

# CACAO TO COCOA TO CHOCOLATE: HEALTHY FOOD?

Roya Kelishadi MD

## ABSTRACT

Chocolate is derived from cocoa beans - the fruit of the cacao tree or *Theobroma cacao* (the latin term: food of the gods). Recent published articles demonstrate that the quality and quantity of the antioxidants in cocoa and chocolate are very high and their flavonoids are believed to reduce the number of free radicals in the body that contribute to medical problems, such as cardiovascular disease and cancer and also to offer some anti-aging health benefits. Cocoa can lower the leukotriene/ prostacyclin ratio and is shown to have beneficial effects on platelets and possibly inflammation and vessel dilation. They inhibit low-density lipoprotein (LDL) oxidation, raise the high-density lipoprotein (HDL) level and reduce the thrombotic tendency. Their antioxidant catechin content is four times that of tea. They help the body process nitric oxide. Their flavanols and procyanidins have inhibitory effects on hemolysis, they can also attribute as a defense against reactive oxygen species (ROS) and can inhibit their carcinogenic processes. Also they are shown to inhibit growth and polyamine biosynthesis of human colonic cancer cells. They contain tryptophan and anandamide, which lessen anxiety, promote relaxation and trigger the production of endorphins. Cocoa can prevent dental caries and may play a regulating role in the function of the immune system and prevent infectious and autoimmune diseases. It stimulates lactase enzyme activity.

Although caffeine may be harmful in large dose, chocolate contains it in small amount in comparison to coffee and tea. Negative effects of chocolate on childhood hyperactivity and migraine as well as tension headaches are controversial. Since the theobromine content of chocolate relaxes the esophageal sphincter, patients suffering from heartburn should avoid it. Cocoa can trigger some allergic reactions such as atopic dermatitis.

This article reviews the potential health benefits and disadvantages of cocoa & chocolate and suggests that their flavonoid-rich types are health beneficial and when consumed in moderation, along with other plant foods, can be part of a healthy diet.

**Keywords:** Cacao, Cocoa, Chocolate, Antioxidants, Flavanols, Caffeine

**ARYA Journal 2005, 1(1): 29-35**

**C**hocolate originates in cocoa beans, the fruit of the cacao plant. Through different processing, cocoa and chocolate are derived from the seeds of the cacao tree or *theobroma cacao*- its scientific name. The Swedish botanist, Carolus Linnaeus classified it in the 1700s, the Latin term *theobroma* means "food of the gods". Cocoa seeds (Cocoa beans) are obtained from this tree which is usually 4-6m high<sup>1</sup>. Cocoa is produced in South America (Ecuador, Colombia, Brazil, Venezuela and Guiana), Central America, the West Indies, West Africa (Nigeria and Ghana), Ceylon and Java<sup>1,2</sup>.

**Collection and preparation:** Cocoa fruits are

15-25 cm long and are borne on the trunk as well as on the branches. Collection continues through the year, but the largest quantities are obtained in the spring and autumn. The fruits have a thick, coriaceous rind and whitish pulp in which 40-50 seeds are embedded. Cocoa seeds are flattened ovoid in shape, 2-3 cm long and 1.5 cm wide. The seeds contain 35 to 50% of a fixed oil, about 15% of starch, 15% of proteins, 1 to 4% of theobromine, and 0.07 to 0.36% of caffeine<sup>3</sup>. In different countries the seeds are prepared in different ways, but the following may be taken as typical: the fruits are opened and the seeds, embedded in the whole pulp or roughly separated from it, are allowed to ferment. Fermentation occurs in tubs, boxes or cavities; the process lasts 3-9 days, and the temperature is not allowed to rise above 60°C. During this process, a liquid drains from the seeds, which change in color from white or red to purple, and also acquire a different odor and taste. They are

### Corresponding Author:

Roya Kelishadi MD. Associate Professor. Pediatrician, Head of Preventive Pediatric Cardiology Department, Isfahan Cardiovascular Research Center, Isfahan, Iran. PO. BOX: 81465-1148  
Email: kelishadi@med.mui.ac.ir

then roasted at 100-140°C, at which point loses water and acetic acid and acquire their characteristic odor and taste. The seeds are cooled as rapidly as possible and the taste removed by a nibbling machine. The nibs or kernels are separated from the husk by winnowing<sup>1,2</sup>.

**Constituents:** Cocoa kernels contain 0.19-3.0% of theobromine and the husks contain 0.19-2.98% of this alkaloid. The seeds also contain 0.05-0.36% caffeine, cocoa fat or butter (nibs 45-53%, husk 4-8%)<sup>1,3</sup>. Chocolate liquor, formed by grinding the roasted, cracked cacao bean, is the base for cocoa and chocolate products. To make cocoa, the chocolate liquor is put under pressure and most of the cocoa butter is squeezed out leaving a cake that is pulverized and sifted into a powder. While cocoa butter is removed in the making of cocoa, it is added in the making of chocolate<sup>4-6</sup>. Chocolate is a combination of chocolate liquor, sugar, cocoa butter, and some added flavors<sup>7-10</sup>. There are different types of chocolate:

1. Bitter chocolate is made by mixing cocoa paste with small amounts of sugar; 2. Milk chocolate is a mixture of cocoa paste, cocoa butter, sugar, and substantial quantities of powdered milk, 3. White chocolate is obtained by mixing cocoa butter, sugar and milk<sup>3</sup>. Chocolate is best stored at 60 to 75 degrees Fahrenheit in an odor-free place away from heat and sunlight. The humidity of the storage place should be no more than 50 percent<sup>9,10</sup>.

**Uses:** Cocoa has nutritive, stimulant and diuretic properties. Theobromine is used as a diuretic. It has less action on the central nervous system than caffeine but is more diuretic. In its isomer, theophylline, the diuretic effect is even more marked<sup>1,2</sup>.

**Nutritional Value:** Because of their fat content, cocoa and chocolate are high in calories. One hundred grams of chocolate (sweet or semisweet) provides about 470 to 528 kcal of energy. Cocoa powders contain about 215 to 300 kcal per 100gm (3.5 oz). Cocoa and chocolate supply some carbohydrate and protein as well as significant amounts of some minerals such as chromium, iron, magnesium, phosphorus and potassium<sup>3,4</sup>. Chocolate contains a number of other substances in small, but effective, quantities: **Theobromine:** which stimulates the central nervous system, facilitates muscular exertion, acts as a diuretic and appetite stimulant. **Caffeine:** which increases resistance to fatigue and watchfulness, although may be harmful in

large doses; chocolate contains it in small amount. An average size chocolate bar contains approximately 6 mg of caffeine, compared to 100-150 mg in a cup of coffee. **Phenyl ethylamine:** which is chemically similar to amphetamines, therefore acting as a psycho-stimulant? **Tryptophan:** an essential amino acid that increases the production of serotonin, an anti-depressant and a natural stress-reducer. In fact, a decrease in serotonin levels in the brain may trigger cravings for starches, sweet foods and chocolate. **Endorphins:** natural opiates that are released by the brain in increased amounts when eating chocolate, thereby elevating one's mood and reducing pain.

**Phenols:** which are also found in tea, fruits and vegetables, and may help reduce the risk of cardiovascular disease (CVD)? **Catechins:** which are antioxidants that may help protect the body against CVD and possibly cancer, are found in substantially higher quantities in chocolate than in black tea. **Anandamide:** which acts on the same brain receptors as marijuana? Plus, chocolate has two ingredients that inhibit the natural breakdown of Anandamide and hence may prolong the feeling of well-being<sup>1,3,4,10</sup>.

#### **A. Cocoa's Potential Health Benefits:**

Many people refer to cocoa and chocolate as "feel good" foods. Now researchers are finding that they may also be good for the body as well. Their benefits can be categorized as follows:

**1. Cocoa and antioxidants:** Researches show that the cocoa bean, and its tasty products such as chocolate, and the beverage cocoa, is rich in specific antioxidants (catechins, epicatechin, procyanidins and polyphenols) similar to those found in vegetables and tea. These natural antioxidants are believed to reduce the number of free radicals in the body and can provide a defense against reactive oxygen species (ROS)<sup>11</sup>. Top antioxidant foods are listed in table 1.

Epidemiologic studies suggest an inverse association between consumption of flavonoid-rich foods such as tea or cocoa and CVD<sup>12-14</sup>. Possible mechanisms include oxidative damage to LDL<sup>15</sup>, attenuating the inflammatory process in atherosclerosis<sup>16, 17</sup>, reducing thrombosis, promoting normal endothelial function, and blocking expression of cellular adhesion molecules<sup>18</sup>.

Flavonols and procyanidins isolated from cocoa exhibit strong antioxidant properties<sup>19</sup>. In acute feeding studies, flavonoid-rich cocoa and chocolate increased plasma antioxidant capacity

**Table 1.** Top Antioxidants foods

Top Antioxidant Food	ORAC* Units per 100 grams
Dark Chocolate	13,120
Milk Chocolate	6,740
Prunes	5,770
Raisins	2,830
Blueberries	2,400
Blackberries	2,036
Kale	1,770
Strawberries	1,540
Spinach	1,260
Raspberries	1,220
Brussel Sprouts	980
Plums	949
Alfalfa Sprouts	930
Broccoli Florets	890
Oranges	750
Red Grapes	739
Red Bell Pepper	710
Cherries	670
Onion	450
Corn	400
Eggplant	390

\*ORAC (Oxygen Radical Absorbance Capacity) is a measure of the ability of the foods to subdue harmful oxygen free radicals that can damage our bodies. Source: Data from the U.S. Department of Agriculture and the *Journal of the American Chemical Society*

reduced platelet reactivity<sup>20, 21</sup>.

Based on limited data, approximately 150 mg of flavonoid is needed to trigger an immediate (acute) antioxidant effect and changes in prostacyclin. Some dose-response evidence demonstrates a continuing (chronic) antioxidant effect with approximately 500 mg flavonoids. Brewed tea typically contains approximately 172 mg total flavonoids per 235 ml (brewed for 2 min); hence, consumption of 1 and 3.5 cups of tea would be expected to elicit acute and chronic physiologic effects, respectively<sup>12</sup>.

In vitro effects of catechins and their oligomers linked by C4 --> C8 bonds are major antioxidative components of chocolate and cocoa. Their effects on protecting human LDL from oxidation are also confirmed in human studies<sup>(22, 23)</sup>. The antioxidant catechin content of dark chocolate (0.535mg/g) is four times that of tea (139-mg/L)<sup>24</sup>. Catechin intake is shown to be inversely associated with ischemic heart disease mortality; but not associated with stroke incidence or mortality<sup>25</sup>.

The study of Wan and his colleagues showed that cocoa powder and dark chocolate may favorably affect CVD risk status by modestly reducing LDL oxidation susceptibility, increasing

serum total antioxidant capacity and HDL-cholesterol concentrations, and not adversely affecting prostaglandins<sup>26</sup>.

Vinson et al have shown that the flavonoids in chocolate are more potent than ascorbic acid in protecting circulating lipids from oxidation<sup>27</sup>.

The study of Rein and his colleagues showed that polyphenol rich cocoa consumption suppressed ADP- or epinephrine-stimulated platelet activation and platelet microparticle formation<sup>28</sup>. This study and the work of Holt and his colleagues<sup>29</sup> have shown that cocoa consumption has an aspirin-like effect on primary homeostasis.

It is found that a substance in cocoa helps the body process nitric oxide (NO), a compound critical for healthy blood flow and blood pressure. In a recent study, researchers gave volunteers cocoa with either a high or low amount of flavones. Those who drank cocoa with more flavonals showed more NO activity<sup>30</sup>.

A few studies show that ROS associated with the carcinogenic processes is also inhibited by antioxidants found in cocoa, although there have not been many studies on a possible lower risk of various types of cancer either in humans or in animal models consuming cocoa butter or chocolates<sup>31</sup>.

Their flavonals and procyanidins are shown to inhibit growth and polyamine biosynthesis of human colonic cancer cells. Procyanidin Enriched (PE) cocoa extracts can cause a 70% growth inhibition with a blockade of the cell cycle at the G2/M phase. PE extracts caused a significant decrease of ornithine decarboxylase and Sadenosylmethionine decarboxylate activities, two key enzymes of polyamine biosynthesis. This led to a decrease in the intracellular pool of the polyamines, the metabolism of which might be an important target in the antiproliferative effects of cocoa polyphenols<sup>32</sup>.

The permeable membranes of the cells produced by the lymph glands contain a high content of poly-unsaturated fatty acids. Consequently, they are very sensitive to lipid peroxidation.

The imbalance of the immune system leads to over production of oxygen radicals and peroxides that can cause acute inflammations leading to auto-immune diseases. It has been shown that antioxidants such as those found in cocoa may play an important regulating role in the functioning of the immune system and preventing infectious and autoimmune diseases<sup>33</sup>. Free radicals are also generally believed to play an important role in

the ageing of cells <sup>(31)</sup>. Extensive research has found that it may be possible to extend the life expectancy of a healthy human being by 5-10 years by adhering to an active life-style and a well balanced diet, high in antioxidants such as the cocoa poly-phenols <sup>31,34</sup>.

Evaluating the inhibitory effects of cocoa flavones (-) epicatechin and (+) catechin, and procyanidin oligomers (dimer to decamer) on rat erythrocyte hemolysis, showed membrane protective effects and enhanced resistance to hemolysis <sup>35</sup>. These compounds are also shown to cause dose-dependent inhibition of isolated rabbit 15-lipoxygenase-1 with the larger oligomers being more active <sup>36</sup>. They also inhibited the formation of 15-hydroxy-eicosatetraenoic acid from arachidonic acid in rabbit smooth muscle cells transfected with human 15-lipoxygenase-1<sup>37</sup>. Moreover they can inhibit recombinant human platelet 12-lipoxygenase <sup>38</sup>. These observations suggest their putative beneficial effects on the cardiovascular system in man too <sup>39,40</sup>.

New researches show a lowering of the leukotriene/prostacyclin ratio in human volunteers who consumed 37 g/day of chocolate which may have beneficial effects on platelets and possibly inflammation and vessel dilation. On this basis, several pharmaceutical companies are isolating and developing some of the components of chocolate as cardiovascular pharmaceuticals <sup>41</sup>.

It has been known for some time that cocoa and polyphenol extracts of cocoa can prevent dental caries. It is believed that their polyphenol inactivates the enzyme responsible for catalyzing the production of poly-saccharoses from sugar - the binding agent that attaches the dental plaque to the teeth <sup>42, 43</sup>. Health educators should be aware that many adolescents have poor knowledge of the cariogenic & anticariogenic status of some of the foods they consume<sup>44</sup>.

Commercially available cocoa and or chocolate vary widely in flavonoid content. Some products contain essentially no flavonoids (0.09 mg procyanidin/g) and others contain relatively high amounts (4 mg procyanidin/g) compared to other plant foods. Thus, approximate estimates of flavonoid rich chocolate needed to exert acute and chronic effects are 38 and 125 g, respectively.

**2. Cocoa and Atherogenesis:** Chocolate is about 30% fat, mainly from cocoa butter, which contains about 60% saturated fatty acids (35% stearic acid and 25% palmitic acids) and about 40% unsaturated fatty acids — mainly oleic acid <sup>45</sup>. The

fat in chocolate from cocoa butter is comprised of oleic acid, a monosaturated fatty acid (with beneficial cardiovascular effects), as well as stearic and palmitic acids, chemically classified as saturated fatty acids <sup>46</sup>. Several studies have also provided evidence that unlike other saturated fats, stearic acid has a neutral effect on blood cholesterol. Other test tube and clinical feeding studies have shown that stearic acid can decrease platelet activity <sup>47</sup>. Cocoa butter is significantly less cholesterolemic and atherogenic than palm oil or coconut oil. The difference between the atherogenic effects of cocoa butter and palm oil may lie in the fact that about half of the fatty acids of palm oil are C 16 or shorter, whereas 76% of the fatty acids of cocoa butter are C 18 or longer <sup>48</sup>.

### **3. Cocoa and the Effect on Exercise Recovery:**

Studying the effects of chocolate supplementation before exercise on improving recovery of physiological and metabolic changes induced by exercise, has shown that plasma glucose levels of subjects increased significantly (5.42 +/- 0.83 mmol/L) at 15 min after ingestion of a chocolate bar and maintained in moderate high levels (4.92 +/- 0.57 mmol/L) until 30 min after an hour's running while the glucose levels were low and dropped to under normal ranges (3.84 +/- 0.31 mmol/L) at 30 min after exercise as they were with a supplement of placebo. It is concluded that a chocolate bar supplementation before exercise benefits by creating the necessary prerequisite for exercise and recovery <sup>49</sup>.

### **4. Cocoa and Chronic Fatigue Syndrome:**

There are several bioactive compounds in chocolate that promote alertness<sup>50</sup>, lessen pain and promote well-being<sup>51</sup>: its tryptophan lessens anxiety by producing serotonin; endorphins reduce sensitivity to pain<sup>52</sup>, anandamide acts like a cannabinoid to promote relaxation <sup>53</sup>.

### **5. Cocoa and Human Lactose Intolerance:**

On the basis of evidence of the suppressing effect of cocoa on human lactose intolerance, a feeding study was conducted; the addition of cocoa significantly reduced breath hydrogen level (BHL) as well as the symptom score of both bloating and cramping. This suppressive effect was independent of the presence of sucrose and carrageenan <sup>54</sup>. Studies show that cocoa stimulates lactase enzyme activity and makes milk easier to digest if one is lactose- intolerant subjects <sup>55</sup>. No single food will confer immunity from illness, but flavonoid-rich cocoa and

chocolate, which are plant foods, can be components of a healthy diet if eaten in moderation along with other plant foods such as fruits and vegetables.

## **B. Cocoa's Potential Health Disadvantages:**

**1. Cocoa and Caffeine:** Coffee and/or caffeine consumption has been linked to many human diseases in epidemiologic studies. Causal relationships have been difficult to substantiate<sup>56</sup>. Recent studies, showing a significant effect over long follow-up periods have again raised the question of a role for caffeine consumption in the pathogenesis of atherosclerotic heart disease<sup>56, 57</sup>. In the Bogalusa Heart Study, snacks contributed large quantities of caffeine intake in children. One of the most frequent sources of caffeine was chocolate-containing foods, and tea<sup>58</sup>. There have been many studies on children of different ages. While newborn infants metabolize caffeine slowly, children from less than 1 year to adolescence metabolize caffeine about twice as fast as non-smoking adults. The numerous studies showing safety of caffeine in adults, combined with the direct studies in children showing they are similar and not more susceptible to caffeine than adults<sup>59</sup>. The epidemiological studies describe exposures of women to caffeine during pregnancy, as well as the occurrence of congenital malformations, fetal growth retardation, small-for-date babies, miscarriages (spontaneous abortions), behavioral effects, and maternal fertility problems that presumably resulted from the caffeine consumption. A few epidemiological studies were concerned with the genetic effects of preconception exposures to caffeine. Animal studies, conducted mostly in pregnant rats and mice, were designed to produce malformations<sup>60</sup>. It should be noted that evaluation of the developmental risks of caffeine based solely on epidemiological studies is difficult because the findings are inconsistent. Even more important, is the fact that caffeine users are subject to multiple confounding factors that make analyses difficult and prevent investigators from reaching definitive conclusion<sup>61</sup>. Anyhow chocolate contains caffeine in small amount in comparison to coffee and tea; the values for different food products is suggested as follows: coffee (5 oz) 85 mg for ground roasted coffee, 60 mg for instant and 3 mg for decaffeinated; tea (5 oz): 30 mg for leaf/bag and 20 mg for instant; colas: 18 mg/6 oz serving; cocoa/hot chocolate: 4 mg/5 oz;

chocolate milk: 4 mg/6 oz; chocolate candy: 1.5-6.0 mg/oz<sup>60,61</sup>.

## **2. Cocoa and Childhood Hyperactivity:**

Chocolate is one the foods suggested to enhance the incidence of this syndrome<sup>62</sup>; but since none of the studies found any negative effect of foods on behavior, some investigators recommend that for children with behavioral problems, diet oriented treatment does not appear to be appropriate<sup>63</sup>.

**3. Cocoa and Headache:** Some authors reported that migraine-and tension type headache attacks might be provoked by foods including chocolate<sup>64</sup>. Another study provides some objective evidence that chocolate is able to provoke a migraine attack in certain patients who believe themselves sensitive to it<sup>65</sup>. There are also evidences contrary to above studies that chocolate is not a common trigger of headaches<sup>66</sup>.

**4. Cocoa and Heartburn:** Chocolate is a common culprit in heartburn because it contains concentrations of theobromine, which relaxes the esophageal sphincter muscle, letting stomach acid squirt up into the esophagus. In patient's suffering from heartburn, it is advised to go easy on chocolate<sup>67</sup>.

**5. Cocoa and Allergic Reactions:** Chocolate is one of the most common triggers of cutaneous symptoms in children with atopic dermatitis (AD)<sup>68</sup>. Food-induced vacuities seems to be rare and is considered by some as controversial, but there is a report describing two children with severe vacuities caused by specific foods such as chocolate<sup>69</sup>. A review performed on allergic reactions to cocoa has concluded that although there are specific contraindications to the ingestion of chocolate by selected individuals, these do not apply to the general population with a frequency that is suggested by the pervasive mistrust of chocolate<sup>70</sup>.

**6. Chocolate Craving:** Based on correlational data, little evidence is found for a relation between addiction to chocolate and the pharmacological (e.g., xanthine-based) effects of chocolate and the liking for chocolate<sup>71</sup>. Frequent and repeated exposure to foods produces stimulus satiation or monotony, but an apparent dissociation between pleasantness and intake of chocolate is shown and may reflect different processes underlying liking and wanting<sup>72</sup>.

**Conclusion:** Cocoa is one of a whole host of flavonoid-rich foods. Such phenolics confer chocolate fat particular resistance to peroxidation, and in vitro & in vivo studies

indicate that they are endowed with biological activity, mainly including antioxidant capacity and immunoregulatory effects. As its fortification with iron had positive effects<sup>73, 74</sup>, researches should be performed on the flavanol content of different types of consumed cocoa and chocolate and related food industries should be encouraged to prepare cocoa products rich in flavonoids. Cocoa and chocolate studies suggest health benefits but as always, moderation is the key to success for a healthy diet.

## REFERENCES

- 1- Ensminger AH, Ensminger ME, Konlande JE, Robson J RK. *The Concise Encyclopedia of Foods & Nutrition*. Philadelphia CRC press, 1995; 206-7.
- 2- Evans WC. *Trease and Evans' Pharamagonosy*, Philadelphia WB Saunders Co, 14th ed, 1998: 402-3.
- 3- Rizza RA, Liang V, Mc Mahon M, Harrison G. *Encyclopedia of foods; A guide to healthy nutrition*. London Academic Press 2000; 403-5.
- 4- Delzenne NM. *Chocolate, an ancient remedy still enjoyed today*. *J Pharm Belg* 2001; 56 (5):- 119-24.
- 5- <http://www.chocolate.org/>
- 6- <http://www.virtualchocolate.com/>
- 7- <http://www.chocolate-alliance.com/>
- 8- <http://www.exploratorium.edu/chocolate/>
- 9- <http://www.faqs.org/faqs/food/chocolate/resources/part1/>
- 10- <http://www.acri-cocoa.org/acri/index.cfm/>
- 11- Visioli F, Borsani L, Galli C. *Diet and prevention of coronary heart disease: the potential role of phytochemicals*. *Cardiovasc Res* 2000; 47(3): 419-25.
- 12- Kris-Etherton PM, Keen CL. *Evidence that the antioxidant flavonoids in tea and cocoa are beneficial for cardiovascular health*. *Curr Opin Lipidol* 2002; 13(1): 41-9.
- 13- Lazarus SA, Hammerstone JF, Schmitz HH. *Chocolate contain additional flavonoids not found in tea*. *Lancet* 1999; 354: 1825-8.
- 14- Waterhouse AL, Shirley JR, Donovan JL. *Antioxidants in chocolate*. *Lancet* 1996; 348: 834-7
- 15- Morel I, Lescoat G, Cillard P, Cillard J. *Role of flavonoids and iron chelation in antioxidant action*. *Methods Enzyme* 1994; 234: 437-43.
- 16- Salah N, Miller NJ, Paganga G, et al. *Polyphenolic flavonols as scavenger of aqueous phase radicals and as chain-breaking antioxidant-ants*. *Arch Biochem Biophys* 1995; 322: 339-46.
- 17- Vinson JA, Jang J, Dabbagh YA, Serry MM, Cai S. *Plant polyphenols exhibit lipoprotein-bound antioxidant activity using in vitro oxidation model for heart disease*. *J Agric Food chem*. 1995; 43: 2798 -9.
- 18- Knekt P, Jarvinen R, Reunanen A, Maatela J. *Flavonoid intake and coronary mortality in Finland: a cohort study*. *Brit Med J* 1996; 312:478-81.
- 19- Hertog M, Kromhout D, Aravanis C, et al. *Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study*. *Lancet* 1993; 342: 1007-11.
- 20- Hollman PC, Hertog MGL, Katan MB. *Role of dietary flavonoids in protection against cancer and coronary heart disease*. *Biochem Soc Transact* 1996;24:785-9.
- 21- Hollman PC, Katan MB. *Dietary flavonoids: intake, health effects and bioavailability*. *Food Chem Toxic* 1999; 37: 937-42.
- 22- Osakabe N, Yasuda A, Natsume M, Taki-zawa T, Terao J, Kondo K. *Catechins and their oligomers linked by C4 --> C8 bonds are major cacao polyphenols and protect low-density lipo-protein from oxidation in vitro*. *Exp Biol Med (Maywood)* 2002; 227(1): 51-6.
- 23- Kondo K, Hirano R, Matsumoto A, Igarashi O, Itakura H. *Inhibition of LDL oxidation by cocoa*. *Lancet* 1996 Nov 30; 348(9040):1514-7.
- 24- Arts IC, Hollman PC, Kromhout D. *Chocolate as a source of tea flavonoids*. *Lancet* 1999; 354 (9177): 488-91.
- 25- Arts IC, Hollman PC, Feskens EJ, Bueno de Mesquita HB, Kromhout D. *Catechin intake might explain the inverse relation between tea consumption and ischemic heart disease: the Zutphen Elderly Study*. *Am J Clin Nutr* 2001; 74(2): 227-32.
- 26- Wan Y, Vinson JA, Etherton TD, Proch J, Lazarus SA, Kris-Etherton PM. *Effects of cocoa powder and dark chocolate on LDL oxidative susceptibility and prostaglandin concentrations in humans*. *Am J. Clin Nutr* 2001; 74(5): 596-602.
- 27- Vinson JA, Proch J, Zubik L. *Phenol antioxidant quantity and quality in foods: cocoa, dark chocolate, and milk chocolate* *J Agric Food Chem*. 1999 ; 47(12): 4821-4.
- 28- Rein D, Paglieroni TG, Wun T, Pearson DA, Schmitz HH, Gosselin R, Keen CL. *Cocoa inhi-bits platelet activation and function*. *Am J Clin Nutr* 2000; 72(1): 30-5.
- 29- Holt RR, Schramm DD, Keen CL, Lazarus SA, Schmitz HH. *Chocolate consumption and platelet function*. *JAMA* 2002; 287(17): 2212-5.
- 30- Zhu QY, Holt RR, Lazarus SA, Orozco TJ, Keen CL. *Inhibitory effects of cocoa flavones and procyanidin oligomers on free radical-induced erythrocyte hemolysis*. *Exp Biol Med (May-wood)* 2002; 227(5): 321-9.
- 31- <http://www.newhope.com/>. *The Sept/Oct 2001 Issue of Functional foods & Nutra-ceuticals*.
- 32- Carnesecchi S, Schneider Y, Lazarus SA, Coehlo D, Gosse F, Raul F. *Flavanols and proc-yanidins of cocoa and chocolate inhibit growth and polyamine biosynthesis of human colonic cancer cells*. *Cancer Lett* 2002; 175(2): 147-55.
- 33- Sanbongi C. *Combat cell damage*. *Cell Immune* 1997 May 1; 177 (2): 129-36.
- 34- Waterhouse, AL. *Source of good antioxidants*. *The Lancet* 1996; 348: 807.
- 35- Weisburger JH. *Chemo preventive effects of cocoa polyphenols on chronic diseases*. *Exp Biol Med (Maywood)* 2001; 226(10): 891-7.
- 36- Schewe T, Sadik C, Klotz LO, Yoshimoto T, Kuhn H, Sies H. *Polyphenols of cocoa: inhibition of mammalian 15-lipoxygenase*. *Biol Chem* 2001; 382(12): 1687-96.
- 37- Bearden MM, Pearson DA, Rein D. *Potential cardiovascular health benefits of procyanidins present in chocolate and cocoa*. In: *Parliament TH. Ho CT. Schieberle P. et al. Caffeinated beverages: health benefits, physiological effects and chemistry*. Washington. DC: American Chemical Society 2000: 177-86.
- 38- Adamson GE, Lazarus SA, Mitchell AE, et al. *HPLC method for the quantification of procyanidins in cocoa and chocolate samples and correlation to total antioxidant capacity*. *J Agric Food Chem* 1999; 47: 4184-8.
- 39- Piskula MK, Teraco J. *Accumulation of (-) epicatechin metabolites in rat plasma after oral administration and*

- distribution of conjugation enzymes in rat tissues. *J Nutr* 1998; 128: 1127-8.
- 40- Richelle M, Tavazzi I, Enslen M, Offord EA. Plasma kinetics in man of epicatechin from black chocolate. *Eur J Clin Nutr* 1999; 53: 22-6.
- 41- Wang JF, Schramm DD, Holt RR, et al. A dose-response effect from chocolate consumption on plasma epicatechin and oxidative damage. *J Nutr* 2000; 130: 2115S-9S.
- 42- Gravenmade EJ, Jenkins GN. Isolation, purification and some properties of a potential cariostatic factor in cocoa that lowers enamel solubility. *Caries Research* 1986; 20: 433-6.
- 43- Kashket S. Tooth decay. *Arch Oral Biol* 1985; 30: 359-63.
- 44- Kinirons MJ, Stewart C. Adolescents' knowledge of common foods and drinks and the importance of the pattern of consumption: a study undertaken in an area of high dental needs. *Community Dent Health* 1998; 15(3): 175-8.
- 45- Osakabe N, Yamagishi M, Sanbogi C, Natsume M, Takizawa T, Osawa T. The antioxidative substances in cocoa liquor. *J Nutr Sci. Vitamin* 1998; 44: 313-21.
- 46- Kritchevsky D, Tepper SA, Bises G, Klurfeld DM. Experimental atherosclerosis in rabbits fed cholesterol-free diets. *Atherosclerosis* 1982; 41(2-3): 279-84.
- 47- Bruinsma K, Taren DL. Chocolate: food or drug? *J Am Diet Assoc* 1999; 99(10): 1249-56.
- 48- Kris-Etherton PM, Derr J, Mitchell DC, et al. The role of fatty acid saturation on plasma lipids, lipoproteins and apolipoproteins: I. Effects of whole food diets high in cocoa butter, olive oil, soybean oil. Dairy butter and milk chocolate on the plasma lipids of young men. *Metabolism* 1993; 42: 121-9.
- 49- Chen JD, Ai H, Shi JD, Wu YZ, Chen ZM. Effect of a chocolate bar supplementation on moderate exercise recovery of recreational runners. *Biomed Environ Sci* 1996; 9(2-3): 247-55.
- 50- Zurer, P. Chocolate may mimic marijuana in brain. *Chemical and Engineering News* 1996; 74 (Sept. 2): 31.
- 51- <http://faculty.washington.edu/chudler/choco.html>.
- 52- Brostoff J. Second World Congress on CFS and Related Disorders held in Brussels, Belgium, Allergy in CFS September 1999.
- 53- DiTomaso E, Beltramo M, Piomelli D. Brain cannabinoids in chocolate. *Nature* 1996; 382: 677-8.
- 54- Lee CM, Hardy CM. Cocoa feeding and human lactose intolerance. *Am J Clin Nutr* 1989; 49 (5): 840-4.
- 55- Dehkordi N, Warren AP, Chawan CB. Lactose malabsorption as influenced by chocolate milk, skim milk, sucrose, whole milk and lactic cultures. *J Am Diet Assoc* 1995; 95(4): 484-6.
- 56- Chou TM, Benowitz NL. Caffeine and coffee: effects on health and cardiovascular disease. *Comp Biochem Physiol C Pharmacol Toxicol Endocrinol* 1994; 109(2): 173-89.
- 57- Chou T. Wake up and smell the coffee. Caffeine, coffee, and the medical consequences. *West J Med* 1992; 157(5): 544-53.
- 58- Arbeit ML, Nicklas TA, Frank GC, Webber LS, Miner MH, Berenson GS. Caffeine intakes of children from a biracial population: the Bogalusa Heart Study. *J Am Diet Assoc* 1988; 88(4): 466-71.
- 59- D'ius PB. Caffeine and children (Review article). *Vopr Pitan* 1997; (1): 39-41
- 60- Christian MS, Brent RL. Teratogen update: evaluation of the reproductive and developmental risks of caffeine. *Teratology* 2001; 64(1): 51-78.
- 61- Barone JJ, Roberts HR. Caffeine consumption. *Food chem toxicol* 1996; 34(1): 119-29.
- 62- Berdonces JL. Attention deficit and infantile hyperactivity. *Rev Enferm* 2001; 24(1): 11-4. 63- Krummel DA, Seligson FH, Guthrie HA. Hyperactivity is Candy Causal? *Crit Rev Food Sci Nutr* 1996; 36 (1-2): 31-47.
- 64- Savi L, Rainero I, Valfre W, Gentile S, Lo Giudice R, Pinessi L. Food and headache attacks. A comparison of patients with migraine and tension-type headache. *Panminerva Med* 2002; 44(1): 27-31.
- 65- Gibb CM, Davies PT, Glover V, Steiner TJ, Clifford Rose F, Sandler M. Chocolate is a migraine-provoking agent. *Cephalalgia* 1991; 11(2): 93-5.
- 66- Marcus DA. Chocolate doesn't cause headaches. *Cephalalgia* 1997; 17: 855-62.
- 67- Murphy DW, Castell DO. Chocolate and heartburn, evidence of increased esophageal acid exposure after chocolate ingestion. *Am J Gastroenterol* 1988; 83(6): 633-6.
- 68- Steinman HA, Potter PC. The precipitation of symptoms by common foods in children with a topic dermatitis. *Allergy Proc* 1994; 15(4): 203-10.
- 69- Businco L, Falconieri P, Bellioni-Businco B, Bahna SL. Severe food-induced vasculitis in two children. *Pediatr Allergy Immunol* 2002; 13(1): 68-71.
- 70- Fries JH. Chocolate: a review of published reports of allergic and other deleterious effects, real or presumed. *Ann Allergy* 1978; 41(4): 195-
- 70- Fries JH. Chocolate: a review of published reports of allergic and other deleterious effects, real or presumed. *Ann Allergy* 1978; 41(4): 195-207.
- 71- Rozin P, Levine E, Stoess C. Chocolate craving and liking. *Appetite* 1991; 17(3): 199-212.
- 72- Hetherington MM, Pirie LM, Nabb S. Stimulus satiation: effects of repeated exposure to foods on pleasantness and intake. *Appetite* 2002; 38(1): 19-28.
- 73- Hurrell RF, Reddy MB, Dassenko SA, Cook JD. Ferrous fumarate fortification of a chocolate drink powder. *Br J Nutr* 1991; 65(2): 271-83.
- 74- Davidson L, Walczyk T, Morris A, Hurrell RF. Influence of ascorbic acid on iron absorption from an iron-fortified, chocolate-flavored milk drink in Jamaican children. *Am J Clin Nutr* 1998; 67(5): 873-7