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FLAVONOIDS

Flavonoids are the water soluble coloring pigments found in fruits and vegetables. They are the counterpart to the fat soluble coloring pigments called carotenoids. Flavonoids exert antioxidant activity in the water soluble compartments of tissue while carotenoids exert antioxidant activity in the fatty tissues.

There are literally thousands of flavonoids (over 4,000) with varying degrees and kinds of activity. These flavonoids are responsible for the blue, purple, and emerald green hues of many foods. There are a variety of flavonoids including flavones, flavanones, flavanols, catechins, anthocyanins, and closely related ellagic acid.

Flavonoids are very effective at inhibiting the formation and activity of peroxynitrite, a powerful oxidant. Nitric oxide is produced by the inner lining of the arteries, macrophages, neutrophils, and brain synaptosomes. When nitric oxide combines with superoxide peroxynitrite is formed.

This is a particularly damaging oxidant due not only to the kind of potential damage it can do but also due to where this damage can take place. Potential sites of damage include the inner lining of the blood vessels, the brain and the immune system.¹ Peroxynitrite can damage not only fats, but also DNA and proteins in the cell.²

Researchers have found increased

nitration in neurons in Alzheimer's disease. The researchers concluded, "These findings provide strong evidence that peroxynitrite is involved in the oxidative damage of Alzheimer's disease. Moreover, the widespread occurrence of nitrotyrosine in neurons suggests that oxidative damage is not restricted to long-lived polymers such as NFTs (neurofibrillary tangles), but instead reflects a generalized oxidative stress that is important in disease pathogenesis." The accumulation of nitrotyrosine is an indicator that damage has been done by peroxynitrite rather than other free radicals.³

Peroxynitrite has also been implicated as an important oxidant in inflammatory lung disease.⁴

One summary concludes, "In vivo, peroxynitrite generation represents a crucial pathogenic mechanism in conditions such as stroke, myocardial infarction, chronic heart failure, diabetes, circulatory shock, chronic inflammatory diseases, cancer, and neurodegenerative disor-



ders. Hence, novel pharmacological strategies aimed at removing peroxynitite might represent powerful therapeutic tools in the future."⁵

Flavonoids may also protect from nitrogen compounds like nitrosamines and nitrites present in bacon, hot dogs and luncheon meats. A number of years ago a study revealed that when children consumed more than 12 hot dogs a month their risk of childhood leukemia increased almost six times. If fathers consumed more than 12 hots dogs a month the risk of leukemia in their children increased 11 times. The nitrogen compounds were destroying the DNA in the sperm increasing the chances of cancer in their children at an early age.⁶

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FLAVONOIDS AND CANCER

Considerable research has shown that flavonoids inhibit the development of cancer. Both citrus and soy flavonoids have been shown to inhibit the appearance of cancer in laboratory animals. The flavonoids inhibited both estrogen-receptor positive and estrogen-receptor negative cancers. The flavonoids also acted synergistically in their inhibition of cancer with tocotrienols, part of the vitamin E family of nutrients.

These researchers wrote, "It is known that combinations of drugs are often more effective in the treatment of cancer than the individual drugs by themselves, and it seems reasonable to think that this principle may also apply to dietary compounds with anticancer activity. Eating a mixture of foods containing these different compounds may thus help to prevent cancer..."¹

The irony of antioxidant studies by researchers is that they often attempt to study these compounds in isolation in spite of the fact that they work together. One could not accurately assess the functionality of the hand by a thorough analysis of the workings of one or two fingers. Yet in study after study researchers attempt to do this very thing with nutrients.

In 1996 the Southern Research Institute of Birmingham, Alabama, following National Cancer Institute Protocols, conducted studies on a number of different compounds to assess anti-cancer activity. One of these products was the GNLD Flavonoid Complex. The researchers found a linear response between the level of flavonoid exposure and the inhibition of breast cancer growth.A report of the findings states, "The concentrations used for regression were 150 µg/ml and 200 µg/ml. Percent inhibition at these points were 41.5% and 82.1%, respectively. This study demonstrates that a flavonoid rich blend of fruit and vegetable extracts strongly inhibits the growth of human breast cancer cells." This summary may have actually understated the inhibitory effect of the flavonoids in this tissue culture study because at a level of 250 µg/ml inhibition of breast cancer cell growth was 96%.²

Flavonoid Complex is a valuable source of antioxidants which have profound anti-carcinogenic properties. The anti-carcinogenic activity of flavonoids has transformed them in the eyes of the scientific community from unimportant food constituents to a status of being semi-essential nutrients. One researcher wrote, "the cytostatic and anti-carcinogenic activity of food flavonoids which distinguishes these compounds from all other nutrients is a fundamental phenomenon which warrants in itself the conclusion that flavonoids must be looked upon as 'semi-essential' food components."3 Other researchers write, "Of the many actions of flavonoids, antioxidant and antiproliferative effects stand out."4

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FLAVONOIDS AND HEART DISEASE

The benefit of flavonoids is not limited to protection against cancer. These compounds also provide significant protection against heart disease. Flavonoids strengthen the walls of blood vessels, inhibit oxidation of cholesterol, and decrease the stickiness of blood platelets.¹

The antioxidant properties of flavonoids are primarily responsible for the cardioprotective effects of flavonoids. The flavonoids in tea appear to be particularly protective as illustrated by the following comment, "Of the flavonoids and flavonoidrelated compounds, flavonols found in tea are the most powerful natural antioxidants. These results provide a mechanism for the beneficial epidemiological effect of dietary flavonoids on heart disease."2 It should be noted that inhibition of heart disease with flavonoid intake appears to occur in a dose related manner--the higher the intake the lower the risk of heart disease.

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ALCOHOLISM

Flavonoids may be valuable tools for reducing alcohol intake. In one study alcohol consumption of Syrian golden hamsters was reduced by 50% with the addition of two



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flavonoids (daidzin and daidzein) to the diet. These flavonoids have been traditionally used in Chinese medicine to treat alcohol abuse.¹

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Flavonoids and Inflammation

One of the more prominent properties of the flavonoid family of nutrients is their powerful anti-inflammatory effects. One researcher writes, "...the inhibitory action on inflammatory cells, especially mast cells, appears to surpass any other clinically available compound...the therapeutic potential of select flavonoids is fairly obvious. The areas that hold the most promise are chronic inflammatory and allergic diseases, as well as coronary artery disease and breast cancer. Well designed clinical trials are overdue possibly because there is no intellectual property protection."¹ Note that flavonoid anti-inflammatory activity might rival that of a number of pharmaceutical drugs, but there is no motivation to study the possibility because there is no ability to patent flavonoids assuring a healthy profit. Flavonoids should rank right along with omega-3 fatty acids and vitamin C as powerful natural anti-inflammatories.

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ANTIOXIDANT ACTIVITY

Essential fatty acids can spontaneously oxidize (autoxidize) destroying their nutritional value. Flavonoids have been shown to prevent the autoxidation of linoleic acid, the root compound of the biologically essential omega-6 fatty acids. The antioxidant efficiency was in the following order: fustin< catechin < quercetin < rutin.¹



This study demonstrates that there is a wide range of activity among different flavonoids and also that they can exert powerful protective effects toward the fatty tissues of the body even though they themselves are not fat soluble.

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PINE BARK FLAVONOIDS

If one reads discussions of flavonoids one is sure to encounter extravagant claims made for pine bark flavonoids (pycnogenol). Most of the medical claims for pine bark are based upon extrapolations from research on other flavonoid products.

For example, pine bark has been touted as being 50 times more powerful than vitamin E. Unfortunately, this claim is based on a study which used green tea and persimmons. The study itself is flawed because flavonoids are water soluble and vitamin E is fat soluble. This is like comparing the properties of olive oil and vinegar.

The study cited looked at six different flavonoid compounds, yet only one was six times more effective than vitamin E. It was also more effective than vitamin E in quenching only one type of free radical.¹

The defect in relying upon pine bark as a source of flavonoids lies in the fact that pine bark is not a normal part of the human diet. As a matter of fact one is hard put to find anything that feeds on pine bark. Pine bark also has a limited flavonoid profile while scientific research has repeatedly demonstrated that a diverse intake of antioxidants is far more effective than an intake of only one or two. **REFERENCE:**

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GNLD AND FLAVONOIDS

GNLD has provided flavonoids in supplement form since the introduction of their first vitamin C product. In those early days flavonoids were considered nutritionally unimportant. I remember listening to a debate on the radio between a supplement supplier who incorporated flavonoids in his product and a prominent radio talk show host who was a physician. The physician was arguing that the incorporation of flavonoids into a vitamin C product was of no value. Most physicians would not dare make that accusation today. GNLD continues to supply citrus flavonoids with the Super C and All C products.

The combination of vitamin C with flavonoids has been shown to improve the bioavailability of vitamin C by 35% over vitamin C alone and also results in significantly higher blood levels four to six hours after intake.¹

GNLD Super C locks the vitamin C in a protein mesh which digests slowly providing a threshold control or monitored release of the vitamin. This provides a distinct advantage because the half-life of vitamin C in the blood appears to be only about 30 minutes. Hickey and Roberts write, "Single large dose will only give about four to six hours of protection as this is the period during which blood levels are raised." They also observe, "A single megadose will provide only a fraction of the potential benefit of split or slow release doses."²



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GNLD's second flavonoid introduction was Flavonoid Complex which widened the sources of flavonoids available. This supplement added flavonoids from cranberries, kale, green tea, beet, elderberry, red grape, black grape, lemon, grapefruit, and orange. The research on this product is discussed in this paper.

One of the flavonoid classes with the highest antioxidant activity is the flavonol category. Foods rich in flavonols include cranberry, kale, and tea. Quercetin and kaempferol, the two most common flavonoids in kale, have antimutagenic and anticarcinogenic effects as well as substantial antioxidant activity.³ Among the anticancer compounds, kale was only surpassed by onion in its quercetin content in one study and no food came close to kale's kaempferol content. ⁴

Elderberry contains four flavonoids which have been shown to incorporate themselves into the lining of blood vessels providing significant protection.⁵ Elderberry flavonoids also have antiviral properties, having been shown to reduce the duration of influenza infections by four days.⁶

Grapes are a source of resveratrol and other valuable flavonoids. The flavonoids in grapes and wine are believed to be responsible for the French paradox--high fat intake, but low incidence of heart disease.

Cranberry flavonoids possess a powerful ability to inhibit the formation of biofilms, a means by which bacteria gain a foothold in the body. Cranberries have long been known to inhibit infections of the urinary tract.

GNLD's third flavonoid product introduction was TRE. This supplement is a liquid similar to a fine wine or concentrated fruit juice without the alcohol content of wine or the sugars of fruit juices. Research on this product is available in a separate newsletter.

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