



Science of the Mangosteen and the Role of Inflammation on Chronic Disease

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The Mangosteen fruit has extremely powerful **NATURAL** anti-inflammatory properties & more than 40 different antioxidants.

Are you one of the tens of millions of people in the U.S. with chronic pain and wondering what to do? Are you aware that inflammation is now felt to be a central component in many diseases.

Cancer

Inflammation increases the spread of abnormal cells & provides the fuel that facilitates their transformation into cancer cells

Heart Disease

Inflammation is a major cause of heart attacks and strokes

Alzheimer's

Inflammation chews up nerve cells

Diabetes

Inflammation promotes insulin resistance keeping insulin from functioning

Allergies & Asthma

Chronic Inflammation is related to Allergies & Asthma in the lungs

Arthritis & Auto-Immune Disease

Inflammation affects the joints and other tissues

Why Are Xanthones So Powerful

Mangosteen contains over 40 DIFFERENT Xanthone, a powerful new class of antioxidants.

What separates Mangosteen from all other antioxidants are the 40+ POWERFULL Xanthones, EACH Xanthone having, DIFFERENT properties, as well as the same Catechins found in Green Tea, as well as Proanthocyanidins, Polysaccharides, and Polyphenols! Mangosteen has MULTIPLE potential health benefits, unique for antioxidants!

- **Antiaging**
- Cardioprotective
- Antidepressant
- Anti-arthritic & osteoporotic
- Antibacterial & Antiviral
- Anti-Alzheimer's
- Antifungal & TB
- Supports Body to Reduce Pain

The Problem - Inflammation and Pain

The traditional approach to treating inflammation and pain is with anti-inflammatory drugs (such as aspirin, Ibuprofen and Naproxen) and with "COX-2 Inhibitors" (such as Vioxx and Celebrex). These man-made drugs have SERIOUS side effects including ulcers, bleeding problems and the increase in heart attacks with the "man made" Cox 2 inhibitors.

More than 50 million people are estimated to take aspirin as an anti-inflammatory for its cardioprotective effects. The major

risk of anti-inflammatory drugs (including aspirin) is the risk of bleeding. In a prospective evaluation of 18,820 hospitalized patients, 1225 were admitted because of adverse drug reactions.

Pharmaceutical drugs cause 350,000 drug-related deaths per year just from the side effects, the 3rd leading cause of death, equivalent to 3 jumbo jets crashing DAILY.

Adverse Reactions to Aspirin

Low-dose aspirin was identified as one of the most common causes of adverse drug reactions, with 18% of the hospitalizations and 61% of the fatalities associated with aspirin. In the Woman's Health initiative, even a 100-mg aspirin on alternate days was associated with increased risk of GI bleeding compared to placebo.

The Solution - Mangosteen Research

There is over 100 years of scientific research on the power of mangosteen and xanthones. Dr. James Duke, who retired in 1995, long before the 1st commercial Mangosteen juice arrived, is one of America's foremost ethnobotanists. He worked for 35 years for the USDA and the University of Maryland. One of his major accomplishments is a remarkable phytochemical & botanical database which is now well known on the Internet. This list identifies 138 separate qualities for Mangosteen based on scientific research.

Mangosteen juice has been shown in scientific studies to be a powerful NATURAL Anti-Inflammatory (a NATURAL COX-2 INHIBITOR), WITHOUT any side effects.

Mangosteen juice is one of the only NATURAL COX-2 inhibitors on the market.

SAFETY: A toxicity study was done on rats using the original Mangosteen juice (equivalent of 5 bottles per day). The outcome: healthy rats.

Why take a supplement "if you feel healthy" or if your symptoms don't go away?

There are 4 stages of disease:

Phase 1 - disease is present but can't be diagnosed (heart disease has been seen as young as age 3)

Phase 2 - physiological abnormalities can be diagnosed if looked for, but NO symptoms exist.

Phase 3 - symptoms finally occur. This is when most people finally seek medical attention.

Phase 4 - the disease progresses and may be fatal.

Are you starting to see that as diseases develop, the symptoms may be SILENT for many years?

Mangosteen juice provides a golden opportunity for you to intervene and potentially prevent or even reverse the disease from progressing.

Why Is Free-Radical Damage and Chronic Inflammation a problem

Free-radical damage and chronic inflammation interact together in a vicious cycle leading to many diseases. Free radicals are unstable molecules which steal an electron from other normal healthy cells to attempt to become normal. Free radicals attack healthy cells throughout the body (silent process) all day and all night long, damaging organs, other cells and even the DNA.

Inflammation is the key component of the immune system's defenses. We can't live with it or without it. **Persistent repeated assaults on our immune system, like eating unhealthy foods, smoking cigarettes, excess cholesterol, STRESS etc., produces**

Xanthones SLOW DOWN the free-radical destruction of our body's 10 trillion cells with NO known side effects.

chronic inflammation that smolders like a low flame on the back of the stove until the pot burns. Let's look at a couple of major causes of disease and death.

1. Reduction Of Cancer Using Anti-Inflammatories:

There is a direct connection between certain cancers and inflammation. For example, by keeping inflammation down, women can decrease their risk of breast cancer.

In the Woman's Health Initiative¹, 72,242 women (ages 50 - 79) took anti-inflammatories only twice a week, reducing their risk of breast cancer 21-28% over a 5 to 9 year period. (Low-dose Aspirin & Tylenol gave NO protection.) Taking anti-inflammatories more than twice / week led to potential side effects.

If taking an anti-inflammatory twice per week could reduce women's risk of breast cancer, what could possibly happen if women took a natural anti-inflammatory twice a day, not twice a week?

Lisa Coussens, a cancer biologist at UCSF, notes that people with chronic Inflammatory Bowel Diseases have a tremendously increased risk of colon cancer. Other inflammation also associated with cancer, includes cigarette smoke in the lungs, persistent infections like Hepatitis C in the liver, and chronic heartburn from reflux esophagitis.

2. Relationship Of Inflammation To Heart Disease & Strokes:

In the U.S. each year, there are 700,000 NEW heart attacks, 500,000 recurrent attacks, and 175,000 silent first heart attacks and strokes. **Half the people with heart attacks have NORMAL cholesterol levels.**

Inflammation is the cornerstone behind heart disease and strokes. A few years ago, most regarded heart disease as an accumulation of cholesterol deposits on the walls of the coronary arteries. We now know that these cholesterol deposits trigger free-radical damage, leading to chronic inflammation at the site of these arterial blockages.

As the chronic inflammation builds, these plaques push the walls of the artery outward. Eventually these plaques become unstable and can rupture, leading to a clot, producing a heart attack (in the heart) or a stroke (in the brain), which can lead to sudden death.

Many of the "plaques" that clog arteries are actually quite small and inflammation causes them to burst, triggering massive clots that cut off the blood supply to the arteries of the heart.

Half the people with heart attacks have NORMAL cholesterol levels. According to many researchers chronic inflammation may be a bigger risk of heart attack or stroke than smoking or high cholesterol.



Most people have inflammation in their arteries!

Because there are no symptoms such as pain, we're not prompted to do anything about this "silent disease." Medical personnel, usually, do not use preventive checks and wait until you have a heart attack or stroke.

Mangosteen & C-Reactive Protein

Peter Libby MD², Chief of Cardiology at Brigham and Women's Hospital in Boston, notes that ruptured plaques from inflammation are the cause of 70% of all heart attacks, not clogged arteries. This means that by the time you see the first narrowing in the artery, chronic inflammation is everywhere. This explains why patients keep coming back with repeat heart attacks and other problems after treatment.

CRP (C-reactive protein), a simple blood test, measures the index of inflammation in the arteries. As inflammation increases, the CRP increases (normal CRP = 0.2 mg/L). Middle-aged men with a CRP greater than 3.0 mg/L were three times more likely to suffer a heart attack in the next six years than men with normal levels. Experts say that a CRP of 3.0 mg/L or higher triples your heart attack risk. People with a CRP less than 0.5 mg/L rarely have heart attacks.

Steve Nissen MD², Chairman of Cardiology at Cleveland Clinic, points out that you can bypass the arteries, but if you don't stop the disease from progressing, the plaque will continue to build up elsewhere over time. **He says one must stop the inflammation.**

He further reports that the same drugs that we use to lower CRP are the same statin drugs we used to lower cholesterol. He points out that we thought the statin drugs were just lowering cholesterol, but we now know that **the more you lower the CRP, the more you reduce inflammation and lower your risk of death, heart attack and stroke.**

Vaughn Johnson, D.O., a family physician in Salt Lake City, Utah, did a simple study of 47 patients with elevated C-Reactive Protein. He placed them on two ounces once a day of Mangosteen juice. No other interventions or changes were made. One month later, 38 patients returned (9 did not).

All 38 patients' abnormally elevated CRP had decreased to normal levels on Mangosteen juice in one month!

The following table lists typical results.

Sample #	Initial CRP Level	CRP Level 30 Days Later
1	55.0 mg/L	2.7 mg/L
2	26.0 mg/L	1.3 mg/L
3	12.6 mg/L	1.8 mg/L
4	8.4 mg/L	2.2 mg/L
5	6.8 mg/L	1.1 mg/L

The above 5 samples were selected because after the test month each person stopped taking the original Mangosteen product & took "other" Mangosteen products. All five returned to their abnormal high risk CRP level after using the other Mangosteen products usually containing extracts. Dr. Johnson then put each of these patients back on the initial Mangosteen juice and all of the CRP numbers came back down. **Dr. Johnson concluded that all Mangosteen supplements are not created equal.**

Additional Considerations

Dr. Greg Cole¹ at UCLA points out that a diet rich in fruits and vegetables is also helpful.

He has studied curcumin, from the curry spice turmeric, and found it to be a natural COX-2 inhibitor. He considers it safer than Vioxx. While drugs usually block a single action, reducing its activity dramatically, Cole says that natural anti-inflammatories modify a broader range of inflammatory compounds. He notes that you'll get greater safety and efficacy by reducing five inflammatory mediators by 30% than one by reducing one by 100 percent. **Dr. Cole is saying that natural anti-inflammatories are safer, and also very effective while having multiple action sites.**

Conclusions

The anti-inflammatory/analgesic market is a \$50 billion market expected to rise to \$108 billion in the next few years; the New York Times says it will be years before there will be a safe solution – **YET WE HAVE A POTENTIAL SAFE SOLUTION NOW, WITH NO SIDE EFFECTS OR DRUG INTERACTIONS!**

EVEN IF THE SYMPTOMS ONE HAS DON'T GO AWAY, Mangosteen JUICE SHOULD BE CONTINUED to potentially prevent chronic inflammation along with their bodies own defenses.

By decreasing inflammation, men & women can potentially reduce their risk of many chronic diseases of aging caused by free-radical damage & chronic inflammation.

Many people use Mangosteen juice and a few do not immediately feel better. Often to alleviate symptoms it is necessary to take a higher amount for a longer time, "at least 60-90 days". Mangosteen juices anti-inflammatory effects are powerful, but if your symptoms are still present do not stop prematurely, you have a lot to gain. Remember there are no known side effects.

Consider most people have a 75% chance of ultimately dying from heart disease, strokes or cancer; the long term potential benefits of using Mangosteen juice daily, forever, are enormous.

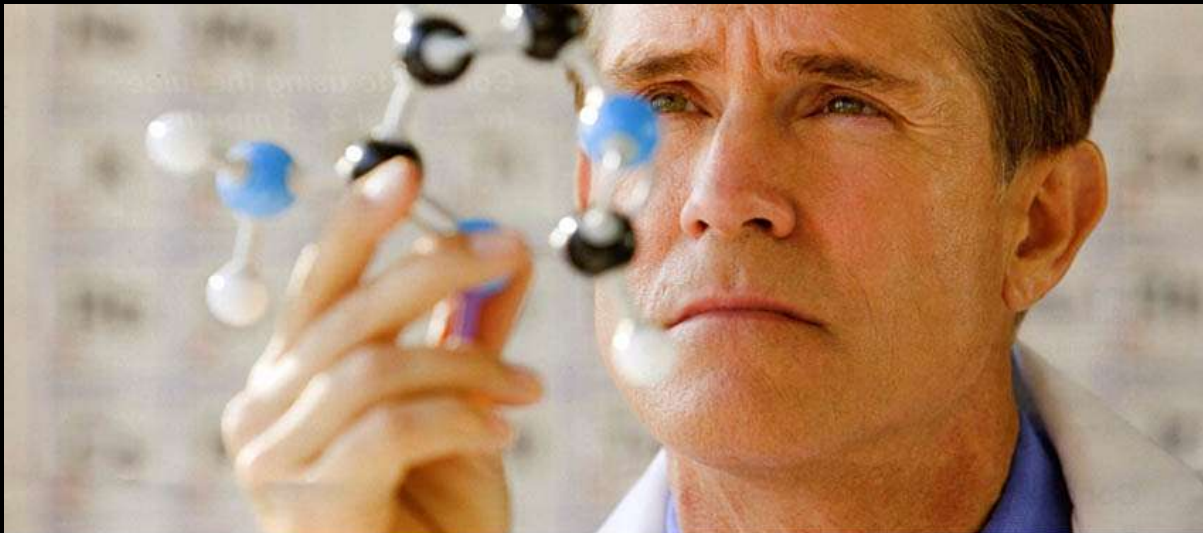
Commit to using the juice for at least 2 - 3 months.

Why would anyone want to use a drug when a food or fruit juice can provide the same result or better? The antioxidant efforts of Xanthones may take months if not years to return the body to a NORMAL HEALTHY body – be patient!

Children and elderly people who hate swallowing pills can take Mangosteen juice. It's exciting to have a supplement with NO side effects and NO contraindications.

The MANGOSTEEN FRUIT has extremely powerful NATURAL anti-inflammatory properties.





Mangosteen Annotated Research References

In The News:

¹ Quieting Body's Defenses—Anne Underwood -Newsweek www.msnbc.msn.com/id/8271053/site/newsweek/

² Watching: The Hidden Epidemic - Heart Disease In America – Larry King – PBS documentary www.mymangosteen.com/pbs

Inflammation Research:

Inhibition of cyclooxygenase and prostaglandin E2 synthesis by gamma-mangostin, a xanthone derivative in mangosteen, in C6 rat glioma cells Keigo Nakatani, Norimichi Nakahata, Tsutomu Arakawa, Hideyuki Yasudac and Yasushi Ohtsumi Biochem Pharmacol. 2002 Jan 1; 63(1):73-9.

The fruit hull of mangosteen fruit, *Garcinia mangostana* L., has been used for many years as a medicine to treat skin infection, wounds, & diarrhea in Southeast Asia. They studied the effect of gamma-mangostin, a xanthone, showing it had Cox-2 inhibition & potent inhibitory activity of prostaglandin E2 (PGE2) release.

Inhibitions of histamine release & prostaglandin E2 synthesis by mangosteen, a Thai medicinal plant. Nakatani K, Atsumi M, Arakawa T, Oosawa K, Shimura S, Nakahata N, Ohtsumi Y. Biol Pharm Bull. 2002 Sep; 25(9):1137-41.

The investigators found the mangosteen fruit extract strongly inhibited histamine release and prostaglandin E2 synthesis. This has great importance in preventing allergies.

Histaminergic and serotonergic receptor blocking substances from the medicinal plant *Garcinia mangostana*. Chairungsilend N, Furukawa K, Ohta T, Nozoe S, Ohtsumi Y. Planta Med. 1996 Oct; 62(5):471-2.

They determined that alpha & gamma-mangostin are a histaminergic & a serotonergic receptor blocking agent, respectively. That is, they have the ability to prevent allergies and inflammation.

Cancer And Hematology (Blood) Disorders:

Garcinone E, xanthone derivative, has potent cytotoxic effect against hepatocellular carcinoma cell line. Ho CK, Huang YL, Chen CC. Planta Med. 68 (11): 975-9, 2002.

The investigators tested 6 xanthones from the fruit *Garcinia mangostana* on 14 different human liver cancer cells and cancer cells of the lung & stomach. They found Garcinone E had greater tumor-killing action than usual chemotherapeutic agents (Metotrexate, Vincristine, 5-FU, Cisplatin, Mitoxantrone) and less than Taxol. QUOTE: "Unlike other anti-cancer drugs such as Metotrexate and Vincristine, the cytotoxic effect of Garcinone E does not vary greatly among different cancer cell lines and could achieve total killing of the target cells... Garcinone E should be a more effective drug than Metotrexate, Vincristine, 5-FU & Cisplatin, suggesting that it is potentially more effective than some of the commercially available anti-neoplastic agents presently in use."

Antiproliferation, antioxidation and induction of apoptosis by *Garcinia mangostana* (mangosteen) on SKBR3 human breast cancer cell line P. Moongkarnkarni, N. Kosema, S. Kadlungkub, O. Luanratanae, N. Pongpanc and N. Neungtond Journal of Ethnopharmacology Volume 90, Issue 1, Jan. 2004, Pgs 161-166

They found that an extract from the Mangosteen fruit inhibited the growth of breast cancer cells. They also showed that the extract had potent antioxidant and cancer cell death properties

Induction of apoptosis by xanthones from mangosteen in human leukemia cell lines. Matsumoto K, Akao Y, Kobayashi E, Ohguchi K, Ito T, Tanaka T, Iinuma M, Nozawa Y. J Nat Prod. 2003 Aug; 66(8):1124-7.

They examined the effects of six xanthones on the cell growth inhibition of human leukemia cell line HL60. Alpha-mangostin showed the most potent ability to cause the death of cancer cells.

Alpha-mangostin induces Ca²⁺-ATPase-dependent apoptosis via mitochondrial pathway in PC12 cells. Sato A, Fujiwara H, Oku H, Ishiguro K, Ohtsumi Y J Pharmacol Sci. 2004 May; 95(1):33-40. ..

Alpha-mangostin had the most potent effect with apoptosis (death) of pheochromocytoma (cancer) cells.

Xanthones as inhibitors of growth of human cancer cell lines and their effects on the proliferation of human lymphocytes in vitro. Pedro M, Cerqueira F, Sousa ME, Nascimento MS, Pinto M Bioorg Med Chem. 2002 Dec; 10(12):3725-30.

This showed inhibition research of in-vitro growth of three human cancer cell lines (breast cancer, kidney cancer, melanoma).

Antiplatelets activity of some xanthone derivatives. Rajar G, Zolkowska D, Kleinrok Z, Marona H. Acta Pol Pharm. 1999 Jul-Aug; 56(4):319-24.

Researchers studied the effects of twelve xanthone-derived compounds on platelet aggregation. They found five of them inhibited thrombin-induced platelet aggregation (inhibited clot formation).

Heart Disease, Cholesterol, High Blood Pressure and Diabetic Research:

High-Sensitivity C-Reactive Protein: A Novel and Promising Marker of Coronary Heart Disease By Nader, Rifai & Paul M. Ridker Clinical Chemistry 47: 403-411, 2001 Major review of CRP in heart dis & cancer

Inhibition of lipoprotein oxidation by prenylated xanthones derived from mangostin. Mahabarakam W, Proudfoot J, Taylor W, Croft K. Free Radic Res. 2000 Nov;33(5):643-59.

Oxidative damage plays a critical role in cardiovascular and other chronic diseases. They have previously shown that the xanthone mangostin can inhibit the oxidation of LDL, low density lipoprotein (bad cholesterol). Researchers studied more xanthone-derived compounds and found enhanced antioxidant activities.

(Research References Continued)

Note: If the oxidation of LDL cholesterol can be prevented or inhibited, then the LDL cholesterol cannot exert its "bad" effect and cause heart disease.

Mangostin inhibits the oxidative modification of human low density lipoprotein. Williams P, Ongsakul M, Proudfoot J, Croft K, Bellin L. Free Radic Res. 1995 Aug; 23(2):175-84.

They concluded that mangostin is acting as a free radical scavenger ("mop up" sponge) to protect the LDL from oxidative damage in this in vitro system. In other words, it's a potent antioxidant.

Relationship between protective effect of xanthone on endothelial cells and endogenous nitric oxide synthase inhibitors. Jiang DJ, Hu GY, Jiang JL, Xiang HL, Deng HW, Li YJ. Bioorg Med Chem. 2003 Nov 17; 11(23):5171-7.

Xanthone-preserved endothelial cells inhibited the increased adhesion of monocytes to endothelial cells induced by oxidized LDL. It was key in preventing plaque formation, subsequent blockage of arteries, and heart disease.

Antihypertensive and vasorelaxing activities of synthetic xanthone derivatives. Wang LW, Kang JJ, Chen JJ, Teng CM, Lin CN. Bioorg Med Chem. 2002 Mar; 10(3):567-72.

All compounds tested exhibited effective hypotensive (lower blood pressure) activity in anesthetized rats.

Antidiabetic activity of a xanthone compound, mangiferin. Miura T, Ishii H, Hashimoto I, Iwamoto N, Kato M, Kubo M, Ishihara E, Ishida T, Tanigawa K, Suzuki. Phytomedicine. 2001 Mar; 8(2):85-7.

Mangiferin, a xanthone, lowered the blood glucose (sugar) level in type II diabetic mice and likely exerts its anti-Diabetic activity by decreasing insulin resistance.

Synthesis and antithrombotic effect of xanthone derivatives. Lin CN, Hsieh HK, Lion SJ, Ko HH, Lin HC, Chung MI, Ko FN, Liu HW, Teng CM. J Pharm Pharmacol. 1996 Sep; 48(9):887-90.

They found several xanthone-derived compounds to possess potent antithrombotic (anticoagulating) activities.

Protecting women's hearts: An interview with Mayo Clinic specialist - Excellent practical review - approach prevention in heart disease www.mayoclinic.com/invoke.cfm?id=HB00040

(4) A Randomized trial of Low Dose Aspirin in Primary Prevention of Cardiovascular Disease - Ridker, PM, Cook NR, NEJM 2005; 352:1293 - 1304. Mangosteen Annotated Research References - continued

Infections:

Antibacterial activity of xanthenes from guttiferaceous plants against methicillin-resistant *St. aureus*. Iimura M, Tosa H, Tanaka T, Asai F, Kobayashi Y, Shimano R, Miyauchi K. J Pharm Pharmacol. 1996 Aug; 48(8):861-5.

This showed that extracts of *Garcinia mangostana* possessed strong inhibitor in-vitro effects against both methicillin-resistant and methicillin sensitive *Staphylococcus aureus* (which is a large cause of antibiotic resistance).

Alpha mangostin vs Vancomycin resistant *Enterococci* (VRE) March 2005 Dbarmarate, H.R.W. Phytomedicine, International Journal of Phytotherapy & Phytopharmacology; 3/1/2005

Alpha-Mangostin, from the stem bark of *Garcinia mangostana* L., was found to be active against Vancomycin resistant *Enterococci* (VRE) and Methicillin resistant *Staphylococcus aureus* (MRSA). Our studies showed synergism between [alpha]-mangostin and gentamicin, and against Vancomycin resistant *Enterococci*, and [alpha]-mangostin and Vancomycin hydrochloride (VCM) against MRSA, as well as partial synergism between [alpha]-mangostin and commercially available antibiotics such as ampicillin and minocycline. Antibiotic resistance is a huge problem in healthcare throughout the world and Alpha-Mangostin has a huge potential solution.

Antimycobacterial Activity of Prenylated Xanthenes from Fruits of *Garcinia mangostana* S. Suktamarn, N. Suwannapoch, W. Phakhodee, J. Thanuhiranlert, P. Ratananukul, N. Chimnoi, & A. Suktamarn Chem. Pharm. Bull. 51(7) 857-859 (2003)

Investigators found that alpha- and beta-mangostins and garcinone B exhibited strong inhibitory effect against *Mycobacterium tuberculosis* (TB).

Plant-derived leading compounds for chemotherapy of (HIV) infection. Vlietinck AJ, De Bruyne T, Apers S, Pieters LA. Planta Med. 1998 Mar; 64(2):97-109.

They found the xanthone mangostin could inhibit the replication cycle of HIV (AIDS virus).

Active constituents against HIV-1 protease from *Garcinia mangostana*. Chen SX, Wan M, Loh BN. Planta Med. 1996 Aug; 62(4):381-2.

They found that extract of *Garcinia mangostana* showed potent inhibitory activity against HIV-1 protease (AIDS virus) which affects the replication of HIV.

Xanthenes as antimalarial agents; studies of a possible mode of action. Ignatshchenko MV, Winter RW, Bachinger HP, Hinrichs DJ, Riscoe MK. (Portland, Oregon) FEBS Lett. 1997 Jun 2; 409(1):67-73.

Researchers showed potent anti-malarial activities for the xanthenes studied.

Brain and Neurologic Disorders:

Synthesis and anticonvulsant effects of some aminoalkanoic derivatives of xanthone. Marona H. Pharmazie. 1998 Oct; 53(10):672-6.

Researchers studied compounds derived from xanthenes for anticonvulsant (inhibited seizure) activities. They found several xanthone-derived compounds to be active in anticonvulsant tests.

Other References

Other references by doctors discussing Mangosteen and Xanthenes. Doctors Templeman & Morton are world experts on Mangosteen fruit research.

"Mangosteen - The X Factor DVD (classroom)" by Fredric Templeman, M.D. & David Morton Ph.D.

"Mangosteen - The Gift Your Body Deserves" by J. Fredric Templeman, M.D.

"Tame the Flame - Mangosteen's Remedy for Chronic Disease" by Sam Walters, N.D.

"Alternative Medicine in a Bottle" by Les Berenson MD, FACP Above books, CDs, and DVDs are available online at * www.mangosteentools.com or by phone at 888-461-7090.

Ask the person who gave you this literature about Mangosteen juice.

It combines the WHOLE FRUIT PUREE of the Mangosteen, in combination with other natural fruit juices and no added sugar for a delicious taste.



Les Berenson is a board certified Internal Medicine physician who has practiced Wellness and Preventive Medicine for over 25 years. He was elected to Fellowship by the American College of Physicians. During his medical career, his passion and practice was to help people learn to prevent heart disease, cancer and chronic disease as well as possibly get off medications by doing lifestyle changes. Over the years, his interests have shifted towards Complimentary Medicine because of the significant beneficial results with dramatically REDUCED SIDE EFFECTS and COSTS.



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