Biology 2003.

"This is one of the first randomized, double-blind, placebo-controlled studies to use a juice-in this case Concord grape juice" explains study author Kevin Maki, Ph.D., Director, Nutrition and Metabolism Research Unit, Radiant Research, Chicago. "In our study, blood pressure was measured as part of the basic health information of the study participants. When we reviewed the data, we saw reductions of nearly six points in both systolic and diastolic blood pressure measurements among the hypertensive men drinking Concord grape juice. Those on the calorie-matched placebo showed no significant change."

The study, presented at the annual meeting of FASEB, the Federation for American Societies of Experimental Biology, looked at 80 healthy males, ages 45 to 70. For 12 weeks, half drank an average of 12 ounces of Concord grape juice per day and half drank the same amount of a placebo beverage designed to look and taste like grape juice. Median baseline systolic blood pressure was 132 mm Hg. At the conclusion of the study, the 19 participants with above-median systolic blood pressure who drank Concord grape juice showed a drop from an average baseline systolic blood pressure of 142.7 mm Hg to 137.0 ($p < 0.05$), and from 87.9 to 82.1 mm Hg ($p < 0.05$) for diastolic blood pressure. The 17 participants with above-median blood pressure who consumed the placebo showed no change from baseline. The systolic and diastolic differences between treatments were significant ($p < 0.05$).

"While additional studies are necessary to confirm these results, it is exciting that drinking Concord grape juice every day may be an easy way for hypertensive individuals to significantly lower their blood pressure," notes Maki. The US National High Blood Pressure Education Program estimates that lowering systolic blood pressure by 5 points would result in a 14% reduction in deaths from stroke and a 9% reduction from heart disease.

Bron: cocordgrape.org

Study Shows Drinking Concord Grape Juice Slowed LDL Oxidation; Inhibiting One Mechanism By Which "Bad" Cholesterol May Contribute To Cardiovascular Disease

Rate at which body oxidizes cholesterol may contribute to cardiovascular disease

Concord, MA (November 26, 2002)-Lowering LDL cholesterol is a well-accepted means of reducing the likelihood of heart disease. Now, in a new research study drinking Concord grape juice slowed the oxidation of LDL in the body, which according to the study's author, may complement LDL reduction in the battle for a healthy heart.

"We know that high levels of LDL cholesterol in the body contribute to heart disease," explains Ishwarlal Jialal, M.D., Ph.D., Professor, Department of Pathology and Internal Medicine, University of California, Davis. "What is also important to understand is that the LDL is relatively harmless unless it oxidizes within the arterial wall. So on one hand, we should strive to maintain health LDL levels in the body. At the same time, taking steps to impede the oxidation of LDL is a complementary pathway to cardiovascular health."

Subjects who drank Concord grape juice for two weeks showed a marked improvement in the resistance of their LDL cholesterol to oxidation. The study is published in the December issue of the American Journal of Clinical Nutrition.

As LDL cholesterol (the so-called "bad" cholesterol) circulates in the blood stream, it will occasionally penetrate the lining of the artery and occupy space within the arterial wall. In normal circumstances, it returns to the blood stream and continues to circulate. However, there is growing evidence that when the LDL oxidizes while in the arterial wall, it can initiate a cascade of events that lead to inflammation, atherosclerosis, and, eventually, arterial blockage that can lead to a heart attack or stroke. The more resistant the LDL is to oxidation—as in this study with people drinking Concord grape juice—the less likely the LDL is to contribute to this process.

"We compared subjects who drank Concord grape juice with similar individuals consuming vitamin E and found comparable effects on resistance to LDL oxidation—an important indicator of oxidative stress—and on ORAC capacity," says Jialal. "We also found that the juice decreased plasma protein oxidation—another oxidative stress marker—better than the vitamin E."

Dr. Jialal goes on to suggest that consuming Concord grape juice for longer periods of time—the subjects participated in the study for only two weeks—may provide increased protection from oxidative stress and inflammation.

"The take-away from this study is that we saw a potent antioxidant effect in both plasma and LDL cholesterol while seeing no corresponding increase in levels of vitamin E or C," explains Dr. Jialal. "This means that we can attribute the antioxidant effect directly to absorbed flavonoids found in the Concord grape juice,"

The research was funded by the National Institutes of Health and Welch Foods, Inc

Purple Grape Juice May Provide Welcome Option for Women Worried About Urinary Tract Infections, According to Welch's.

Compounds in grape juice as effective as those in cranberry juice in reducing bacterial adhesion associated with UTI
CONCORD, Mass.--(BW HealthWire)--Nov. 8, 2001-- In laboratory tests, compounds found in purple grape juice were as effective as those found in cranberry juice in blocking the bacterial adhesion that is thought to contribute to urinary tract infections. Urinary tract infections are a painful condition that affects nearly ten million Americans each year, mostly women, and are the country's second most commonly treated infection.

"It is well accepted that drinking cranberry juice reduces the incidence of urinary tract infection in women," explains David Mark, Ph.D., R&D manager, Health and Nutrition, for Welch Foods Inc., which sponsored the study. "This effect is attributed to compounds in the juice called proanthocyanidins. In our in vitro study, the proanthocyanidins from purple grape juice showed similar anti-adhesive qualities as those from cranberry juice."

Urinary tract infections occur when E. coli, a common bacterium, adheres to the lining of the bladder, colonizes and infects the bladder and urinary tract. The study, conducted five separate times, compared proanthocyanidins from Welch's Purple 100% Grape Juice against those from both Ocean Spray Cranberry Juice Cocktail and 100% cranberry juice in their effect against E. coli and found that the grape juice proanthocyanidins provided comparable bacterial anti-adhesion. The study was designed to replicate previous published research on the anti-adhesive properties of proanthocyanidins extracted from cranberries, by measuring the inhibition of E. coli adhesion to target cells in cell cultures.

"We think this is good news for the consumer," adds Mark. "More and more Americans are drinking purple grape juice for their heart health. Now people concerned about urinary tract health may have another effective, good tasting option to consider."

Purple grape juice has been shown to enhance cardiovascular function in a number of previous preliminary clinical studies. One serving of Welch's Purple 100% grape juice contains 100% of the RDA of vitamin C and counts towards the USDA goal of five servings of fruits and vegetables a day. According to a USDA study, purple grape juice also has three times the antioxidant power of such popular juices as grapefruit, orange, tomato and apple. It also carries the American Heart Association's HeartCheck symbol.
Bron: Concordgraper.org

-- Researchers see beneficial effects of juice at lower doses than previously tested --

Concord, MA (September 1, 2001)-Patients with narrowing of the coronary arteries who drank purple grape juice daily for eight weeks showed significant improvement in their arterial function, according to researchers at the University of Wisconsin School of Medicine. The researchers also found that purple grape juice achieves its effect independently of vitamin E, and at quantities lower than previously tested.

The study, published in the September issue of *The American Journal of Cardiology*, looked at the effect of drinking purple grape juice on flow mediated vasodilation—a measurement of the ability of the artery to relax and expand to accommodate increased blood flow. This represents a good gauge for measuring general arterial health, and the arteries of patients with vascular coronary disease typically do not relax well.

Eighteen men and four women with severely compromised arterial function drank purple grape juice over an eight week span. Half the participants consumed about 21 ounces of juice, depending on body weight. The others consumed half that dose—on average about ten ounces of juice a day. At the end of eight weeks, both groups showed a similar response—roughly doubling their flow mediated dilation (from 1.3% to 2.9%).

"It is interesting to see that the response to juice was approximately the same at both the higher and lower doses," notes James H. Stein, M.D., Assistant Professor of Medicine and senior author of the study. "The previous work we have done has been at slightly higher dosing levels. Now we are seeing that patients with severe vascular disease are responding to smaller quantities of juice—doses averaging ten ounces per day, depending on body weight."

As part of the study design, vitamin E supplementation (400 IU) was included in the subjects's diet after four weeks. The study found that the effects of the juice were independent of the presence of vitamin E.

While a previous study reported a larger increase in flow mediated dilation, the researchers point to several factors contributing to this study's results. First, participants in this study had, on average, more severe arterial disease. Second, juice in this study was stored in a manner that may have adversely affected its potency. Third, study subjects, because of the severity of their disease, were typically taking statins, beta-blockers or calcium channel blockers, common prescription drugs which may also, according to the researchers, have had a mediating effect on some of the findings reported in the study.

Researchers also found that after eight weeks of juice consumption, increases in lipid levels and triglycerides were not significant. Changes in insulin and glucose levels were also not statistically significant.

Two Recent Studies Point To "Heart-Healthy" Effects Of Drinking Purple Grape Juice

Circulation Study Identifies Dual Mechanisms of Action for Beneficial Effects of Purple Grape Juice in Humans

Atherosclerosis Study Shows Purple Grape Juice Inhibits Atherosclerosis and Reduces Cholesterol At Least As Well as Red Wine or Dealcoholized Red Wine in Animal Model

Concord, MA - Two separate studies recently published in leading cardiovascular research journals—one looking at mechanism of action; the other looking at clinical outcomes—point to the "heart healthy" benefits of drinking purple grape juice. In the June 12th issue of *Circulation*, the official journal of the American Heart Association, researchers showed that drinking grape juice not only has a direct effect on important biological functions like blood clotting but it also appears to increase the body's levels of valuable antioxidants while reducing free radical production.

"This study gives us new insight into how purple grape juice may improve cardiovascular function," explains Jane E. Freedman, M.D., assistant professor of medicine and pharmacology at Georgetown University and the lead author of the study. "What we are seeing for the first time is that the flavonoids in purple grape juice work in two related ways: First, they have a protective effect on vitamin E and other antioxidants, allowing them to remain active longer, while at the same time lowering production of superoxide—a free radical. Second, they also seem to have a direct, positive effect on a number of biological functions like nitric oxide production and inhibition of platelets, or the cells that cause clots, both of which are important protective factors as well."

"This study also supports our previous work published in the *Journal of Nutrition*, March, 2000," adds John D. Folts, Ph.D., director of the Coronary Thrombosis Research and Prevention Laboratory at the University of Wisconsin School of Medicine, and a co-author of the *Circulation* study. "That study demonstrated a reduction in clotting in healthy volunteers who consumed purple grape juice daily. More importantly, this study helps explain a mechanism behind the protective effects of purple grape juice."

In the May, 2001 issue of *Atherosclerosis*, researchers compared the effects of drinking purple grape juice, red wine, and dealcoholized red wine in hamsters. They found that purple grape juice, when compared to red wine and dealcoholized red wine, was at least as effective at: Lowering total cholesterol, Decreasing LDL, Reducing atherosclerosis (vs. wine only), Increasing LDL lag times. Bron : Cocordgrape.org

Health Benefits

Promotes Heart Health for All Ages

Preliminary research has shown that drinking antioxidant-rich Concord grape juice encourages clear, flexible arteries, which contribute to healthy circulation, blood pressure, and works against LDL (bad) cholesterol to allow for greater blood flow when needed, such as during increased activity.

Fights the Effects of Aging on Mind and Body

Emerging research not only suggests that what is good for the heart may also be good for the brain, but also suggests that antioxidant-rich foods, such as Concord grape juice may help protect our memory and brain function. A study on memory, health and aging found a link between consumption of antioxidant-rich fruits and vegetables and enhanced cognitive function. Laboratory research also shows that drinking Concord grape juice improves memory and physical dexterity.

Supports a Healthy Immune System and More

Many grape juices made from Concord grapes are an excellent source of vitamin C, which is necessary for a healthy immune system. In addition, the antioxidants in Concord grape juice protect against damage that can weaken the immune system, and preliminary research suggests that these antioxidants may also improve immune cell responsiveness.

Due in large part to the potent antioxidant effect of Concord grape juice, some preliminary cancer research has focused on investigating the role of Concord grape juice in potentially reducing the risks of certain types of cancers, such as breast cancer.

*Independent study of over 1,000 common foods measuring antioxidant capacity per serving. American Journal Clinical Nutrition July 2006.

FRENCH STUDY SHOWS CONCORD GRAPE JUICE HAS A HEART-HEALTHY EFFECT LIKE RED WINE'S

Grape juice made from Concord grapes is shown to stimulate nitric oxide production, which relaxes arteries and is associated with healthy blood pressure

CONCORD, MASS., January 30, 2007 – Many studies have suggested that moderate red wine consumption is beneficial to cardiovascular health. But what if you'd like to skip the alcohol? Take heart: in a laboratory study, just published in the January 2007 issue of Cardiovascular Research, Concord grape juice worked in a similar fashion to red wine to promote healthy arterial function.

Dr. Valérie Schini-Kerth and a team of researchers of the Université Louis Pasteur de Strasbourg found that Concord grape juice stimulated the production of nitric oxide in endothelial cells and produced a vasorelaxation effect. It is known that nitric oxide is important in the body's natural system for maintaining healthy, flexible blood vessels and helps support healthy blood pressure. The findings in this study are particularly noteworthy because the beneficial effects of Concord grape juice were observed in arteries of the heart.

Researchers further discovered that Concord grape juice produced this relaxation effect by stimulating the same chemical reactions in the arteries that are activated by red wine – showing that it's the components of the grape, rather than alcohol, that produces this beneficial effect for the heart.

This study supports other preliminary research in which Concord grape juice had a blood pressure-lowering effect as it provides a possible mechanism for the effect. So, for those looking for an alternative to red wine, grape juice made from Concord grapes provides a delicious, family-friendly, heart-healthy alternative.

Welch Foods Inc. is committed to supporting independent research exploring the role of Concord grape juice in a healthy lifestyle and provided funding and Concord grape juice for this study.

CONTACT: Regina Ragone, MS RD Hunter Public Relations (212) 679-6600



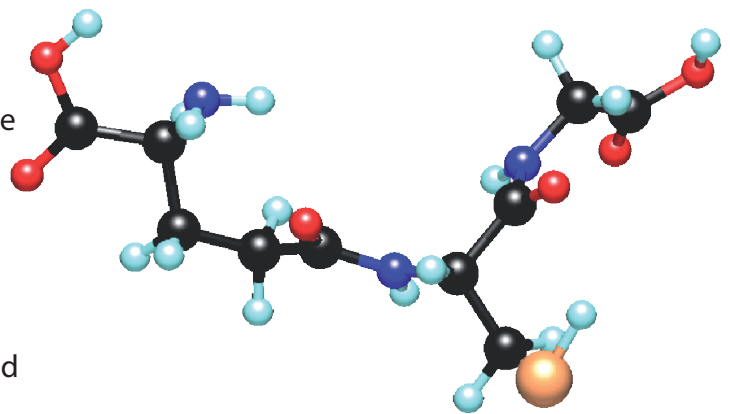
Anti-oxidanten en de rol in ons lichaam

- 1 Beschermende werking tegen oxidatie van LDL (cholesterol verbinding).
- 2 Beschermen van de endotheelcellen waarmee onze aders bedekt zijn.
- 3 Voorkomen dat bloedplaatjes samenklonteren in ons lichaam.
- 4 Vertragen van de oxidatie stimulerende werking van stress hormonen (catecholamines).
- 5 Verminderen van de hoeveelheid vrije radicalen.
- 6 Bescherming van de beschadigende werking als gevolg van Diabetes type II.
- 7 Bescherming van beschadigingen als gevolg van het verouderingsproces.
- 8 Beschermende werking tegen de schadelijke effecten als gevolg van arthritis of Alzheimer.
- 9 Bescherming tegen degeneratieve processen in de hersenen die leiden tot Parkinson of Alzheimer.

In de huidige samenleving zien we dat veel mensen steeds minder groente en fruit eten. Daardoor krijgen ze ook veel minder anti-oxidanten binnen. Een suppletie van anti-oxidanten kan voor sommige mensen heilzaam werken (denk aan ouderen). Bovendien is het raadzaam niet te kiezen voor één anti-oxidant maar voor zoveel mogelijk verschillende vanwege de mogelijk synergetische werking van anti-oxidanten in ons lichaam. Het beste advies lijkt ook hier: eet met mate, maar gezond (groente en fruit) en gevarieerd.

Antioxidantia, een bescherming tegen de constante aanval van de vrije radicalen.

Glutathione Molecule
water oplosbare
anti-oxidant



Leo Goeyens, Wetenschappelijk Instituut Volksgezondheid

De bedreiging van onstabiele moleculen

Een vrij radicaal is een onstabiele molecule, die zelf heel gemakkelijk met andere moleculen reageert. Probleem hierbij is dat die reactie vernietigend is voor de andere moleculen. Het is een "afbraakreactie" en dat kan gevaarlijk zijn. Nemen wij ons voedsel. Eenmaal vers bereid, is het voedsel onderhevig aan wijzigingen, met name chemische wijzigingen, waardoor het op de lange duur helemaal ongeschikt wordt voor consumptie. Blootstelling aan zuurstof uit de lucht, bij voorbeeld, maakt vet ranzig en het voedsel onsmakelijk. De reactie met zuurstof, die we oxidatie noemen, kan nog andere gevolgen hebben. Essentiële bestanddelen kunnen afgebroken worden; soms verandert niet enkel de smaak maar worden er tevens toxische stoffen in het voedsel geïntroduceerd. Het is hoegenaamd niet nutteloos om de bewaardata te respecteren !!!

We staan echter niet helemaal machteloos tegenover deze vorm van bederf. Toevoegingen van antioxidantia vertragen of verhinderen de oxidatie en verhogen dus de shelf life van het voedsel. Het komt er op aan ofwel de zuurstof uit te schakelen en zo de oxidatie te beletten ofwel de vorming van onstabiele vrije radicalen te verhinderen. Hiervoor heeft men de keuze uit een hele reeks van synthetische en natuurlijke antioxidantia. Vitamine C, bij voorbeeld, is een natuurlijke en water-oplosbare antioxidant en dus uitermate geschikt voor de bescherming van opgeloste voeding. Vitamine E is vet-oplosbaar en dus aangewezen voor de bescherming van lipiden (olieën en vetten).

De afbraakreactie, waarvan reeds sprake, vindt overigens ook plaats in de cellen van levende organismen. Ons lichaam evenals dat van onze geliefkoosde huisdieren maakt vrije radicalen aan. Dit is een normaal metabolisch proces; cellen verouderen en sterven af. Alleen, we willen dat verouderingsproces graag onder controle houden en zelfs vertragen in de mate van het mogelijke. In dit verband werden de voordelen van een juist gebruik van antioxidantia uitgebreid beschreven in de medische literatuur. Het lijkt vast te staan dat de toediening van supplementen van antioxidantia de kans op een ondermijnende ziekte op latere leeftijd aanzienlijk vermindert. En aanrijkingen van antioxidantia in het voer van onze poezen en honden zijn vandaag ook niet ongewoon meer.

Gezondheidsbevorderende mechanismen van bioactieve stoffen.

Zoals al gezegd, is er dus nog veel onbekend over bioactieve stoffen en het onderliggende werkingsmechanisme dat zorgt voor het positieve effect op de gezondheid. Er zal dus nog veel onderzoek gedaan moeten worden naar de exacte mechanismen, de meest optimale hoeveelheden, en naar de biobeschikbaarheid (hoeveel kan je lichaam opnemen en gebruiken?). Het probleem is, dat het moeilijk is om aan te tonen dat juist één stofje een bepaald effect op de gezondheid heeft. Misschien is het namelijk wel een ander stofje in het dieet of de leefstijl van een persoon die de werking van het eerste stofje bepaald. Vele factoren kunnen er dus voor zorgen dat er een vertekend beeld ontstaat van wat nu precies de oorzaak is en wat het gevolg. Daarbij kunnen er ethische bezwaren zijn om mensen bijvoorbeeld een bepaald stofje te laten eten als daarvan nog niet bekend is wat de effecten van dat stofje zijn.

Samenvattend kan gezegd worden dat het onderzoek naar bioactieve stoffen en de werking daarvan niet eenvoudig is. Toch zijn er inmiddels positieve effecten aangetoond bij zowel mens- als dieronderzoek voor carotenoïden, flavonoïden, fenolische zuren, glucosinolaten, alkylsulfides, fytoosterolen, terpenen en saponinen.

Over de werking van bioactieve stoffen wordt het volgende verondersteld. Er zijn bioactieve stoffen die werken als een antioxidant. Ook zijn er effecten op de bloedstolling en op de verlaging van het serumcholesterolgehalte waargenomen.

De antioxidatieve werking is een belangrijke factor in de beschermende rol van groente en fruit. Vitamine C en E zijn antioxidanten, maar ook een groot aantal andere bioactieve stoffen, zoals de carotenoïden, hebben een antioxidatieve werking. Antioxidanten beschermen ons tegen vrije zuurstofradicalen. Het is normaal dat deze vrije zuurstof radicalen ontstaan in ons lichaam, maar als er teveel zijn kunnen ze schade aanrichten. Onze lichaamscellen en hun erfelijk materiaal (DNA) kunnen dan beschadigd raken en de kans op kanker, hart- en vaatziekten, staar en veroudering wordt groter.

Het eten van veel groente en fruit verkleint het risico op kanker van mond- en keelholte, slokdarm, maag en longen. De bioactieve stoffen kunnen het kankerproces op verschillende momenten en manieren beïnvloeden: via de genoemde antioxidantwerking, maar ook door inwerking op enzymen, hormonen of het immuumsysteem.

Hart- en vaatziekten kunnen ontstaan doordat vrije radicalen vaatwanden beschadigen. Door de beschadiging ontstaat er plaquevorming en slibben de vaten dicht. Ook de invloed van flavonoïden op de bloedstolling en de verlaging van het cholesterolgehalte door de fytoosterolen lijken hier beschermend te werken.

Flavonoïden

Flavonoïden zijn polyfenolen die aanwezig zijn in plantaardige voedingsmiddelen en dus ook in groenten en fruit. In groenten en fruit zijn deze stoffen verantwoordelijk voor de grote variatie in kleuren, van geel tot rood en donkerpaars. Subgroepen binnen de flavonoïden zijn flavonolen, flavonen, flavanonen, catechinen, anthocyanen en isoflavonoïden. Tot nu toe zijn er al meer dan 4000 soorten flavonoïden beschreven. De belangrijkste bronnen van flavonolen en flavonen zijn niet groente en fruit maar thee, wijn en uien. Studies bij grote groepen mensen naar deze afzonderlijke flavonoïdenrijke voedingsmiddelen laten nog geen consistent beschermend effect op kanker en hart- en vaatziekten zien. Nu moet niet geconcludeerd worden dat groenten en fruit dus niet gezond zijn! Het is namelijk wel degelijk vastgesteld dat groenten en fruit beschermend werken, deze bescherming is mogelijk ook het werk van andere bioactieve stoffen dan flavonoïden. Mogelijk zijn er dus meerdere mechanismen van invloed en hebben verschillende bioactieve componenten onderling effect op elkaar.

Van de andere flavonoïden leveren catechinen en anthocyanen eveneens een belangrijke bijdrage in onze voeding. Catechinen zitten in thee, wijn en fruit. Anthocyanen zorgen voor de rode en paarse kleuren in groenten en fruit.

De hoogste gehalten aan anthocyanen worden gevonden in bessensap, rode wijn, bessen en druiven.



Carotenoïden.

Carotenoïden hebben een antioxidantieve werking. Men vermoedt dat ze een belangrijke rol spelen bij de bescherming van cellen tegen oxidatie. Carotenoïden komen in veel soorten groenten en fruit voor. Er bestaan meer dan 500 varianten, waaronder β -caroteen en luteïne (zie tabel 2). Zo zou een hoge inname van β -caroteen geassocieerd zijn met een verlaagd risico op hart- en vaatziekten. Behalve beschermende effecten werden echter ook negatieve effecten van carotenoïden gevonden.

Net als bij flavonoïden worden niet alle carotenoïden even goed in de darmen geabsorbeerd. Het voedingsmiddel waarin de flavonoïden verpakt zitten, speelt hierin een rol. Zo blijkt de biobeschikbaarheid van β -caroteen uit fruit veel groter dan uit groenten en van het carotenoïde lycopene uit een gekookte tomaat (of tomatenpuree) groter dan uit een rauwe tomaat.

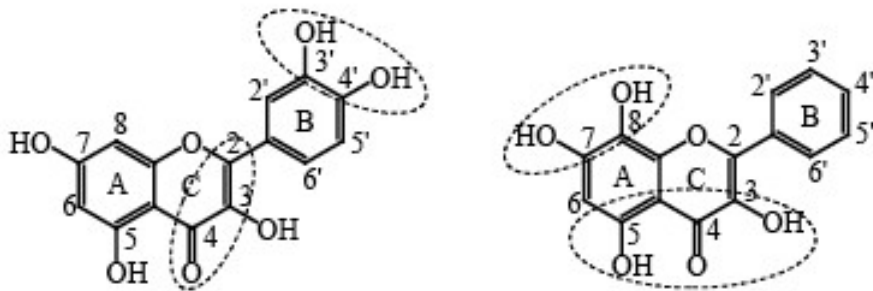
Glucosinolaten

Glucosinolaten komen alleen voor in kruisbloemigen groenten, zoals bloemkool, broccoli en spruitjes. Er bestaan meer dan 100 verschillende soorten glucosinolaten en de gehaltes in de verschillende groenten kunnen aanzienlijk variëren. Door het verwerken en bereiden van deze groenten daalt de biobeschikbaarheid van de isothiocyaten. De isothiocyaten geven spruitjes de specifieke bittere smaak.

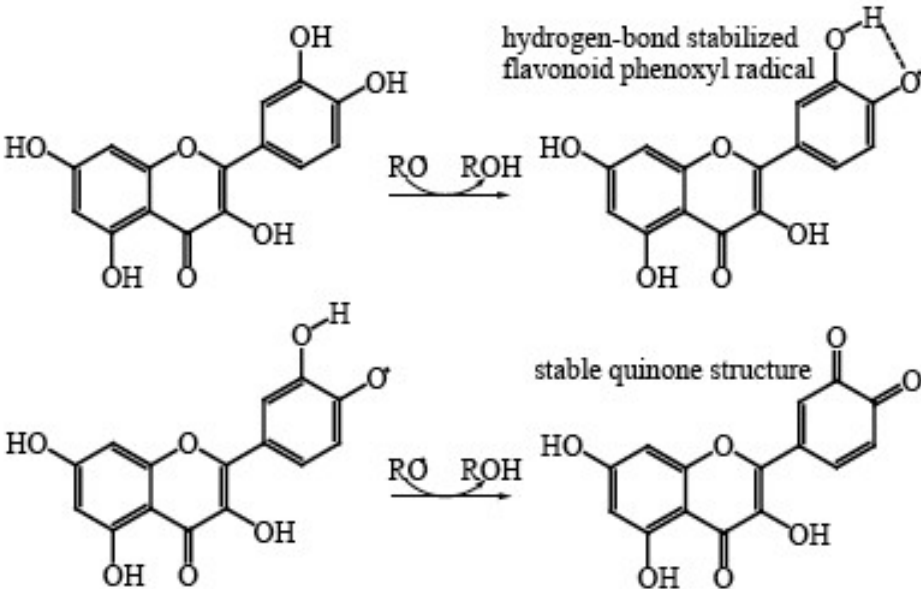
Een hoge consumptie van deze groenten, in het bijzonder van broccoli, blijkt mogelijk het risico te verlagen van verschillende kankersoorten zoals colon- en rectumkanker. Behalve glucosinolaten bevat broccoli echter ook nog andere bioactieve componenten, zoals bijvoorbeeld flavonolen, die eveneens verantwoordelijk kunnen zijn voor een beschermend effect. Daarnaast kunnen verschillende componenten in broccoli elkaar mogelijk ook versterken.

Bron:www.food-info.net

Polyphenols :



Basic structural features of flavonoids with high multifunctional activities, *i.e.* free radical scavenging, metal ion chelating and enzyme inhibiting



Mechanism of antioxidant action of 3',4'-diOH polyphenols (flavonoids)

Polyphenols: antioxidants and beyond^{1,2,3}

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² Presented at the 1st International Conference on Polyphenols and Health, held in Vichy, France, Nov. 18–21, 2004.

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ABSTRACT

Research on the effects of dietary polyphenols on human health has developed considerably in the past 10 y. It strongly supports a role for polyphenols in the prevention of degenerative diseases, particularly cardiovascular diseases and cancers. The antioxidant properties of polyphenols have been widely studied, but it has become clear that the mechanisms of action of polyphenols go beyond the modulation of oxidative stress. This supplemental issue of *The American Journal of Clinical Nutrition*, published on the occasion of the 1st International Conference on Polyphenols and Health, offers an overview of the experimental clinical, and epidemiologic evidence of the effects of polyphenols on health.

Key Words: Polyphenols • flavonoids • antioxidants • health

Polyphenols are the most abundant antioxidants in the diet. Their total dietary intake could be as high as 1 g/d, which is much higher than that of all other classes of phytochemicals and known dietary antioxidants. For perspective, this is 10 times higher than the intake of vitamin C and 100 times higher than the intakes of vitamin E and carotenoids (1, 2). Their main dietary sources are fruits and plant-derived beverages such as fruit juices, tea, coffee, and red wine. Vegetables, cereals, chocolate, and dry legumes also contribute to the total polyphenol intake.

Despite their wide distribution in plants, the health effects of dietary polyphenols have come to the attention of nutritionists only rather recently. Until the mid-1990s, the most widely studied antioxidants were antioxidant vitamins, carotenoids, and minerals. Research on flavonoids and other polyphenols, their antioxidant properties, and their effects in disease prevention truly began after 1995 (Figure 1). Flavonoids were hardly mentioned in textbooks on antioxidants published before that date (3). The main factor that has delayed research on polyphenols is the considerable diversity and complexity of their chemical structures.

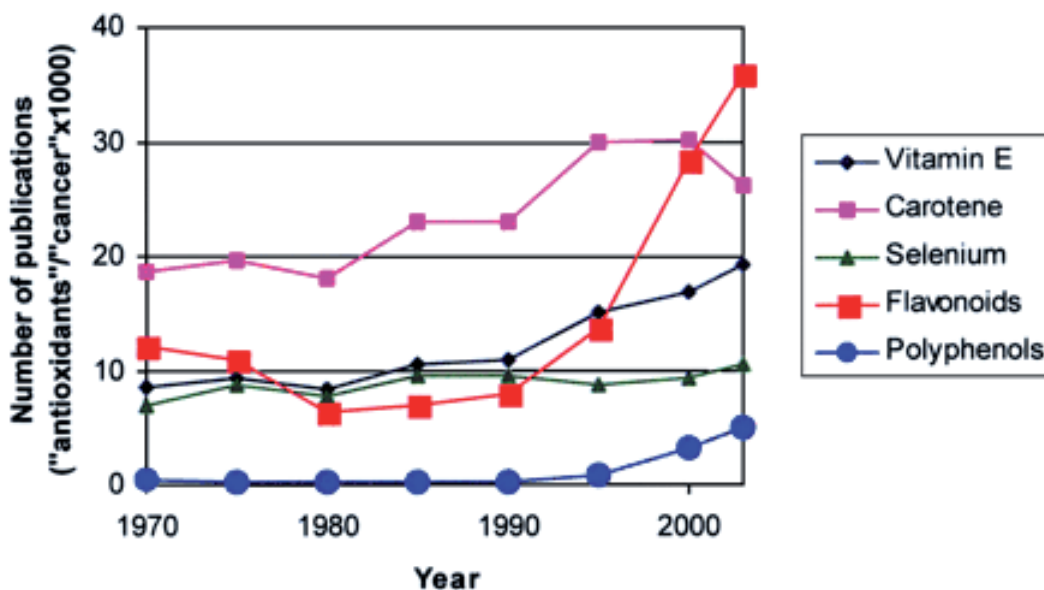


FIGURE 1. Increase in the number of publications regarding various antioxidants in the past 30 y. Publications were those registered in the Medline database. Values were determined as follows: number of results from the query "compound X" AND "year n"/number of results from the query "cancer" AND "year n" x 1000. The key word cancer was used as a reference, to take into account the general increase in the number of publications.

Current evidence strongly supports a contribution of polyphenols to the prevention of cardiovascular diseases, cancers, and osteoporosis and suggests a role in the prevention of neurodegenerative diseases and diabetes mellitus (4). However, our knowledge still appears too limited for formulation of recommendations for the general population or for particular populations at risk of specific diseases. Evidence for a reduction of disease risk by flavonoids was considered "possible" for cardiovascular diseases and "insufficient" for cancers in a recent report from the World Health Organization (5). The objectives of the 1st International Conference on Polyphenols and Health (Vichy, France, November 18–21, 2004) were to offer an overview of our current knowledge on the associations between polyphenol intake and disease and health and to discuss key issues awaiting resolution. More than 350 communications from >30 countries were presented. The articles included in this volume correspond to the invited lectures presented at the conference.

Much of the evidence on the prevention of diseases by polyphenols is derived from *in vitro* or animal experiments, which are often performed with doses much higher than those to which humans are exposed through the diet. One purpose of the conference and of this volume was to review some of the evidence for health effects of polyphenols in humans, from both clinical trials and epidemiologic studies. Polyphenols clearly improve the status of different oxidative stress biomarkers (6). Much uncertainty persists, however, regarding both the relevance of these biomarkers as predictors of disease risk and the appropriateness of the different methods used (7). Significant progress has been made in the field of cardiovascular diseases, and today it is well established that some polyphenols, administered as supplements or with food, do improve health status, as indicated by several biomarkers closely associated with cardiovascular risk (8–10). Epidemiologic studies tend to confirm the protective effects of polyphenol consumption against cardiovascular diseases (11). In contrast, evidence for protective effects of polyphenols against cancers, neurodegenerative diseases, and brain function deterioration is still largely derived from animal experiments and *in vitro* studies (12, 13); we await the discovery of predictive biomarkers for such diseases or large intervention studies, similar to those performed with nonphenolic antioxidants (14).

One of the major difficulties of elucidating the health effects of polyphenols is the large number of phenolic compounds found in food (15), yielding differing biological activities, as shown in several *in vitro* studies (16, 17). Major differences in bioavailability are now well established, and the influence of structural factors is better understood (18). This issue was discussed at length during the conference. The active compounds may not be the native polyphenols found in food, which are most often tested in *in vitro* studies; they are more likely to be metabolites (19). The importance of microbial metabolites has been emphasized in some recent studies, as exemplified by equol, the major metabolite of daidzein (20). Polyphenols are extensively conjugated in the body, and nonconjugated metabolites most often account for a minor fraction of the circulating metabolites. Very little is currently known regarding the biological activities of these conjugated metabolites (1). Glucuronides of isoflavones and epicatechin were shown to have much weaker estrogenic activity and provided no protection against oxidative stress in cells grown *in vitro* (21, 22). These findings suggest that many of the *in vitro* studies published to date must be reevaluated, in light of the new data on polyphenol bioavailability.

A considerable body of literature supports a role for oxidative stress in the pathogenesis of age-related human diseases and a contribution of dietary polyphenols to their prevention. The complex relationships between antioxidant status and disease are still poorly understood and have been studied intensively. For many years, polyphenols and other antioxidants were thought to protect cell constituents against oxidative damage through scavenging of free radicals. However, this concept now appears to be an oversimplified view of their mode of action (23). More likely, cells respond to polyphenols mainly through direct interactions with receptors or enzymes involved in signal transduction, which may result in modification of the redox status of the cell and may trigger a series of redox-dependent reactions (24–26). Both antioxidant and prooxidant effects of polyphenols have been described, with contrasting effects on cell physiologic processes. As antioxidants, polyphenols may improve cell survival; as prooxidants, they may induce apoptosis and prevent tumor growth (12). However, the biological effects of polyphenols may extend well beyond the modulation of oxidative stress. One of the best-known examples involves the interaction of soy isoflavones with estrogen receptors and the effects of these compounds on endocrine function. These effects could explain the prevention by isoflavones of bone resorption among postmenopausal women (27). A detailed understanding of the molecular events underlying these various biological effects is essential for evaluation of the overall impact on disease risk and progression.

The current evidence for protective effects of polyphenols against diseases has generated new expectations for improvements in health, with great interest from the food and nutritional supplement industry regarding promotion and development of polyphenol-rich products. However, it is still impossible to evaluate the individual and societal benefits that increases in polyphenol intake could have for the general population or for particular groups at specific disease risk. Furthermore, a significant increase in the consumption of polyphenols, as for many other phytonutrients, may not be without risks (28). Some hazards associated with the consumption of polyphenols are documented, but evaluation among humans is still very limited. Lastly, we should not forget that many polyphenols have a taste and/or a color (29); food must be not only good for health but also acceptable to consumers.

Integration of the results of past and future experiments in various disciplines, including biochemistry, cell biology, physiology, pathophysiology, epidemiology, and food chemistry, will be needed to identify the most effective polyphenols and to determine the optimal levels of intake for better health. The present research efforts will coordinate with current efforts to identify more accurate biomarkers of risks for nutrition-related diseases and should lead to dietary recommendations and the formulation of new food products contributing to good health.

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Pomegranate Glossary

ACE - ACE stands for angiotensin-converting enzyme. By splitting proteins, these enzymes convert angiotensin I into angiotensin II, a substance that increases salt and water in the body and leads to high blood pressure, a real no-no. ACE inhibitors make blood vessels relax, helping to lower blood pressure and allowing more oxygen-rich blood to reach the heart. Research shows reduced ACE by 36% in ten elderly patients with high blood pressure after drinking an 8 oz. glass a day for only 2 weeks and also lowered their systolic blood pressure by 5%.

Anthocyanins - Naturally occurring polyphenolic compounds give many fruits, vegetables and plants their bright colors. Originally derived from two Greek words meaning plant and blue, anthocyanins are what make eggplants purple and pomegranates red. Many of the antioxidant characteristics in plants are due largely to anthocyanins. In fact, the darker, more deeply red and blue fruits usually have higher values of antioxidants; the rich, red pomegranate is absolutely loaded.

Atherosclerosis - Often called hardening of the arteries, atherosclerosis starts when oxidized cholesterol and other substances build up in the inner lining of an artery. The build-up is called plaque. Damage occurs when the plaque reduces the blood's flow or when the plaque ruptures and causes blood clots. When a blood vessel that feeds the heart is blocked, it can cause a heart attack. If it blocks a vessel feeding the brain, it can cause a stroke. Naturally, the less plaque, the better. And that's where pomegranates comes in.

A pilot study of 19 elderly patients with atherosclerosis showed that an 8 oz. glass of pomegranate concentrate a day can reduce plaque build-up in the arteries by up to 30%.

Antioxidants - Antioxidants are scavengers that may neutralize free radicals before they get a chance to harm you body. They get their name from their ability to inhibit oxidation. There are lots of different substances we call antioxidants, including many vitamins and minerals. Of course, not all antioxidants are created equal, and some of the most powerful, polyphenol antioxidants are found in great abundance in pomegranate hich is why we call "The Antioxidant Superpower".

Carotid IMT - A stroke occurs when an adequate flow of blood to the brain is disrupted. The most common cause of this disruption is a narrowing or blockage of the carotid artery caused by the accumulation of plaque in the artery walls. The carotid arteries are the main blood supply to the brain. The intima-media thickness (IMT) of the carotid arteries is a common way to measure how much plaque is lining the artery walls. The less, of course, the better.

Ellagic Acid - A naturally occurring phenolic compound phytochemical found in many fruits and vegetables, with levels much higher in berries and pomegranates than in apples, pears or walnuts.

Free Radicals - Free radicals are atoms or molecules in your body with an unpaired electron-making them highly unstable. Because electrons normally come in pairs, the free radicals collide with other molecules in an attempt to steal an electron, and may start a chain reaction, damaging your DNA and cells. Emerging science suggests this free radical damage may be linked to disease. Free radical scavengers, or antioxidants, bind with the free radicals before they can do their damage. This brings us back to Pomegranate Juice. The polyphenol antioxidants in Pomegranate concentrated juice have been shown through emerging science to function as potent free radical scavengers.

HDL/LDL - High-density lipoprotein, or HDL cholesterol, is called "good" cholesterol because scientists believe it removes cholesterol from the blood, thereby reducing your risk of heart disease. You want your HDL count to be "high" and your LDL count to be "low." Low-density lipoprotein, or LDL cholesterol, carries the majority of cholesterol through the blood stream. In order for cholesterol to travel through your blood (cholesterol can't dissolve in water or blood), it's coated with a layer of protein to make lipoprotein. Larger, less dense and less stable than HDL cholesterol, LDL can oxidize if attacked by free radicals and build-up on the walls of your arteries. This plaque can narrow the arteries, reduce blood flow or rupture, leading to heart disease or stroke. Which is why LDL cholesterol is known as the "bad" cholesterol.

Hypertension - Also called high blood pressure, it's a major cause of damage to the arteries, heart and kidneys and can lead to atherosclerosis and stroke. 8 When your blood vessels are narrow and filled with plaque, it's harder for blood to flow through them and pressure against your artery wall increases. This can cause high blood pressure.

Nitric Oxide - Produced by several different kinds of cells and present in all humans and most animals, nitric oxide functions as a signaling molecule that tells the body to make blood vessels relax and widen. Nitric oxide controls our blood pressure, giving us more blood when we're exercising and reducing the flow of blood when we're at rest. Since heart attacks happen when the blood can't flow through the blood vessels to the heart, we of course want to encourage lots of nitric oxide in our body... it can help by relaxing the blood vessels, allowing them to open and increasing blood flow.