

# Tart Cherries

## SUMMARY OF CURRENT SCIENTIFIC LITERATURE



**MORE AND MORE PEOPLE ARE COMING TO DISCOVER THE POWERFUL HEALING PROPERTIES OF PLANTS. ONE THAT IS GETTING SOME OF THE MOST ATTENTION IS MORE FAMILIAR THAT YOU MIGHT THINK: TART CHERRIES.** Having found delicious new ways to capture the energy of this fruit, conscientious companies are creating drinks to bring you the health benefits of the tart cherry. They are backed up by new research that shows why we should be drinking tart cherry juice. The reasons are as follows: 1) have high antioxidant potential as measured by laboratory tests and contain a number of compounds that fight free radicals 2) they have been shown to cut down on inflammation of different sorts including decreased muscle soreness, greater strength following exercise, decreased inflammatory markers 3) have important beneficial metabolic effects such as decreasing fat, sugar, and insulin levels in the blood, 4) may show helpful effects on sleep, and finally 5) show encouraging positive effects against cancer such as reducing tumor burden in parts of the gut and slow tumor growth. These are all just the beginning. Now that we have some encouraging results (and with the help of informed consumers), much more attention will be directed toward learning everything there is to know about this important fruit, the tart cherry.

In collaboration with Michelle's Miracle®, researchers at the National College of Natural Medicine in Portland, Oregon have assembled and studied the relevant peer-reviewed medical literature on tart cherries. A review of scientific articles was conducted to identify the depth and breadth of research to date on tart cherries.

### *Antioxidants*

#### *Novel Antioxidant Compounds from Tart Cherries (*Prunus cerasus*) (Wang<sup>1</sup>)*

Though we are familiar with the power of the anthocyanin group of antioxidants and anti-inflammatory compounds in tart cherry, these researchers give us a new group of compounds that appear to have strong antioxidant effects. Two of the compounds 1-(3',4'-dihydroxycinnamoyl)-cyclopenta-2,5-diol (3) and 1(3',4-dihydroxycinnamoyl)-cyclopenta-2,3-diol (4) act like caffeic acid. Caffeic acid acts strongly as an antioxidant because it is hydrophilic, which means it can easily donate a hydrogen atom (a proton) to unstable free radical compounds. In fact, the effectiveness of these caffeic acid look-alikes in tart cherries seems to

depend on very small changes in their chemical structure. For instance, the amount and position of oxygen-hydrogen (hydroxyl) units on the caffeic acid structures act like cannons on a ship ready to take aim at free radicals. And when the smoke cleared, these compounds turned out to be nearly as effective as commercial antioxidants BHT (butylated hydroxytoluene) and TBHQ (tert-butylhydroquinone). What's more, the tart cherry compounds may work in an additional way. They may be "chelating" or picking up metals in the body like iron, which produces free radicals such as the hydroxyl radical that cause oxidative damage.

### Improved Antioxidant and Anti-inflammatory Potential in Mice Consuming Sour Cherry Juice (*Prunus Cerasus cv. Maraska*) (Sarıc<sup>2</sup>)

Several research teams have shown the powerful antioxidant effect of tart cherry cell culture in the lab, and it is now known that the amount of anthocyanins in the fruit goes hand in hand with its ability to reduce cell damage. But a European research team also set out to discover the effects of anthocyanins in living animals. They found that a type of tart cherry worked in a way that is very similar to aspirin. Not only that, but tart cherry juice also has antioxidant power in the blood and livers of mice.

The study group found that tart cherry juice increased the activity of a free radical scavenger called superoxide dismutase. Glutathione peroxidase, another powerful player in the antioxidant pathway, also surged in the liver when researchers gave mice tart cherry juice. This amazing substance might also work in the brain, although the body handles the anthocyanins in tart cherry juice in complex ways that we do not yet understand. And while the type of cherry affects the amount of different beneficial antioxidants, all tart cherries have some of the most powerful kinds, like cyanidin-3-glucoside.

### Cherry Antioxidants: From Farm to Table (Ferretti<sup>3</sup>)

Italian scientists talk about the many functions of tart cherry flavonoids, two of which are plant defense and sun protection. Just like animals, cherry plants break down sugar to create important defense products. The authors begin their article with a review of the important differences between sweet and tart cherries. Both have sugar and acid, but the higher acid in tart cherries is what gives them their sour flavor. Tart cherries also have more vitamin A and beta-carotene in addition to lots of vitamins including

A, B, C, E, and K. They are high in calcium, magnesium, phosphorus, and potassium as well. Most importantly, tart cherries contain higher phenolics (a group of major antioxidants that contain anthocyanins). They even have some melatonin, an antioxidant that helps with sleep and partially controls the sleep-wake cycle. Of course, the amount of total phenolics and total anthocyanins varies among the variety of sweet and sour cherries (two varieties of sweet cherries actually contain more total anthocyanins than 3 of the 4 sour cherries in their study).

More light and warmer growing conditions seem to increase the amount of anthocyanin and total phenolics found in the fruit. Protecting the fruit from "cracking" and allowing them to ripen longer would allow the tart cherries to get the maximum possible phenolic, anthocyanin, and other "phyto-compound" (plant product) content. Overall, the authors highlight the many blood markers of inflammation that improved with tart cherry intake, including an increase in the antioxidant enzymes SOD and glutathione peroxidase. Both of these compounds help to fend off the free radicals that occur in our body because of the oxygen we breathe in and the iron and copper we eat. Tart cherry also decreased lipid peroxidation (cell membrane damage) and F(2)-isoprostane (marker of oxidation) levels. Similarly, while sweet cherries have been shown to bring down C-reactive protein (an inflammatory substance) levels, the same may be true for tart cherries. Anthocyanins may decrease nitric oxide levels. Phenolics found in cherries may inhibit the cyclooxygenase II pathway (the target of aspirin and the new COX-II inhibitors like celecoxib). Finally, anthocyanins seem to have anticancer properties we are just beginning to understand.

### Sour Cherry (*Prunus cerasus L*) Anthocyanins as Ingredients for Functional Foods (Blando<sup>4</sup>)

Researchers in Italy compared the beneficial properties of cherries off the tree to isolated cherry tissue in the lab. Blando and his team did two things: 1) they compared total amounts of anthocyanins in the fruits of several Italian tart cherry species with tart cherry cells that were grown in the lab, stimulated by light and everything a cherry cell needs to grow; 2) The researchers also looked at the antioxidant profile of the Petri dish cherries versus natural cherries grown on trees. Though the total amount of antioxidant and other good compounds varied a lot between the real cherries and lab cherries, the real cherries contained many more anthocyanins. However, the lab cherries were able to change their

anthocyanin profile in interesting ways (creating more cyaniding 3-glucoside), which could be used for our benefit. They also have some antioxidant capacity as measured by the ORAC and TEAC tests, which are common tests used to measure antioxidant power. But this capacity was still not as much as the cherries that were grown naturally. Cherry cells grown in the lab have the right stuff, just not enough of it...yet.

### Degradation Products of Cyanidin Glycosides from Tart Cherries and Their Bioactivities (Seeram<sup>5</sup>)

Researchers in this study looked for breakdown products of the active ingredient in tart cherry juice: cyanidin, a type of anthocyanin that gives cherries their color. Tart cherries must be handled carefully to avoid damaging this ingredient. Interestingly, one of the breakdown products, protocatechuic acid was just about as strong an antioxidant as several artificial products used in research. This breakdown product appears to be formed in the human body, thus eating fresh or minimally prepared cherries is a good idea. Even brief heat can help bring out the “aglycon” or base form of anthocyanin called just “cyanidin”, which also has high anti-inflammatory and antioxidant power. However, in general, tart cherry juice is best when kept at low pH (< 3, such as found in the human stomach unless the patient is on proton pump inhibitors like Prilosec).

### Anthocyanin Content, Lipid Peroxidation and Cyclooxygenase Enzyme Inhibitory Activities of Sweet and Sour Cherries (Mulabagal<sup>6</sup>)

Both sweet and tart cherries have high levels of antioxidants though each type of cherry is higher in certain ones. Red sweet cherries have mostly cyanidin-3-O-rutinoside, with the variety “Kordia” having the most. The tart cherry varieties (Balaton and Montmorency) have higher levels of cyaniding-3-O-glucosylrutinoside, though Balaton has slightly higher levels. Researchers also tested cherry power to block lipid peroxidation, or cell barrier breakdown, with sweet cherry varieties performing a little better than tart cherries at this. Both cherry types blocked COX, which is the cell machine that creates inflammatory compounds from arachidonic acid, a cell membrane fat present in animal cells. A little inflammation can alert the body to painful areas, but too much just causes more body tissue destruction.

### Antioxidant and Antiinflammatory Activities of Anthocyanins and Their Aglycon, Cyanidin, from Tart Cherries (Wang<sup>7</sup>)

Evidence continues to mount for the anti-inflammatory and antioxidant effects of tart cherries. These researchers looked at how well cherries blocked lipid peroxidation, or cell membrane damage. All of the compounds including the foundation structure cyanidin (without sugar attached) and the three major sugar-added compounds, a.k.a. anthocyanins, blocked this peroxidation. In fact, cyanidin did the best, meaning that the effectiveness of all its sugar products (anthocyanins) is probably due to the cyanidin “foundation”.

Sugar products (glycosides) are formed by adding hydrogen or sugars and it seems like the smaller the additional group (moiety), the stronger the antioxidant effect. Even certain glycoside products of cyanidin appear to hold onto iron and other heavy metals (which cause peroxidation). Overall cyanidin actually performed better than aspirin at inhibiting COX. Furthermore, all tart cherry compounds matched standard commercial antioxidants in terms of antioxidant power. The tart cherry compounds even outperformed vitamin E, a known antioxidant that is used for neurodegenerative disease.

## Pain & Inflammation

### Dietary Constituents as Novel Therapies for Pain (Tall<sup>8</sup>)

While there are several “alternative” therapies for pain such as acupuncture, our knowledge of the effects of food on pain is limited. Researchers think that inflammation may play a role in pain, just as it does in other chronic diseases like hardening of the arteries, many types of cancer and Alzheimer’s Disease. They agree with the evidence that tart cherries can reduce inflammation and work as a powerful scavenger of free radicals. They go on to say that tart cherries may also reduce pain caused by heat. This may be because heat causes cell injury that leads to swelling of the tissue and the release of inflammatory enzymes.

Tissue swelling causes inflammation because blood vessels, which normally wash out cellular garbage,

are blocked. With cellular breakdown products kept in the cells and local tissues, things such as reactive oxygen species can overwhelm the body's defenses. More importantly, with this swelling, cells die because they can't get oxygen and other supplies needed to survive. Inflammation causes cellular injury as compounds called interleukins and tumor necrosis factor (not necessarily related to tumors or cancer) contribute to the break down of cells. Under normal circumstances these chemicals are used to break down foreign and infected cells, but can also be produced excessively and directed towards health cells.

### Tart Cherry Anthocyanins Suppress Inflammation-Induced Pain Behavior in Rats (Tal<sup>P</sup>)

This study piggy-backs upon the previous study by Tall in which researchers propose that tart cherry helps with heat-caused pain. Here they have numbers to back up their claims. They first argue that inflammation causes both swelling of the painful area...and of course, pain itself. They then looked at how much tart cherry reduces swelling in a painful hand, for instance. Cherries brought down swelling similar to the common drug indomethacin. However, inflammation doesn't just cause swelling, it causes pain too. When your hand hurts, you pull it away from the source of pain. The researchers did something similar in rats, where they measured how fast the rats pulled their paws away from the source of pain. Tart cherry seemed to increase this time, indicating that it decreased pain, allowing them to manage the pain. This is like numbing pain with ice so that you can stand it longer. In the end, we don't know exactly what in the tart cherries is having the effect. It could be either the anti-inflammatory or antioxidant properties of anthocyanins, or both.

### Tart Cherry Juice Decreases Oxidative Stress in Healthy Older Men and Women (Traustadottir<sup>10</sup>)

Older people are more likely to have oxidative (free radical) damage than younger people. This may be the case for a number of reasons; perhaps older cells are less able to create natural anti-oxidants. Maybe they take more medications (that may cause oxidation), are more dehydrated (cannot eliminate oxidants as well), or have worse diets (so get less antioxidants in their diets). Whatever the reason, these researchers wanted to test to see if tart cherries, especially the anthocyanins in them, could reduce

the amount of oxidation going on in the body. They found that this was true. They gave a group of older people cherry juice and then had them exercise their arms until they became sore. Then they measured the amount of a chemical called isoprostane (something that aspirin for example normally blocks) in the bloodstream. Those older people who received tart cherry juice had lower levels of inflammation. This study is important because, whenever possible, we want to build upon animal research to understand the effects of tart cherry juice in people.

### Antioxidant Polyphenols from Tart Cherries (*Prunus cerasus*) (Wang<sup>11</sup>)

The researchers looked at certain Michigan varieties of tart cherry, the Montmorency and Balaton, and tested their power at preventing oxidation (oxygen damage). In this case, they looked at something called "lipid peroxidation", a type of oxygen damage to cell membranes (which made up of a lot of fatty substances). Iron is a common product that can increase lipid peroxidation. These researchers found that both Balaton and the more common Montmorency tart cherries had compounds that blocked this peroxidation. They further processed the tart cherry juice, separating out eight individual compounds that were especially protective. These include "compound 8" or 6,7-dimethoxy-5,8,4'-trihydroxyflavone, an antioxidant that was strongest of all. "Compound 3" or chlorogenic acid, another compound discovered in tart cherry, had strong action against free radicals. It also delays the release of glucose into the blood after a meal. This means there is less of an "insulin spike" after meals, meaning cherries may help maintain insulin sensitivity. Interestingly, the sum total antioxidant power against lipid peroxidation of the individual eight compounds was greater (246%) than when they were mixed together (90%). However, drinking the mixture is what ensures that we get all of the other benefits of tart cherry juice aside from just compound 8 and 3.

### Antioxidant Properties of Sour Cherries: Role of Colorless Phytochemicals from the Methanolic Extract of Ripe Fruits (Piccolella<sup>12</sup>)

Though we think it is most important to drink the whole tart cherry, it can be helpful to understand the parts that make up the whole. Plant chemicals or "phytochemicals" have activity in their own right. If we can separate these out and test them individually, we can find which are the most powerful. These Italian researchers looked at the antioxidant power of some

of the plant chemicals in native Italian tart cherries. They wanted to see how strong these chemicals were at fighting free radicals and reducing damage to protective cell membranes. They found twenty downstream products that have high antioxidant activity. As we would expect, flavonoids and quinic acid were the strongest antioxidants.

## Muscle Pain

### Efficacy Of Tart Cherry Juice in Reducing Muscle Pain During Running: a Randomized Controlled Trial (Kuehl<sup>13</sup>)

As important as exercise is, it can be a painful process. We need something to help us reach our full potential without getting held back by pain. Unfortunately, many pain medications can be harmful to the stomach lining and can cause other long-term problems like “salicisms” (build-up of aspirin in the body causing toxicity). It would be beneficial to have an alternative for pain relief, especially something that could be taken before exercise to prevent pain. Some of this pain may be due to muscle damage. This damage draws immune cells to the site of injury, making the muscle damage worse through friendly fire. Tart cherries may help prevent this marching army of immune cells and halt the process of destruction.

Researchers at Oregon Health & Science University gave runners tart cherry juice while other runners received placebo juice. Then the researchers asked runners to rate their pain after a long-distance race. Those who got tart cherry juice throughout the week before the race said they hurt less after the race and they seemed to think the juice is what did the trick. The bottom line is: cherry juice helps with pain if you are going to exercise strenuously. People in the study said they would rather drink cherry juice than a non-cherry alternative.

### Efficacy of a Tart Cherry Juice Blend in Preventing the Symptoms of Muscle Damage (DAJ Connolly, MP McHugh, OI Padilla-Zakour<sup>14</sup>)

Researchers in this study gave a group of young men either tart cherry juice or a look-alike juice and compared the men’s muscle strength, how sore their muscles were to the touch, arm pain, and how well they could relax their arms after “eccentric”

(lengthening under tension) exercise (like arm-wrestling). The researchers found that the men reported less overall pain and greater strength if they were taking tart cherry juice, though their arms were not less relaxed or less tender to touch. In fact, those volunteers who drank tart cherry juice were five times less sore than those who drank the false juice. Researchers were not sure what to ascribe this to but felt it had something to do with the cherries. The study might have showed a beneficial effect on muscle tenderness and relaxation if there had been more study participants or if the researchers had done measurements differently. It might have been helpful to use blood tests for muscle breakdown (like creatine kinase) to tell if the cherries were actually stopping muscle breakdown. But researchers could not use these tests because they did not instruct the men to avoid other forms of exercise. Even as exciting as these results are, one of the best things about tart cherries is that they are a delicious way to decrease pain and maintain strength. Other methods such as electrical stimulation may be effective but are not as convenient as eating cherries or drinking good quality cherry juice.

## Metabolic Syndrome

### Regular Tart Cherry Intake Alters Abdominal Adiposity, Adipose Gene Transcription, and Inflammation in Obesity-Prone Rats Fed a High Fat Diet (EM Seymour<sup>15</sup>)

We know that anthocyanins, some of the active ingredients in tart cherry juice, by themselves can help with obesity and other problems related to metabolic syndrome (a complex problem of obesity and inflammation). But until this study, we were not sure how helpful the real cherry juice that we drink is in fighting these same problems. Those familiar with the benefit of cherries are not surprised by what they found. Rats with metabolic syndrome that were given cherry powder over a 3-month period had improved health in many ways. The amount of high fat in the blood decreased with the ingestion of tart cherries. Even better, abdominal (inside) fat came off. This is important as abdominal fat is the most damaging in terms of metabolic syndrome because it is more associated with free fatty acids in the blood, insulin resistance, and imbalanced hormones like

testosterone. Not only did the harmful abdominal fat decrease, but the underlying metabolic problem improved with tart cherry as well. PPAR-alpha, a signal system on fat cells that responds to free fatty acids and increases fat storage (and represents how abnormal the weight gain process is), also decreased. Oftentimes with abdominal obesity and the poor metabolic process that comes with it, there is an increase in inflammatory chemicals. Tart cherry helped produce a decrease in those inflammatory compounds.

### Altered Hyperlipidemia, Hepatic Steatosis, and Hepatic Peroxisome Proliferator-Activated Receptors in Rats with Intake of Tart Cherry (EM Seymour<sup>16</sup>)

Similar to their study on the effects of tart cherry on several components of metabolic syndrome, these Michigan researchers tested what cherries can do for other aspects of metabolic syndrome, including high blood sugar, fatty blood, and high blood pressure. As with inflammation and obesity, tart cherry was shown to reduce blood sugar, fats in the blood, and even insulin levels. As with their previous study, a measure of insulin resistance, PPAR-alpha, also went down.

Insulin resistance is like a runaway train that all-too-often leads to metabolic syndrome or diabetes. It is a vicious cycle where high sugar, high fat, and unbalanced hormones interact to make it more difficult for the body to use the available sugar. This is what happens with “type 2” diabetes: there is plenty of insulin in the body, but the cells cannot respond to it. They actually begin to starve. Meanwhile, the sugar that cannot get into the cells sits around for awhile but eventually is made into more fat. This makes the problem worse. Amazingly, all of the changes that decreased insulin resistance occurred over just three months.

### Tart Cherry Intake Reduces Indices of Metabolic Syndrome in Rats (Seymour<sup>17</sup>)

Researchers at the University of Michigan knew that isolated anthocyanins, the tart cherry compound that gives it its color and disease-fighting power, reduce blood fats, obesity, and hardening of the arteries. What they did not know for sure was whether or not cherries eaten as a food could do the same thing. They did a study to see if whole tart cherries helped the activity of different versions of peroxisome proliferator-activated receptors (PPAR), a fat cell

device that does mostly good things: everything from bringing down blood fats in the body to improving the activity of insulin (which is defective in diabetes). In this way, tart cherry would be acting like several powerful drugs on the market. For example, tart cherry may act like “fibrates”, which promote the activity of one type of PPAR that brings down the body’s level of cholesterol and triglycerides, one of main fats in the blood. Tart cherry may also act like the thiazolidinedione (TZD) drugs for diabetes, which help insulin work better. To test their theory, these researchers took rats with high blood fat and insulin malfunction and gave them tart cherry meal for 3 months. The researchers found that tart cherry promoted the first (fibrate) type of PPAR and showed an encouraging trend in the second (TZD). And because they were using whole cherry meal, the total anthocyanin content was less than past studies that used concentrated cherry extract. This means that maybe different tart cherry compounds are working together to help the PPAR work more effectively.

## Sleep

### Effects of a Tart Cherry Juice Beverage on the Sleep of Older Adults with Insomnia: A Pilot Study (Pigeon<sup>18</sup>)

Americans have tried everything from valium to melatonin to get a good night’s sleep. Recently, a small but good-quality study showed that tart cherry juice helped people stay asleep and increased total time in bed. Researchers got the idea from reports that cherries might help in this area. They took older Americans, who are prone to sleep problems, and gave them cherry juice or a cherry juice look-alike. It turned out that cherry juice helped more with sleep than valerian root, a common treatment for sleep problems, and might be better than melatonin. When combined with current treatments for insomnia, such as counseling and therapy, cherry juice might be even more effective. The study is interesting because it offers some hint as to why tart cherry juice may be helpful. Tart cherries pack a double-punch because they first of all help control inflammation, which itself can be bad for sleep. But because they have some melatonin, this strengthens the anti-inflammatory effect as a gentle sleep aide.

## Detection and Quantification of the Antioxidant Melatonin in Montmorency and Balaton Tart Cherries (*Prunus cerasus*)

(Burkhardt<sup>19</sup>)

We think that melatonin is a powerful part of the sleep cycle in humans, helping us get the rest we need. We all create melatonin in our brains during the dark hours of the night. But new evidence is coming out that some fruits, especially tart cherries, have melatonin in them. In addition, there is evidence that plants with melatonin in them get into the bloodstream when eaten. This then raises levels of melatonin in the blood. Two of the most popular tart cherries, the Montmorency and Balaton varieties, contain high levels of melatonin. What's more, the Montmorency variety has six times more melatonin than the Balaton type. Melatonin seems to scavenge several different types of free radicals, especially the hydroxyl radical. This antioxidant probably has a protective effect in the plant, protecting against its own free radicals. Both types of tart cherry produced the same amount of melatonin no matter when they were harvested. Even unripe fruit had significant levels. Researchers think that light may stimulate melatonin production in plants. Though there was some variation in melatonin production between trees, this might have been due to variable light to different trees.

## Jerte Valley Cherry-Enriched Diets Improve Nocturnal Rest and Increase 6-Sulfatoxymelatonin and Total Antioxidant Capacity in the Urine of Middle-Aged and Elderly Humans (Garrido<sup>20</sup>)

Cherries contain not only melatonin, but also tryptophan and serotonin. All of these compounds are known to be antioxidant and help with sleep. Melatonin levels and sleep quality appear to decline greatly with age. Melatonin acts directly as an antioxidant by scavenging free radicals. But they also work in a roundabout way by increasing levels of other antioxidants. The researchers tested seven different types of cherries on their effect on sleep, levels of melatonin, and total antioxidant power. They found that each of the cherry types improved actual sleep time, total nocturnal activity, assumed sleep, and immobility. Because each cherry increased melatonin levels, the researchers felt that improved sleep was due to this. Finally, total antioxidant activity increased, which was probably due to tryptophan, serotonin, and melatonin in the cherries.

# Cancer

## Dietary Anthocyanin-Rich Tart Cherry Extract Inhibits Intestinal Tumorigenesis in *Apc<sup>min</sup>* Mice Fed Suboptimal Levels of Sulindac (Bobe<sup>21</sup>)

Colon cancer is the third leading cause of cancer-related deaths among American men and women. There are few preventive measures for colon cancer aside from better (earlier and more frequent) screening. There is some evidence that non-steroidal anti-inflammatory drugs (in the class of aspirin) like sulindac can help slow the growth of gut polyps, which can become colon cancer tumors.

Previous researchers have shown that tart cherry anthocyanins are anti-inflammatory, either by blocking COX enzymes or lipid peroxidation. The researchers studied whether or not adding tart cherry extract (containing anthocyanins) to sulindac would block cancer growth even more powerfully. The mice that got both tart cherry and sulindac had fewer small gut tumors and smaller total tumor mass (adding up all tumors in the body). It seems that the tart cherry extract may be working on a different part of the small gut than sulindac. This might explain how tart cherry works with this medication to decrease tumor burden all across the gut.

Lastly, the mice that received tart cherry and sulindac also lost less weight. In someone with cancer, weight loss is an important sign of worsening health. When it comes to cancer, tart cherry anti-oxidants may work even at low doses. This means that you wouldn't need to an unreasonable amount of cherries to get the right effect.

## Tart Cherry Anthocyanins Inhibit Tumor Development In *Apc<sup>Min</sup>* Mice And Reduce Proliferation Of Human Colon Cancer Cells (Kang<sup>22</sup>)

Tart cherries are good for so many things. Studies have shown how good they are as anti-inflammatory agents, much like ibuprofen or aspirin. And we know that anti-inflammatory agents can slow the growth of colon tumors. So why not see if tart cherries could do the same thing: help stop colon cancer in its tracks? There are many ways to test this idea. The researchers in this study used both animals (mice) as well as

individuals groups of tumor cells in the lab to see how tart cherry anthocyanins interacted with tumor growth and spread. But it is always important to have a control group and alternative treatment group if possible, which they also did do. They compared tart cherry extract with the most common preventive, anti-inflammatory treatment for colon tumors, sulindac (a non-steroidal anti-inflammatory agent or NSAID).

The control in their study was standard feed and standard diet plus whole tart cherry. The researchers found that mice who ate anthocyanins, cyanidin, and tart cherry had fewer and smaller tumors in the cecum (the junction between the small and large intestine). They think that anthocyanins act like a wrench in the works of tumor machinery. This is because in the human body anthocyanins can change to look like pieces of human DNA. For this reason they bind to DNA to perform a number of useful functions in plants. But they also have destructive function for uncontrollably dividing cells like cancers.

Another very interesting finding is that anthocyanins lose their sugar part and become cyanidin in the cecum. This happens because of digestive processes in the small intestine. This means that eating the anthocyanins, preferably in the whole form such as juiced fruit, is essential to get the natural breakdown product cyanidin. What's more, it would be difficult to achieve high enough levels of anthocyanin or cyanidin without supplementation (through juice, etc.).

Lastly, these researchers found that anthocyanins, especially cyanidin, slowed the growth of certain cancer cell types. Of course, this would only work in the living human body if cyanidin were stable in the pH of the colon. Though much of cyanidin breaks down in the colon due to bacterial digestion, the normal colon pH of 6 causes the cyanidin to form "pseudobase" compounds, or look-alike DNA, that can stop tumor growth. Another way they may be working in the cecum and colon is by turning off cell growth switches, or "epidermal growth factor receptor kinases". Such alternative methods of stopping tumors are likely going on because anthocyanins and cyanidin do not seem to be working like sulindac. Sulindac is an NSAID and has its greatest effect in the small gut, but it doesn't work well in the cecum or large gut. So tart cherry compounds may not be slowing tumor growth through the "COX" pathway but rather through some pathway we have yet to discover.

## Bibliography

- <sup>1</sup>Novel Antioxidant Compounds from Tart Cherries (*Prunus cerasus*) H Wang et al. *Journal of Natural Products* 1999; 62:86-88
- <sup>2</sup>Improved Antioxidant and Anti-inflammatory Potential in Mice Consuming Sour Cherry Juice (*Prunus Cerasus* cv. Maraska) Saric et al. *Plant Foods Human Nutrition* 2009; 64:231-237
- <sup>3</sup>Cherry Antioxidants: From Farm to Table G Ferretti et al. *Molecules* 2010; 15:6993-7005
- <sup>4</sup>Sour Cherry (*Prunus cerasus* L) Anthocyanins as Ingredients for Functional Foods F Blando, C Gerardi, I Nicoletti. *Journal of Biomedicine and Biotechnology* 2004; 5:253-258
- <sup>5</sup>Degradation Products of Cyanidin Glycosides from Tart Cherries and Their Bioactivities Seeram, L Bourquin, M Nair. *J Agric Food Chem* 2001; 49:4924-4929
- <sup>6</sup>Anthocyanin Content, Lipid Peroxidation and Cyclooxygenase Enzyme Inhibitory Activities of Sweet and Sour Cherries V Mulabagal et al. *Journal of Agricultural and Food Chemistry* 2009; 57:1239-1246
- <sup>7</sup>Antioxidant and Antiinflammatory Activities of Anthocyanins and Their Aglycon, Cyanidin, from Tart Cherries H Wang et al. *Journal of Natural Products* 1999; 62:294-296
- <sup>8</sup>Dietary Constituents as Novel Therapies for Pain J Tall and S Raja. *Clinical Journal Pain* 2004; 20:19-26
- <sup>9</sup>Tart cherry anthocyanins suppress inflammation-induced pain behavior in rat J Tall et al. *Behavioral Brain Research* 2004; 153:181-188
- <sup>10</sup>Tart Cherry Juice Decreases Oxidative Stress in Healthy Older Men and Women T Traustadottir et al. *Journal of Nutrition* 2009; 139:1896-1900
- <sup>11</sup>Antioxidant Polyphenols from Tart Cherries (*Prunus cerasus*) H Wang et al. *Journal of Agricultural and Food Chemistry* 1999; 47:840-844
- <sup>12</sup>Antioxidant Properties of Sour cherries: role of colorless phytochemicals from the methanolic extract of ripe fruits S Piccolella et al. *Journal of Agricultural and Food Chemistry* 2008; 56:1928-1935
- <sup>13</sup>Efficacy of tart cherry juice in reducing muscle pain during running: a randomized controlled trial K Kuehl et al. *Journal of the International Society of Sports Nutrition* 2010; 7:17
- <sup>14</sup>Efficacy of a tart cherry juice blend in preventing the symptoms of muscle damage DAJ Connolly, MP McHugh, OI Padilla-Zakour. *Br J Sports Med* 2006; 40:679-683
- <sup>15</sup>Regular Tart Cherry Intake Alters Abdominal Adiposity, Adipose Gene Transcription, and Inflammation in Obesity-Prone Rats Fed a High Fat

Diet EM Seymour et al. *Journal of Medicinal Food* 2009; 12(5):935-942

<sup>16</sup>Altered Hyperlipidemia, Hepatic Steatosis, and Hepatic Peroxisome Proliferator-Activated Receptors in Rats with Intake of Tart Cherry EM Seymour et al. *Journal of Medicinal Food* 2008; 11(2): 252-259

<sup>17</sup>Tart Cherry Intake Reduces Indices of Metabolic Syndrome in Rats EM Seymour. *International Symposium on Human Health Effects of Fruits and Vegetables* 2007; 2:215-220

<sup>18</sup>Effects of a Tart Cherry Juice Beverage on the Sleep of Older Adults with Insomnia: A Pilot Study W Pigeon et al. *Journal of Medicinal Food* 2010; 13(3):579-583

<sup>19</sup>Detection and Quantification of the Antioxidant Melatonin in Montmorency and Balaton Tart Cherries (*Prunus cerasus*) S Burkhardt et al. *Journal of Agricultural and Food Chemistry* 2001; 49:4898-4902

<sup>20</sup>Jerte Valley Cherry-Enriched Diets Improve Nocturnal Rest and Increase 6-Sulfatoxymelatonin and Total Antioxidant Capacity in the Urine of Middle-Aged and Elderly Humans M Garrido et al. *J Gerontology A Biol Sci Med Sci* Sep 2010; 65A(9):909-914

<sup>21</sup>Dietary Anthocyanin-Rich Tart Cherry Extract Inhibits Intestinal Tumorigenesis in APC minus Mice Fed Suboptimal Levels of Sulindac Bobe et al. *Journal of Agricultural and Food Chemistry* 2006; 54:9322-9328

<sup>22</sup>Tart cherry anthocyanins inhibit tumor development in *Apc* minus mice and reduce proliferation of human colon cancer cells S Kang et al. *Cancer Letters* 2003; 194:13-19