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ALL ABOUT CHOCOLATE by Ann Gerhardt, MD

Bottom Line at the Top: Chocolate contains many bio-active substances, not just flavanols. Its dark color tells very little about the composition and may be healthy, may not. Read on...

Given the prevalence of chocoholics, any hint of chocolate as a health food makes big news, not just once, but every time some new glimmer of hope appears. Since chocolate is a veritable cauldron of naturally occurring bio-active chemicals, we can expect scientific revelations for years to come as each new one is studied.

Cacao beans, the source of chocolate, contain naturally occurring, fountain-of-health chemicals called flavanols. These are the same nutrients presumed to be responsible for the medicinal benefits of green and black tea, apples, grapes and red wine. Flavanols decrease inflammation, act as anti-

oxidants and stimulate nitric oxide production, which opens up blood vessels and normalizes blood pressure.

All cacao beans start out flavanol-rich, some more than others, depending on soil and other factors unique to their origin. Cacao beans from the San Blas islands off the coast of Panama, provide a perfect example. High blood pressure is very rare in San Blas Island Kuna Indians, even in old age. Their resistance to hypertension disappears when they move to Panama City. Scientists propose that their daily habit of drinking 5 cups of San Blas-grown, flavanol-rich cocoa keeps their blood pressure low.

Health benefits of flavanol-rich cocoa: A study of 13 hypertensives, consuming chocolate bars either rich in or devoid of flavanols, showed that **blood pressure** dropped within 14 days of starting only the flavanol-rich bars.

A single ounce of flavanol-rich semi-sweet chocolate abruptly reduces **platelet clotting**. Chronic daily
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Chocolate

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consumption of the same amount maintains the effect.

The fat content of chocolate products varies from 6.6 to 40%, and depends on how much cacao bean fat is retained and how much fat from other ingredients is added. Cacao bean fat is mostly stearic and palmitic acids, which, though saturated, are not terribly horrible for you. There is a small amount of oleic acid (think olive oil) and even less linoleic acid (an essential fatty acid).

In spite of chocolate's considerable fat content, it seems to improve **cholesterol** levels. LDL-cholesterol declined by 6% in non-obese adults consuming 3.5 ounces of Lindt Dark Chocolate per day. At the same time their HDL-cholesterol climbed by 9% (for HDL-C, that's a lot) and markers of inflammation and platelet aggregation slightly decreased. The Lindt chocolate contained 70% cocoa and 800 mg flavanols. In another study in Finland, dark chocolate, with or without additional flavanols, raised HDL-cholesterol 11-13%.

Higher flavanol intake reduced risk of **heart disease** and death over 16 years in 34,489 post-menopausal women in the Iowa Women's Health Study who were free of any heart disease at baseline. The flavanol-rich foods associated with better health were chocolate, bran, apples, pears, red wine, grapefruit and strawberries.

Chocolate is a rich source of **magnesium**, an essential mineral for normal heart, muscle and brain function.

Flavanols have a plasma half-life of approximately six hours, suggesting that any biological effects may wear off quickly. This might be construed as a fault, or an excuse to eat chocolate four times a day.

Dark chocolate: Currently, the common misperception is that if chocolate is dark, it is healthy. **In actuality there is nothing inherent in chocolate's color that gives a clue to its health benefits.**

Flavanols taste bitter and have an astringent (dry) feel on the tongue. **Cacao bean processing intentionally destroys flavanol content to remove the unpleasant taste.** With a process called 'dutching', alkali-potash is added to cocoa nibs to enhance cocoa's taste, texture and appearance, but it eliminates active flavanols and their bitter flavor. It also darkens chocolate (non-dutched cocoa tends to be an almost reddish-brown, color). Really dark, almost black cocoa or chocolate is often less healthy because of fewer flavanols. That doesn't mean that milk chocolate is healthier because of its light color – It is 'dutching', then lightened with milk and other ingredients.

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Avandia, Diabetes & Heart Disease

by Ann Gerhardt, MD

Bottom Line at the Top: Avandia, a diabetes medication, may increase heart disease risk.

Avandia (generic name rosiglitazone) is proof of the not-all-drugs-in-a-class-are-equal lesson. Avandia is a diabetes medication of the TZD class. TZD's treat diabetes by improving insulin sensitivity and fat metabolism. In the RECORD trial diabetics taking Avandia died more often than those taking 2 other common diabetes medications.

Heart disease eventually afflicts all diabetics, if they don't die of something else first. This is because diabetics have abnormal cholesterol and triglyceride profiles, clotting, blood vessel damage and spasticity, inflammation and oxidation. Usually TZD's as a class help to reverse many of these.

Unfortunately, though Avandia lowers blood sugar and improves some aspects of metabolism, it is not one of the TZD's that improves cholesterol and triglycerides. Instead of lowering them, it raises LDL-cholesterol (the bad) and has no effect on triglycerides. At best it modestly improves HDL-cholesterol (the good). The over-all effect of a drug is the sum of all its positive and negative effects. For Avandia, that sum does not improve heart disease.

Actos, the other TZD available in the U.S., lowers triglycerides, raises HDL-cholesterol and only slightly raises LDL-cholesterol. In the PROACTIVE trial, Actos reduced the incidence of heart attack and stroke. ¶

Proof that scientists strain really hard to come up with cumbersome clinical trial names to fit an acronym.

ENHANCE (Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression),

ACCORD, (Action to Control Cardiovascular Risk in Diabetes) and RECORD (Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes)

Chocolate

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Dutching is only one of a number of steps in cacao bean processing that destroy flavanols. Following picking, the cacao seed pods ferment for up to several days prior to drying and packaging for shipping. Fermentation greatly enhances flavor generation, but reduces flavanol content in proportion to its duration.

Chocolate manufacturers roast the dried cacao beans to develop flavor. This further reduces flavanol content, because flavanols are heat-sensitive. The beans are shelled to obtain the cocoa nibs, then ‘dutch’ (or not) and ground to chocolate liquor. Depending on the duration of each of these steps, the flavanol content of cocoa and chocolate products vary greatly and (to the consumer) unpredictably.

The liquor is used to make candy and other chocolate products, or the fat is expressed out, leaving cocoa powder. Candy consists of chocolate liquor plus sugar, soy-lecithin, flavorings and (for milk chocolate) milk. The greater the percentage of the final product that comes from cocoa nibs, the more bitter is the final product, generally changing its designation from semi-sweet to bittersweet.

People vary considerably in their perception of chocolate’s bitterness and astringency – Hence the wide variation in preference for milk vs. dark and the types of dark, ranging from bittersweet up to the very bitter, 90% chocolates.

Cocoa is just chocolate with the fat squeezed out. It is very low calorie, retains the chocolate flavor and may or may not contain flavanols. The expressed fat (cocoa butter) and white chocolate, a confectionary of cocoa butter, vanilla, milk and sugar, contain no flavanols.

According to a Harvard study, most commercially available cocoa in the developed world is devoid of flavanols. While most candy makers do not process the chocolate liquor they use, some do and claim to produce flavanol-rich cocoa. Scharffen Berger chocolate maker prides itself on not dutching its cocoa in order to preserve flavanol content. Mars Company claims to process cacao beans in such a way that flavanols are retained in their proprietary Cocopro cocoa, which they use in some of their products. It does have a high flavanol content, and performs well in controlled trials of biological effects.

Since **color doesn’t reveal much about chocolate’s nutrient content**, what we need to quantify chocolate’s healthfulness is not the word ‘dark’ on the label, but some measure of its active flavanols.

Mood adjuster: Some people use chocolate to ‘drug’ their mood disorders and compulsive behaviors. In spite of the assertion by some that chocolate’s neuroactive substance

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VYTORIN & VASCULAR DISEASE

by Ann Gerhardt, MD

Bottom Line at the Top: The verdict is still out on whether ezetimibe adds anything to simvastatin, when it comes to preventing vascular disease.

Vytorin is a combination of ezetimibe and simvastatin. The ENHANCE trial (**E**zetimibe and **S**imvastatin in **H**ypercholesterolemia **E**nhances **A**therosclerosis **R**egression- a falsely hopeful acronym) compared the ability of Vytorin vs. simvastatin to reduce carotid artery wall thickening in people with genetically high cholesterol. The carotids are the major arteries to the brain. Carotid artery walls thickened by cholesterol and clot can eventually lead to the artery closing off, causing a stroke.

Though Vytorin lowers cholesterol more than does simvastatin, that did not translate into healthier carotid arteries. In fact, the carotids of people taking Vytorin had slightly thicker walls. ENHANCE’s design did not allow statistical comparison of death and stroke rates in the two groups.

Ezetimibe lowers cholesterol by blocking the body’s absorption of cholesterol from food and bile. Cholestyramine, one of the first cholesterol-lowering drugs, has the same mechanism of action and was proven long ago to reduce heart attacks. We don’t use it much, because it is a grainy powder, tastes atrocious and has to be taken with each meal. Efforts to produce a cholesterol absorption blocker in a once-a-day-pill form ultimately resulted in ezetimibe. It reliably lowers cholesterol, though not as much as statins (lovastatin, Lipitor, Zocor, Pravachol, Crestor). So far we lack proof that it, like cholestyramine, reduces vascular disease risk or death.

Ezetimibe only lowers cholesterol, unlike many other drugs

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Joseph Ann Greer, MFT

Marriage Family Therapist
License No. MFC25522



(916) 736-6300
2015 21st Street, Suite 305
Sacramento CA 95818

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content is too low to make us feel anything, **studies prove that people feel less depressed after chocolate consumption.** Some people assert that all palatable foods stimulate endorphin release in the brain, making us feel satisfied and happy.

Enjoying a piece of pizza is different from craving chocolate, and it just might be due to the tyramine, serotonin, dopamine and cannabinoid content, all of which affect mood and brain function. Many anti-depressants work by stimulating brain serotonin and dopamine activity and at least a few people can attest to the high of cannabinoids (the psycho-active component of marijuana).

Chocolate contains compounds that increase our natural cannabinoids in the brain. This may contribute to the serenity that accompanies eating chocolate.

Cannabinoids stimulate appetite, another reason why eating chocolate may make us want to eat more and more of it. The sometime-soon-to-arrive appetite suppressant, rimonabant, works through its effect on the cannabinoid system and, in rats, eliminates chocolate consumption.

Chocolate cannabinoids are not so similar to marijuana's that they might produce a positive drug test. That defense was tried and disproved and the guy went to jail.

Some newly identified components, salsolinol and tetrahydro- β -carbolines, exist in chocolate in significant quantities. They both have properties that might influence behavior and mood.

In addition to calming chemicals, chocolate also contains several stimulants, including caffeine and one used for asthma. Whether the balance of chocolate's biologically active chemicals calms or stimulates any given individual probably relates to that person's own brain chemistry. Chocolate cravings in women often fluctuate with hormonal changes. Women do not have a monopoly on chocolate
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FRUIT CONTAINS FRUCTOSE – IS IT OK??? *by Ann Gerhardt, MD*

Last issue's article about fructose, in "Not All Calories are Created Equal", stimulated readers' interest and questions. This comment sums up most of them:

Q: If honey, fruit, maple syrup and corn all contain fructose, does that overrule the familiar advice to eat lots of fruits and vegetables? Does it overrule my understanding that honey is a better sweetener than refined sugar in cereal or bread? Should I avoid eating polenta? I eat a lot of whole fruits...should I be concerned about eating too much fruit? I'm confident these are healthier than eating an equal weight of Oreos, but your point seems to say that eating a lot of fruit isn't such a good idea either. I would suppose this is a matter of degrees.

A: In the last issue of DrG's MediSense newsletter, I explained that the sugar fructose behaves differently from other sugars in the body. It contributes to insulin resistance and diabetes and increases uric acid production, leading to hypertension and kidney stones. **The U.S. epidemic of obesity and diabetes may in part be related to the abundance of cheap, high fructose corn syrup in sweetened beverages and foods.**

During processing of all-glucose corn syrup, glucose is turned into fructose. The resulting high fructose corn syrup (HFCS) contains 90% fructose. In North America it is diluted to a final concentration of HFCS-55 (55% fructose) or HFCS-42 (42% fructose). HFCS-55 has a slightly higher fructose content than table sugar, at 50% fructose.

Because natural corn, corn syrup and corn sugar is 100% glucose, foods like polenta, popcorn and corn on the cob raise blood sugar and caloric intake without the extra, adverse, metabolic effects of excess fructose.

Foods like fruit, honey, syrup and table sugar also contain fructose, leading to the above question. Fruits contain both free fructose and fructose that is part of sucrose. **Fruit's sugar (and fructose) content varies, depending on the variety, season and geographic area in which the fruit is grown.** An apple's total fructose content ranges from 59 – 72%. Pears contain 63 – 84% fructose and peaches are 50% fructose, while plums, grapes and cherries generally have more glucose than fructose. Even berries are not consistent, with strawberries having the least fructose, raspberries the most and blackberries in between.

Excessive fructose from fruit can and does raise triglyceride levels. It also contributes to insulin resistance in susceptible individuals. People exhibit different sensitivities to fructose, depending on their genetic make-

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Chocolate

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addiction, though. Many men in my practice reluctantly admit to being closet chocoholics. Most likely, a combination of chocolate's taste, mouth-feel, nutrient composition, and psychoactive ingredients induce cravings and make it difficult to stop eating it.

Adverse effects: Chocolate products contain some lead, occasionally enough to exceed the Food and Drug Administration's recommendations. The lead usually comes from contamination by cacao bean shells which have adsorbed lead from the environment.

Chocolate contains oxalate, which may contribute to kidney stones. Individuals prone to calcium oxalate stones should restrict chocolate intake.

Some people react to chocolate with headaches, possibly due to its tyramine content. Cocoa may raise blood pressure, from its phenylethylamine, caffeine and methyl-xanthine content. These are naturally occurring in the cacao bean, not additives acquired during processing.

Cocoa powder added to any food stimulates insulin secretion more than occurs with the food alone. Chocolate also has calories and perpetuates its own consumption, often leading to weight gain. Both of these might lead to metabolic syndrome in genetically prone individuals. ¶

Vytorin

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which reduce blood vessel clogging by mechanisms over and above cholesterol reduction alone. It is possible that ENHANCE's subjects, with genetically high cholesterol, needed more to improve carotid artery walls than ezetimibe's incremental cholesterol-lowering effect. A study comparing Vytorin and simvastatin's effects real outcomes, like death and heart attack, is underway.

Simvastatin's brand name is Zocor. Merck/Schering-Plough makes both Vytorin and Zocor. Zocor's patent has run out so the much cheaper generic simvastatin might cut into Merck/Schering-Plough's sales. The company stands to lose a lot of money if it can't prove that Vytorin is any better than simvastatin when it comes to saving lives. ¶

Fructose

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up. **Some people, with absolutely no tendency to metabolic syndrome, can eat fruit, honey and syrup all day and suffer no fat or sugar problems.** Others need to limit their intake to 2 fruits per day and consume minimal sweets, desserts, juice, honey, table sugar and syrup.

A trim, physically active, male patient of mine, consuming a very healthy diet and > 5 fruits per day, had fasting triglyceride levels of ~ 500 mg/dl (truly normal = <60, American normal = <150). His sugar was rising and he was headed for diabetes. Limiting the fruit brought the triglyceride level down to 150 mg/dl. He has a genetic make-up that makes him particularly sensitive to fructose and prevents his triglycerides from approaching normal without starvation.

We all ingest some fructose. Not all people will react to it by developing high triglycerides, metabolic syndrome or diabetes. Those require a certain genetic predisposition and lifestyle factors like being a couch potato, obese or a sugar addict. People with 'diabetes genes' probably differ in their sensitivity to fructose. Most will tolerate modest amounts; others more or less.

Maple sugar contains sucrose, with 50% fructose. Honey's sugar composition varies according to type of flower the bees visited, geographic location, and even the individual hive. Cotton honey contains the least fructose (51%) and tupelo honey the most (65%), with common clover honey in between, at 53%. Small differences in fructose-to-glucose ratios in honey does not substantially impact the amount that they raise blood sugar levels.

With a roughly equivalent fructose:glucose ratio to HFCS-55, we might assume that honey similarly affects insulin sensitivity and promotes the metabolic syndrome. I don't know that that study has been done. As with HFCS and other sources of fructose, I would expect the metabolic effect would be related to quantity consumed. One soda contains as much fructose as 2.5 tablespoons of honey. Three sodas per day is not uncommon: Consuming ½ cup of honey every day is.

A typical soda contains 39 – 48 grams of sugar, more than twice the sugar content of most fruits. The problem with HFCS isn't an extraordinary fructose *percentage*, but that it has so much fructose per serving and is so much cheaper and easier to consume than natural foods.

The alternative to HFCS? Fruit, honey and maple syrup are not pure sugar. Plant saps, honey and fruits contain vitamins, bioflavonoids and even amino acids, which add considerably to health value. Choose fruit, syrup and honey over sugar as sweeteners, and limit the total quantity. ¶

EXERCISE EXCUSE CANTATA

A song by Ann Gerhardt MD

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New Year's Resolution Time: The usual time to decide to exercise, then to create delusional excuses for not doing it, that you think your doctor might believe. I put these real excuses patients tried (and failed) with me to music.

I work long days.
Gym at work is too far away.
Just can't seem to run.

I'm lazy. Day's hazy.
My daughter just had a baby.
Sweating isn't fun.

Chorus *Doctor says I have to move it
What's so good 'bout moving fast?
When I get the urge to work out
The couch holds me 'til it's past.*

Busy. Stressed. No time.
Eat, sleep, work, shop, internet, TV
Can't find time to train.

I can't lift weights.
Five green aliens late one dark night
took control o' my brain.

Chorus

Pool's closed. No suit.
Don't want anyone to see me.
Chlorine makes me wheeze.

Too fat. Too skinny.
The gym smells and it is boring.
Muscles turned to cheese.

Chorus

Too tired. Need shoes.
My dog now has old-age blues.
Got no place to walk.

It's hot. I hurt.
Houseguests, neighbors, kids & husband
only want to talk.

Chorus

It's raining. Too windy.
Never thought of an umbrella.
Can't mix rain with sweat.

Movement makes me sick.
No amount will compensate for
pounds of fudge I ate.

Chorus

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DOES 'NORMAL' BLOOD SUGAR INCREASE HEART DISEASE RISK IN DIABETICS???

by Ann Gerhardt, MD

Bottom Line at the Top: Two recent studies of diabetes control, taken together, suggest that trying to normalize blood sugar alone does not prevent heart disease. We are still missing the exact formula to do so.

The National Heart, Lung, and Blood Institute (NHLBI) is sponsoring the ACCORD study (Action to Control Cardiovascular Risk in Diabetes) to see if very low blood sugar prevents heart disease in diabetics. Heart disease is the number one killer of diabetics. The study follows two groups of patients taking medication to lower hemoglobin A1c (HgbA1c), a measure that reflects sugar control for the preceding 3 months. The 'tight-control' group has aimed for HgbA1c less than 6%, and the 'usual-care' group has settled for 7 – 7.9%, the level of success most commonly achieved by diabetics. The American Diabetes Association has long recommended a goal of HgbA1c < 7%.

The study's **Data and Safety Monitoring Board stopped the 'tight control' goal, because after 4 years those patients were dying at the rate of 3 more deaths per 1000 participants each year.** They don't yet know why more of the people with good sugar (glucose) control died more often. One obvious possibility is use of Avandia (see related article in this issue), but there was no difference in the numbers of people taking it in the two groups. The NHLBI reports that the tight control group had more trouble with extremely low blood sugars. This makes sense, since HgbA1c is just an average of the highs, lows and middles: A lower average frequently means more lows. It is not clear if low blood sugar played a role in the deaths. The data has not yet been published, pending further analysis.

I have a theory: Diabetes experts have long contended that diabetics have more heart disease because of high blood sugar. A perfectly normal HgbA1c in a non-diabetic is < 5%. In the ACCORD study, more people died with

Continued on page 7

Blood Sugar/Heart Disease *continued from page 6*
HgbA1c levels that were approaching perfectly normal. So what is the difference between diabetics and non-diabetics with normal blood sugar?

The diabetics in this study achieved their normal levels with medication. Non-diabetics don't take those medications, maintaining normal glucose levels with normal metabolism and possibly even a healthy lifestyle.

Many diabetes medications make it very difficult to lose weight, and in fact may drive up hunger and body weight from fat. More fat, particularly in the spare-tire area common in diabetics, perpetuates metabolic abnormalities common to 'apple' shaped people. Those include worse inflammation, oxidation, blood vessel spasm, cholesterol, triglycerides and clotting, all of which contribute significantly to heart disease.

I posit that driving diabetics' blood sugar to normal levels with medication increases abdominal fat mass, which leads to heart-disease-causing metabolism, independent of blood sugar.

It will be very interesting to see what happened to the weight and waistlines of ACCORD's tight-control group. If the investigators also measured parameters of inflammation, oxidation and clotting, it would add invaluable information and possibly the explanation for ACCORDS's findings.

A Danish study recently published in the New England Journal of Medicine tried to address many factors as well as lowering glucose. They added aspirin, cholesterol-lowering medication and a specific type of blood pressure drug that prevents kidney disease to the 'tight-control' group.

In its initial phase there were equal numbers of heart disease deaths in the 'tight-control' and usual care groups. Though the goal for 'tight' control was HgbA1c<6.5%, people only achieved an average of 7.9%, and the 'usual-care' group wasn't too far off.

During the follow-up phase, the 'usual-care' group's average HgbA1c *improved* and most added the same extra medications to help metabolism, but they had many more heart disease deaths. Both groups increased weight and waistline.

The official conclusion of the study was that tight control helps over the long-haul, but the 'tight-control' group's glucose control wasn't so tight – It ended up the same as the other 'usual-care' group.

The only real difference between the two groups at the end of follow-up was the higher rate of aspirin use by the group with less heart disease. So either aspirin is the answer, or we are missing something completely. While we look for it, diabetics do much better if they rid themselves of diabetes with lifestyle changes. ¶

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