Effects of long-term administration of a cocoa polyphenolic extract (Acticoa powder) on cognitive performances in aged rats.

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Numerous studies have indicated that increased vulnerability to oxidative stress may be the main factor involved in functional declines during normal and pathological ageing, and that antioxidant agents, such as polyphenols, may improve or prevent these deficits. We examined whether 1-year administration of a cocoa polyphenolic extract (Acticoa powder), orally delivered at the dose of 24 mg/kg per d between 15 and 27 months of age, affects the onset of age-related cognitive deficits, urinary free dopamine levels and lifespan in old Wistar-Unilever rats. Acticoa powder improved cognitive performances in light extinction and water maze paradigms, increased lifespan and preserved high urinary free dopamine levels. These results suggest that Acticoa powder may be beneficial in retarding age-related brain impairments, including cognitive deficits in normal ageing and...
perhaps neurodegenerative diseases. Further studies are required to elucidate the mechanisms of cocoa polyphenols in neuroprotection and to explore their effects in man.

**American Journal of Clinical Nutrition**
January 2008; 87(1): 175-180
*(Abstract Available)*

**Chocolate consumption and bone density in older women**

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Background: Nutrition is important for the development and maintenance of bone structure and for the prevention of osteoporosis and fracture. The relation of chocolate intake with bone has yet to be investigated. Objective: We investigated the relation of chocolate consumption with measurements of whole-body and regional bone density and strength. Design: Randomly selected women aged 70–85 y (*n* = 1460) were recruited from the general population to a randomized controlled trial of calcium supplementation and fracture risk. We present here a cross-sectional analysis of 1001 of these women. Bone density and strength were measured with the use of dual-energy X-ray absorptiometry, peripheral quantitative computed tomography, and quantitative ultrasonography. Frequency of chocolate intake was assessed with the use of a questionnaire and condensed into 3 categories: <1 time/wk, 1–6 times/wk, ≥1 time/d. Results: Higher frequency of chocolate consumption was linearly related to lower bone density and strength (*P* < 0.05). Daily (≥1 times/d) consumption of chocolate, in comparison to <1 time/wk, was associated with a 3.1% lower whole-body bone density; with similarly lower bone density of the total hip, femoral neck, tibia, and heel; and with lower bone strength in the tibia and the heel (*P* < 0.05, for all). Adjustment for covariates did not influence interpretation of the results. Conclusions: Older women who consume chocolate daily had lower bone density and strength. Additional cross-sectional and longitudinal studies are needed to confirm these observations. Confirmation of these findings could have important implications for prevention of osteoporotic fracture.

**Appetite**
*(Abstract Available)*

**Repeated cue exposure effects on subjective and physiological indices of chocolate craving.**

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The aim of this study is to investigate the effects of repeated unreinforced exposure to chocolate cues in persons reporting chocolate craving. Participants in the experimental group (n=40) received 10 consecutive brief exposures to chocolate cues in each of two sessions, separated by 1-3 days. Control participants (n=18) received two exposures at the start and end of each session. Chocolate craving was measured (alternately) through subjective report and the amount of saliva secretion to chocolate cues. Results showed a between-sessions decrease in both craving measures in the experimental group, whereas no differences in craving between sessions were observed in the control group. These results provide evidence for the effects of cue exposure treatment in chocolate craving.

**Eating Behaviors**  
January 2008; 9(1): 1-12

(Abstract Available)

A multidimensional ambivalence model of chocolate craving: Construct validity and associations with chocolate consumption and disordered eating.

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This study tested the construct validity of a multidimensional ambivalence model of chocolate craving, and examined the concurrent and discriminant validity of the model with respect to chocolate consumption and disordered eating behaviors. The Orientation to Chocolate Questionnaire (OCQ) was administered to 312 university students (79.5% female) along with measures of chocolate consumption and disordered eating. Results supported a three-factor model of chocolate craving incorporating approach and avoidance inclinations and feelings of guilt. These craving dimensions differentially predicted frequency and quantity of chocolate consumption as well as a range of disordered eating behaviors. Chocolate-related guilt was a consistent indicator of dysfunctional eating patterns, but was unrelated to external or functional eating. Approach inclinations positively predicted consumption-oriented eating behaviors and negatively predicted avoidance-oriented behaviors. Active avoidance inclinations facilitated restraint and inhibited frequency of consumption, but were unrelated to quantity consumed. In line with contemporary theories of substance craving, chocolate craving can be conceptualized as a net action disposition resulting from the relative strength of the competing processes underlying indulgence and restraint.

**Molecular Nutrition & Food Research**  
January 2008; 53(1): 79-104

(Abstract Available)

Flavan-3-ols: nature, occurrence and biological activity.

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Representing the most common flavonoid consumed in the American diet, the flavan-3-ols and their polymeric condensation products, the proanthocyanidins, are regarded as

Page 3 of 24
functional ingredients in various beverages, whole and processed foods, herbal remedies and supplements. Their presence in food affects food quality parameters such as astringency, bitterness, sourness, sweetness, salivary viscosity, aroma, and color formation. The ability of flavan-3-ols to aid food functionality has also been established in terms of microbial stability, foamability, oxidative stability, and heat stability. While some foods only contain monomeric flavan-3-ols [(-)-epicatechin predominates] and dimeric proanthocyanidins, most foods contain oligomers of degree of polymerization values ranging from 1-10 or greater than 10. Flavan-3-ols have been reported to exhibit several health beneficial effects by acting as antioxidant, anticarcinogen, cardiopreventive, antimicrobial, anti-viral, and neuro-protective agents. This review summarizes the distribution and health effects of these compounds.

**Prostaglandins, Leukotrienes and Essential Fatty Acids**
January 2008; 78 (1): 81-84
(Abstract Available)

**Stearic acid potently modulates the activity of cyclooxygenase-1, but not cyclooxygenase-2, in the form of its CoA ester**

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The effects of palmitic acid (PA), stearic acid (SA) and oleic acid (OA), and their respective CoA esters, PA-CoA, SA-CoA and OA-CoA, on the activities of cyclooxygenase (COX)-1 and -2 were examined. Ten units of purified COX-1 or -2 were preincubated with drugs in the presence of hematin (0.1μM) and phenol (2mM) as cofactors for 10min at 37 degrees C, and then incubated with 100μM arachidonic acid for 2min at 37 degrees C. The amounts of prostaglandins formed were measured by HPLC. PA, SA and OA had no effect on the COX-1 and -2 activities, but their respective CoA esters, PA-CoA, SA-CoA and OA-CoA, suppressed COX-1 activity with no significant effect on COX-2 activity. The inhibitory effect of SA-CoA was much stronger than that of PA-CoA and OA-CoA.

**Predictive Relationship between Polyphenol and Nonfat Cocoa Solids Content of Chocolate**
January 9, 2008; 56(1): 206-265
(Abstract Available)

**At a Glance:**
“...NFCS is linearly related to total polyphenols. Total polyphenol content appears to be systematically slightly higher for milk chocolates than estimated by the dark chocolate model.”

**Article Type:** Antioxidant Activity/Analytical

**Funding Source:** Not Stated


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Chocolate is often labeled with percent cocoa solids content. It is assumed that higher cocoa solids contents are indicative of higher polyphenol concentrations, which have potential health benefits. However, cocoa solids include polyphenol-free cocoa butter and polyphenol-rich nonfat cocoa solids (NFCS). In this study the strength of the relationship between NFCS content (estimated by theobromine as a proxy) and polyphenol content...
was tested in chocolate samples with labeled cocoa solids contents in the range of 20-100%, grouped as dark (n = 46), milk (n = 8), and those chocolates containing inclusions such as wafers or nuts (n = 15). The relationship was calculated with regard to both total polyphenol content and individual polyphenols. In dark chocolates, NFCS is linearly related to total polyphenols (r^2 = 0.73). Total polyphenol content appears to be systematically slightly higher for milk chocolates than estimated by the dark chocolate model, whereas for chocolates containing other ingredients, the estimates fall close to or slightly below the model results. This shows that extra components such as milk, wafers, or nuts might influence the measurements of both theobromine and polyphenol contents. For each of the six main polyphenols (as well as their sum), the relationship with the estimated NFCS was much lower than for total polyphenols (r^2 < 0.40), but these relationships were independent of the nature of the chocolate type, indicating that they might still have some predictive capabilities.

Journal of Ethnopharmacol
January 17, 2008; 115(2): 238-248
(Abstract Available)

Repression of calcitonin gene-related peptide expression in trigeminal neurons by Theobroma cacao extract

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ETHNOPHARMACOLOGICAL RELEVANCE: Cocoa bean preparations were first used by the ancient Maya and Aztec civilizations of South America to treat a variety of medical ailments involving the cardiovascular, gastrointestinal, and nervous systems. Diets rich in foods containing abundant polyphenols, as found in cocoa, underlie the protective effects reported in chronic inflammatory diseases. Release of calcitonin gene-related peptide (CGRP) from trigeminal nerves promotes inflammation in peripheral tissues and nociception. AIM OF THE STUDY: To determine whether a methanol extract of Theobroma cacao L. (Sterculiaceae) beans enriched for polyphenols could inhibit CGRP expression, both in vitro and an in vivo approach was taken. RESULTS: Treatment of rat trigeminal ganglia cultures with depolarizing stimuli caused a significant increase in CGRP release that was repressed by pretreatment with Theobroma cacao extract. Pretreatment with Theobroma cacao was also shown to block the KCl- and capsaicin-stimulated increases in intracellular calcium. Next, the effects of Theobroma cacao on CGRP levels were determined using an in vivo model of temporomandibular joint (TMJ) inflammation. Capsaicin injection into the TMJ capsule caused an ipsilateral decrease in CGRP levels. Theobroma cacao extract injected into the TMJ capsule 24h prior to capsaicin treatment repressed the stimulatory effects of capsaicin. CONCLUSIONS: Our results demonstrate that Theobroma cacao extract can repress stimulated CGRP release by a mechanism that likely involves blockage of calcium channel activity. Furthermore, our findings suggest that the beneficial effects of diets rich in cocoa may include suppression of sensory trigeminal nerve activation.

British Journal of Nutrition
January 2008; 99:(1) 1-11
(Abstract Available)
Cocoa and Health: a decade of research

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It has been over 10 years since the first mention in a medical journal about cocoa and chocolate as potential sources of antioxidants for health. During this time, cocoa has been found to improve antioxidant status, reduce inflammation and correlate with reduced heart disease risk; with these results, and its popularity, it has received wide coverage in the press. However, after 10 years of research, what is known about the potential health benefits of cocoa and what are the important next steps in understanding this decadent source of antioxidants?

Mutation Research
January 2008; 650(1): 48-54
(Abstract Available)

Protection of DNA from gamma-radiation induced strand breaks by Epicatechin.

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Epicatechin (EC), a polyphenolic antioxidant compound found in tea, apples and chocolate offered protection to DNA against ionizing radiation induced damages. Under in vitro conditions of radiation exposure, plasmid pBR322 DNA was protected by EC in a concentration dependent manner. The dose modifying factor for 0.2mM EC for 50% protection of the plasmid DNA was found to be 6.0. EC when administered to mice 1h prior to exposure to 4Gy gamma-radiation protected cellular DNA against radiation-induced strand breaks in peripheral blood leukocytes, as revealed in alkaline comet assay studies. Thus, EC was found to protect DNA from gamma-radiation induced strand breaks under in vitro as well as in vivo conditions of radiation exposure.

Physiology Behavior
January 2008; 93(1-2): 235-42
(Abstract Available)

Genetic and environmental contributions to food use patterns of young adult twins.

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The contribution of genetic factors to individual differences in food use was estimated in a large population-based twin cohort of young adults (22- to 27-year-old). Male and female twins (n=2009 complete twin pairs) evaluated use-frequencies of 24 food items using 5 categories (1=never-5=several times a day) in a postal questionnaire. Foods were categorized by factor analysis. Estimates of the relative proportions of additive genetic, shared environmental, and unshared environmental effects on the use-frequency of food items and factor scores were obtained by quantitative genetic modeling of twin data based on linear structural equations. Four factors of food use were identified: "healthy" foods, high-fat foods, sweet foods, and meats. The variance of the use-frequency of food items and food categories was explained by additive genetic and unshared environmental influences, whereas shared environmental factors did not contribute to food use. The average proportions of genetic effects on the total variance of the use-frequency of food items and food categories were 40% and 45%, respectively. Sex differences were observed in the magnitude of genetic influences for use-frequency of four food items (chocolate, other sweets, fried foods, and meat), and in genetic factors underlying the use of three (fresh vegetables, fruits, and cheeses) items. In conclusion, family environment does not appear to influence the food use of young adults and thus nutritional education should be targeted at this age group to support development of healthy eating patterns. In addition, the results illuminate the importance of the sex-specific genetic effects on food use.

British Journal of Nutrition
February 2008; (In Press)
(Abstract Available)

The effects of milk as a food matrix for polyphenols on the excretion profile of cocoa (-)-epicatechin metabolites in healthy human subjects.

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The effect of different food matrices on the metabolism and excretion of polyphenols is uncertain. The objective of the study was to evaluate the possible effect of milk on the excretion of (-)-epicatechin metabolites from cocoa powder after its ingestion with and without milk. Twenty-one volunteers received the following three test meals each in a randomised cross-over design with a 1-week interval between meals: (1) 250 ml whole milk as a control; (2) 40 g cocoa powder dissolved in 250 ml whole milk (CC-M); (3) 40 g cocoa powder dissolved in 250 ml water (CC-W). Urine was collected before consumption and during the 0-6, 6-12 and 12-24 h periods after consumption. (-)-Epicatechin metabolite excretion was measured using liquid chromatography-MS. One (-)-epicatechin glucuronide and three (-)-epicatechin sulfates were detected in urine excreted after the intake of the two cocoa beverages (CC-M and CC-W). The results show that milk does not significantly affect the total amount of metabolites excreted in urine. However, differences in metabolite excretion profiles were observed; there were changes in the glucuronide and sulfate excretion rates, and the sulfation position between the period of excretion and the matrix. The matrix in which polyphenols are consumed can affect their metabolism and excretion, and this may affect their biological activity. Thus, more studies are needed to evaluate the effect of these different metabolite profiles on the body.
European Journal of Cancer Prevention
(Abstract Available)

Protective effect of Acticoa powder, a cocoa polyphenolic extract, on prostate carcinogenesis in Wistar-Unilever rats.

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The effects of Acticoa powder on prostate carcinogenesis were investigated using the N-methylnitrosourea and testosterone propionate prostate tumor model. Sixty male Wistar-Unilever rats were randomly divided in four groups of 15 rats: one control group not induced but treated with vehicle (not induced+vehicle) and three chemo-induced groups. Two weeks before prostate tumor induction and then throughout the experiment, chemo-induced rats were orally treated with Acticoa powder at 24 (chemo-induced+Acticoa powder24) or 48 (chemo-induced+Acticoa powder48) mg/kg or with vehicle (chemo-induced+vehicle), daily from Monday to Friday. Survival, body weight, food and water consumption were recorded throughout the experiment. Six rats per group were randomly killed 9 months after the prostate tumor induction for histopathological analysis of prostates. A reduction in the incidence of prostate tumors was observed for the chemo-induced+Acticoa powder48-treated group in comparison with the chemo-induced+vehicle-treated group and no tumors were observed in the chemo-induced+Acticoa powder24-treated group as in the not induced+vehicle-treated group after 9 months. The nine remaining rats per group were maintained in a long-term survival study. The life span of the chemo-induced+Acticoa powder24-treated group was significantly increased in comparison with the chemo-induced+Acticoa powder48 and the chemo-induced+vehicle-treated groups, close to the one of the not induced+vehicle-treated group. A significant reduction in the incidence of prostate tumors was also observed for the chemo-induced+Acticoa powder24 and chemo-induced+Acticoa powder48-treated groups in comparison with the chemo-induced+vehicle-treated group. In conclusion, Acticoa powder at 24 mg/kg protected rats from prostate carcinogenesis when chronically given before the initiation and promotion phases of induction.

Environmental Monitoring and Assessment
February 6, 2008; (In Press)
(Abstract Available)

Trace metal contents in chewing gums and candies marketed in Turkey.

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Cu, Ni, Pb, Fe, Mn, Cr and Cd contents were determined in 17 different brands of chewing gum and candy samples available in local markets of Kayseri, Turkey. Concentration of selected trace metals were estimated using flame atomic absorption spectrometer after dry and wet digestion methods. Out of 17 brands of chewing gums and candies analysed, four were cocoa based, two were sugar based and other were of fruit
based. Copper level ranged from 0.219 to 2.455 mug/g with an average of 1.390 mug/g. Nickel ranged from 0.120 to 2.588 mug/g with an average of 0.846 mug/g. Lead level ranged from 0.031 to 2.46 mug/g with an average of 0.746 mug/g. Iron level ranged from 3.963 to 9.863 mug/g with an average of 6.618 mug/g. Manganese level ranged from 1.872 to 5.067 mug/g with an average of 3.196 mug/g. Chromium ranged from 0.740 to 6.265 mug/g with an average of 2.473 mug/g and cadmium level ranged from 0.027 to 0.825 mug/g with an average of 0.296 mug/g. Cocoa based samples were found to have higher contents of the analysed metals than sugar and fruit based samples.

**Talanta**
February 15, 2008; 74(5): 1166-1174
(Abstract Available)

**Evaluation of solid-phase micro-extraction coupled to gas chromatography-mass spectrometry for the headspace analysis of volatile compounds in cocoa products.**


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The aroma profile of cocoa products was investigated by headspace solid-phase micro-extraction (HS-SPME) combined with gas chromatography-mass spectrometry (GC-MS). SPME fibers coated with 100 microm polydimethylsiloxane coating (PDMS), 65 microm polydimethylsiloxane/divinylbenzene coating (PDMS-DVB), 75 microm carboxen/polydimethylsiloxane coating (CAR-PDMS) and 50/30 microm divinylbenzene/carboxen on polydimethylsiloxane on a StableFlex fiber (DVB/CAR-PDMS) were evaluated. Several extraction times and temperature conditions were also tested to achieve optimum recovery. Suspensions of the samples in distilled water or in brine (25% NaCl in distilled water) were investigated to examine their effect on the composition of the headspace. The SPME fiber coated with 50/30 microm DVB/CAR-PDMS afforded the highest extraction efficiency, particularly when the samples were extracted at 60 degrees C for 15 min under dry conditions with toluene as an internal standard. Forty-five compounds were extracted and tentatively identified, most of which have previously been reported as odor-active compounds. The method developed allows sensitive and representative analysis of cocoa products with high reproducibility. Further research is ongoing to study chocolate making processes using this method for the quantitative analysis of volatile compounds contributing to the flavor/odor profile.

**European Journal of Clinical Nutrition**
February 2008; 62(2): 247-253
(Abstract Available)

**Chocolate, well-being and health among elderly men.**

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OBJECTIVE: We hypothesized that chocolate preference would be related to health and psychological well-being in old men. DESIGN, SETTING AND PARTICIPANTS: We have followed up a socio-economically homogenous group of men, born in 1919-1934, since the 1960s. In 2002-2003, a mailed questionnaire was used to assess the health and well-being (including questions related to positive life orientation, visual analogue scales and the Zung depression score) of survivors. In addition, candy preference was inquired. Those men who reported no candy consumption (n=108) were excluded from the analyses. OUTCOME MEASURES: Psychological well-being in old age. RESULTS: The response rate was 69% (1367 of 1991). Of the respondents, 860 and 399 preferred chocolate and other type of candy, respectively. The average age in both candy groups was 76 years. Of the respondents, 99% were home-dwelling, 96% were retired and 87% were presently married, without differences between the candy groups. Men preferring chocolate had lower body mass index and waist circumference, and they also reported more exercise and better subjective health (P=0.008) than other candy consumers. Variables related to psychological well-being were consistently better in those preferring chocolate. The differences were statistically significant in feeling of loneliness (P=0.01), feeling of happiness (P=0.01), having plans for the future (P=0.0002) and the Zung depression score (P=0.02). CONCLUSIONS: In this socioeconomically homogenous male cohort, chocolate preference in old age was associated with better health, optimism and better psychological well-being.

Behaviour Research and Therapy
March 2008; 46(3): 375-391
(Abstract Available)

Return of experimentally induced chocolate craving after extinction in a different context: Divergence between craving for and expecting to eat chocolate.

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Unlike in fear conditioning, little attention has been devoted to extinction and renewal in appetitive conditioning, despite its relevance for extinction-based addiction treatments. We developed a paradigm, using a specific tray as a conditioned stimulus (CS) for eating chocolate (unconditioned stimulus, US), to investigate the effects of context change on acquisition and extinction of conditioned chocolate craving using an ABA renewal design. In Study 1 (n=32), participants successfully acquired chocolate craving, but unlike what is commonly observed in fear conditioning, craving did not extinguish. In Study 2, we separately assessed craving and US expectancy in a between-subjects design (n=64). US-expectancy data showed acquisition, extinction and renewal in the ABA group. The craving data did not follow this pattern, suggesting different mechanisms for craving and US expectancy. Similarities and differences between craving and US expectancy, as well as practical implications, are discussed.

Journal of Agricultural and Food Chemistry
March 12, 2008; 56(5): 1602-1605
(Abstract Available)

Effect of Antibloom Fat Migration from a Nut Oil Filling on the Polymorphic Transformation of Cocoa Butter.
In confectionery products, loss in texture contrast between chocolate and filling and the appearance of fat bloom on the surface of the chocolate can be caused by fat migration. Bloom is often linked to the transformation of the cocoa butter beta V polymorph into beta VI. A previous study showed that small additions (1%) of nut oil can have a significant impact on the rate of transformation and that migration of nut oil from a filling would increase polymorphic transformation of cocoa butter. In the present study, antibloom fat was added to the filling in a model system. The antibloom fat migrated with the nut oil and inhibited the transformation of cocoa butter from the beta V polymorph into beta VI. Despite experiencing migration of greater amounts of nut oil, cocoa butter closest to the filling transformed more slowly than that farther away (i.e., the reverse of the situation in the absence of antibloom fat).

**Appetite**
March- May 2008; 50(2-3): 415-421

(Abstract Available)

**Resistance can be futile: Investigating behavioural rebound.**

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One hundred and thirty-four non-dieting participants spent 5min thinking aloud under three different conditions. Participants either suppressed or expressed thoughts of eating chocolate, or verbalised with no further instructions. After thinking aloud, all participants took part in a taste preference task where they tried two brands of chocolate and answered questions about their preference. Unbeknownst to participants the variable of interest was the amount of chocolate eaten, not their preference. Results indicated an interaction between condition (suppression vs. expression vs. control) and gender. Both male and female participants showed a behavioural rebound effect, consuming significantly more chocolate after suppression than participants in the verbalise only control group. However, in the expression group, a clear difference between males and females was manifested, while females ate a similar amount of chocolate in the expression and verbalise only control groups, males ate the most chocolate in the expression group and this was significantly greater than the amount eaten after suppression or the verbalise only control group.

**Appetite**
March- May 2008; 50(2-3): 499-505

(Abstract Available)

**The Attitudes to Chocolate Questionnaire: Psychometric properties and relationship to dimensions of eating.**
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The aim of the present study was to evaluate the psychometric properties of the Attitudes to Chocolate Questionnaire (ACQ). We analyzed the factor structure of the ACQ by conducting exploratory and confirmatory factor analyses in a sample of healthy adults and a sample of dietician students. Further, the relationship between the resulting ACQ factors and dimensions of eating behavior, personality, emotionality, and tests of the pleasantness, sweetness, and intensity of sugar and chocolate was examined. The results yielded a clear two-factor structure of the ACQ: The first factor (guilt) was composed of items concerning negative consequences of chocolate eating including the feeling of guilt. The second factor (craving) comprised items related to craving and emotional chocolate eating. Guilt correlated significantly with "emotional eating", "restrained eating", and with neuroticism. Craving correlated significantly with "emotional eating" and "external eating", with neuroticism, and with the "difficulty identifying feelings" facet of the Toronto Alexithymia Scale; further, it correlated highly with the average reported chocolate consumption and with the ratings of the intensity of taste of sugar. In conclusion, results support the validity of the German version of the ACQ and showed a stable factor structure and a good internal consistency.

Cardiovascular Research
March 2, 2008 (In Press)
(Abstract Available)

Cocoa Procyanidins Inhibit Expression and Activation of MMP-2 in Vascular Smooth Muscle Cells by Direct Inhibition of MEK and MT1-MMP Activities.

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Aims: Expression and activation of matrix metalloproteinase (MMP)-2 play pivotal roles in the migration and invasion of human aortic vascular smooth muscle cells (VSMC) originating from normal human tissue, which is strongly linked to atherosclerosis. The present study investigated the possible inhibitory effects of cocoa procyanidins on thrombin-induced expression and activation of MMP-2 in VSMC. Methods and results: Cocoa procyanidin fraction (CPF) and procyanidin B2, one of major procyanidins in cocoa (3 mug/ml and 3 muM, respectively), strongly inhibited thrombin-induced activation and expression of pro-MMP-2 in VSMC, as determined by zymography. The thrombin-induced invasion and migration of VSMC were inhibited by CPF or procyanidin B2 (p < 0.05), as assessed by a modified Boyden chamber and wound healing assays, respectively. An enzymatic assay data demonstrated that CPF and procyanidin B2 directly inhibited membrane type-1 (MT1)-MMP activity (p < 0.05), and this inhibition of CPF was greater than those of red wine polyphenols. Western blot data showed that CPF and procyanidin B2 inhibited thrombin-induced phosphorylation of extracellular signal-regulated protein kinase but not mitogen-activated protein kinase kinase (MEK) in VSMC. Kinase and pull-down data revealed that CPF and procyanidin B2 inhibited MEK1 activity and directly bound with glutathione-S-transferase-MEK1. In addition, the thrombin-induced invasion and migration and the activation and expression of pro-MMP-2 in
VSMC were attenuated by U0126 (a well-known inhibitor of MEK1). Conclusions: Cocoa procyanidins are potent inhibitors of MEK and MT1-MMP, and subsequently inhibit the expression and activation of pro-MMP-2, and also the invasion and migration of VSMC, which may in part explain the molecular action of antiatherosclerotic effects of cocoa.

**Archives of Biochemistry and Biophysics**
March 6, 2008; (In Press)
(Abstract Available)

**Cocoa flavanols lower vascular arginase activity in human endothelial cells in vitro and in erythrocytes in vivo.**

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The availability of l-arginine can be a rate-limiting factor for cellular NO production by nitric oxide synthases (NOS). Arginase competes with NOS for l-arginine as the common substrate. Increased arginase activity has been linked to low NO levels, and an inhibition of arginase activity has been reported to improve endothelium-dependent vasorelaxation. Based on the above, we hypothesized that an increase in the circulating NO pool following flavanol consumption could be correlated with decreased arginase activity. To test this hypothesis we (a) investigated the effects of (-)-epicatechin and its structurally related metabolites on endothelial arginase expression and activity in vitro; (b) evaluated the effects of dietary flavanol-rich cocoa on kidney arginase activity in vivo; and (c) assessed human erythrocyte arginase activity following flavanol-rich cocoa beverage consumption in a double-blind intervention study with cross-over design. The results demonstrate that cocoa flavanols lower arginase-2 mRNA expression and activity in HUVEC. Dietary intervention with flavanol-rich cocoa caused diminished arginase activity in rat kidney and, erythrocyte arginase activity was lowered in healthy humans following consumption of a high flavanol beverage in vivo.

**Archives of Biochemistry and Biophysics**
March 10, 2008
(Abstract Available)

**How do dietary flavanols improve vascular function? A position paper.**

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Epidemiological and clinical studies revealed that high-flavanol diet or isolated (-)-epicatechin improves the function of the vascular endothelium, as assessed by flow-mediated dilation, through elevation of bioavailability and bioactivity of NO(*). We have demonstrated that exposure of human endothelial cells to (-)-epicatechin elevates the cellular levels of NO(*) and cyclic GMP and protects against oxidative stress elicited by proinflammatory agonists. (-)-Epicatechin acts like a prodrug, since these effects involve O-methylation of the flavanol and are attributed to apocynin-like inhibition of endothelial...
NADPH oxidase. Thus, generation of superoxide and peroxynitrite is diminished and, consequently, the cellular NO(*) level is preserved or augmented. We propose therefore that endothelial NO(*) metabolism rather than general antioxidant activity is a major target of dietary flavanols and that NADPH oxidase activity is a crucial site of action. Moreover, flavonoid glucuronides appear to serve as plasma transport metabolites to target cells rather than solely as excretion products. Implications for the interpretation of the role of dietary polyphenols for cardiovascular health are discussed.

**Epidemiology**
March 25, 2008 (In Press)
(Abstract Available)

**Chocolate Consumption in Pregnancy and Reduced Likelihood of Preeclampsia.**

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BACKGROUND: Preeclampsia is a major pregnancy complication with cardiovascular manifestations. Recent studies suggest that chocolate consumption may benefit cardiovascular health. METHODS: We studied the association of chocolate consumption with risk of preeclampsia in a prospective cohort study of 2291 pregnant women who delivered a singleton livebirth between September 1996 and January 2000. Chocolate consumption was measured by self report in the first and third trimesters, and by umbilical cord serum concentrations of theobromine, the major methylxanthine component of chocolate. Preeclampsia was assessed by detailed medical record review for 1943 of the women. We derived adjusted odds ratios (aOR) and 95% confidence intervals (CIs) from logistic regression models controlling for potential confounders. RESULTS:: Preeclampsia developed in 3.7% (n = 63) of 1681 women. Cord serum theobromine concentrations were negatively associated with preeclampsia (aOR = 0.31; CI = 0.11-0.87 for highest compared with lowest quartile). Self-reported chocolate consumption estimates also were inversely associated with preeclampsia. Compared with women consuming under 1 serving of chocolate weekly, women consuming 5+ servings per week had decreased risk: aOR = 0.81 with consumption in the first 3 months of pregnancy (CI = 0.37-1.79) and 0.60 in the last 3 months (0.30-1.24). CONCLUSIONS: Our results suggest that chocolate consumption during pregnancy may lower risk of preeclampsia. However, reverse causality may also contribute to these findings.

**Journal of Nutrition**
March 2008; 138(3): 497-501
(Abstract Available)

Mammalian sirtuin 1 is involved in the protective action of dietary saturated fat against alcoholic fatty liver in mice.

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This study was undertaken to elucidate the mechanism underlying the protective effect of a high saturated fat (HSF) diet against the development of alcoholic fatty liver in mice. We tested the effects of a HSF diet on the ethanol-mediated increase in hepatic sterol regulatory element binding protein 1 (SREBP-1) activity. Thirty-two male mice were divided into 4 groups and fed liquid diets consisting of either a high polyunsaturated fat (40% of energy from corn oil) or a HSF (40% of energy from cocoa butter) diet with or without ethanol for 4 wk. In the ethanol-containing diets, ethanol was substituted for an equivalent amount of carbohydrate to provide 27.5% of the total energy. Control mice were pair-fed the same volume of liquid diets as the ethanol-fed mice. The HSF diet suppressed the increase in mature SREBP-1 protein and prevented increased mRNA of the SREBP-1-regulated lipogenic enzymes in the ethanol-fed mice (P < 0.05). Sirtuins 1 (SIRT1), a NAD+-dependent class III histone deacetylase, was upregulated by ethanol administration in mice fed the HSF diet (P < 0.05). The HSF diet blocked histone H3 at lysine 9 (lys9) hyperacetylation and attenuated association of acetylated histone H3-Lys9 with the promoters of mitochondrial glycerol-3-phosphate acyltransferase and stearoyl-CoA desaturase 1 in the livers of the ethanol-fed mice. These results suggest that the protective effects of HSF diet against the development of alcoholic liver steatosis may occur via regulation of the hepatic SIRT1-SREBP-1-histone H3 axis, suppressing the expression of genes encoding lipogenic enzymes and slowing the synthesis of hepatic fatty acids.

Mutation Research  
April 2, 2008; 640(1-2): 123-130  
(Abstract Available)

Cocoa procyanidins protect PC12 cells from hydrogen-peroxide-induced apoptosis by inhibiting activation of p38 MAPK and JNK.

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Oxidative stress induced by reactive oxygen species has been strongly associated with the pathogenesis of neurodegenerative disorders, including Alzheimer's disease. In this study, we investigated the possible protective effects of a cocoa procyanidin fraction (CPF) and procyanidin B2 (epicatechin-(4beta-8)-epicatechin) - a major polyphenol in cocoa - against apoptosis of PC12 rat pheochromocytoma (PC12) cells induced by hydrogen peroxide (H(2)O(2)). CPF (1 and 5muM) and procyanidin B2 (1 and 5muM) reduced PC12 cell death caused by H(2)O(2), as determined by MTT and trypan blue exclusion assays. CPF and procyanidin B2 attenuated the H(2)O(2)-induced fragmentation of nucleus and DNA in PC12 cells. Western blot data demonstrated that H(2)O(2) induced cleavage of poly(ADP-ribose)polymerase (PARP), downregulated Bcl-X(L) and Bcl-2 in PC12 cells. Pretreatment with CPF or procyanidin B2 before H(2)O(2) treatment diminished PARP cleavage and increased Bcl-X(L) and Bcl-2 expression compared with those only treated with H(2)O(2). Activation of caspase-3 by H(2)O(2) was inhibited by pretreatment with CPF or procyanidin B2. Furthermore, H(2)O(2)-induced rapid and significant phosphorylation of c-Jun N-terminal protein kinase (JNK) and p38 mitogen-activated protein kinase (MAPK), and both of these effects were attenuated by CPF or
procyanidin B2 treatment. These results suggest that the protective effects of CPF and procyanidin B2 against H(2)O(2)-induced apoptosis involve inhibiting the downregulation of Bcl-X(L) and Bcl-2 expression through blocking the activation of JNK and p38 MAPK.

Journal Agricultural Food and Chemistry
April 16, 2008 (In Press)
(Abstract Available)

At a Glance:
Flavanol content of major brands of cocoa in the Spanish market were tested. Dutching resulted in a 60% loss of mean flavanol content with epicatechin & quercetin presenting greatest losses.


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Major brands of cocoa powder products present in the Spanish market were analyzed for monomeric flavanols [(+)-catechin and (-)-epicatechin] and flavonols [quercetin-3-glucuronide, quercetin-3-glucoside (isoquercitrin), quercetin-3-arabinoside, and quercetin]. In addition, the influence of the manufacturing process of cocoa powder products, in particular, the alkalization treatment (Dutching), on the original content of these flavonoids has been studied. (-)-Epicatechin was in the range of 116.02-730.26 microg/g, whereas (+)-catechin was in the range of 81.40-447.62 microg/g in the commercial cocoa products studied. Among flavonols, quercetin-3-arabinoside and isoquercitrin were the major flavonols in the cocoa powder products studied, ranging from 2.10 to 40.33 microg/g and from 3.97 to 42.74 microg/g, respectively, followed by quercetin-3-glucuronide (0.13-9.88 microg/g) and quercetin aglycone (0.28-3.25 microg/g). To our knowledge, these results are the first quantitative data in relation to the content of individualized flavonol derivatives in commercial cocoa powder products. The alkalization treatment resulted in 60% loss of the mean total flavonoid content. Among flavanols, (-)-epicatechin presented a larger decline (67%, as a mean percentage difference) than (+)-catechin (38%), probably because of its epimerization into (-)-catechin, a less bioavailable form of catechin. A decline was also confirmed for di-, tri-, and tetrameric procyanidins. In the case of flavonols, quercetin presented the highest loss (86%), whereas quercetin-3-glucuronide, quercetin-3-arabinoside, and isoquercitrin showed a similar decrease (58, 62, and 61%, respectively). It is concluded that the large decrease found in the flavonoid content of natural cocoa powder, together with the observed change in the monomeric flavanol profile that results from the alkalization treatment, could affect the antioxidant properties and the polyphenol bioavailability of cocoa powder products.

American Journal of Clinical Nutrition
April 2008; 87(4): 872-880
(Abstract Available)

A double-blind, placebo-controlled, randomized trial of the effects of dark chocolate and cocoa on variables associated with neuropsychological functioning and cardiovascular health: clinical findings from a sample of healthy, cognitively intact older adults.

Crews, D., Harrison, D., and Wright, J.
Background: In recent years, there has been increased interest in the potential health-related benefits of antioxidant- and phytochemical-rich dark chocolate and cocoa. 

Objective: The objective of the study was to examine the short-term (6 wk) effects of dark chocolate and cocoa on variables associated with neuropsychological functioning and cardiovascular health in healthy older adults.

Design: A double-blind, placebo-controlled, fixed-dose, parallel-group clinical trial was used. Participants (n = 101) were randomly assigned to receive a 37-g dark chocolate bar and 8 ounces (237 mL) of an artificially sweetened cocoa beverage or similar placebo products each day for 6 wk.

Results: No significant group (dark chocolate and cocoa or placebo)-by-trial (baseline, midpoint, and end-of-treatment assessments) interactions were found for the neuropsychological, hematological, or blood pressure variables examined. In contrast, the midpoint and end-of-treatment mean pulse rate assessments in the dark chocolate and cocoa group were significantly higher than those at baseline and significantly higher than the midpoint and end-of-treatment rates in the control group. Results of a follow-up questionnaire item on the treatment products that participants believed they had consumed during the trial showed that more than half of the participants in both groups correctly identified the products that they had ingested during the experiment.

Conclusions: This investigation failed to support the predicted beneficial effects of short-term dark chocolate and cocoa consumption on any of the neuropsychological or cardiovascular health-related variables included in this research. Consumption of dark chocolate and cocoa was, however, associated with significantly higher pulse rates at 3- and 6-wk treatment assessments.
every 2 wk. Regular consumption of the PS-containing chocolate bar resulted in reductions of 2.0 and 5.3% in serum total and LDL cholesterol (P < 0.05), respectively. Consumption of CF also reduced systolic blood pressure at 8 wk (-5.8 mm Hg; P < 0.05). Results indicate that regular consumption of chocolate bars containing PS and CF as part of a low-fat diet may support cardiovascular health by lowering cholesterol and improving blood pressure.

**Shokuhin Eiseigaku Zasshi**
April 2008; 49(2): 111-115
(Abstract Available)

[Investigation of ochratoxin a, B and citrinin contamination in various commercial foods]

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Ochratoxin A (OTA), ochratoxin B (OTB) and citrinin (CIT) in commercial foods were simultaneously determined and confirmed with high-performance liquid chromatography (HPLC) and liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS). The samples examined were made up of cereal, fruit, coffee, and cacao products. The limits of quantification (S/N ≥ 10) of OTA, OTB and CIT were 0.1 microg/kg or less. Aflatoxins (AF), deoxynivalenol (DON) and fumonisins were also surveyed. Of 157 samples examined, 44 were contaminated with OTA at levels of 0.11 to 4.0 microg/kg. At least 2 positive samples were labeled as domestics. In most positive samples, the OTA level was low, less than 1 microg/kg. The highest incidence of OTA was observed in cacao powder (10/12), followed by instant coffee (5/7), cocoa (5/8) and raisin (6/13). OTB was found in fruit and cacao products containing relatively high levels of OTA. Co-occurrence of OTA, CIT and DON was found in cereal products, and co-occurrence of OTA and AF was found in cacao products. Approximately 30% of naturally contaminated OTA in roasted coffee bean moved into the extract solution when brewed with paper filter.

**International Journal of Obesity**
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(Abstract Available)

Effect of cocoa flavanols and exercise on cardiometabolic risk factors in overweight and obese subjects.

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Objective: Impaired endothelial function in obesity may reduce blood flow to sites of metabolism, contributing to impaired fat oxidation and insulin resistance. This study
investigated the effects of cocoa flavanols and regular exercise, interventions known to improve endothelial function, on cardiometabolic function and body composition in obese individuals.

**Design:** Overweight and obese adults were randomly assigned to high-flavanol cocoa (HF, 902 mg flavanols), HF and exercise, low-flavanol cocoa (LF, 36 mg flavanols), or LF and exercise for 12 weeks (exercise duration was 3 x 45 min per week at 75% of age-predicted maximum heart rate). Body composition was assessed by dual-energy X-ray absorptiometry at 0 and 12 weeks. Brachial artery flow-mediated dilatation (FMD), supine blood pressure (BP) and fasting plasma insulin, and glucose levels were assessed at 0, 6 and 12 weeks, respectively. Insulin sensitivity/resistance was determined using the modified homeostasis model assessment of insulin resistance (HOMA2).

**Results:** A total of 49 subjects (M=18; F=31) completed the intervention. Baseline averages were as follows: body mass index=33.5 kg/m$^2$; BP=123/76 mm Hg; HOMA2=2.4; FMD=4.3%; rate of fat oxidation during exercise=0.34 g min$^{-1}$; abdominal fat=45.7% of total abdominal mass. Compared to LF, HF increased FMD acutely (2 h post-dose) by 2.4% (P<0.01) and chronically (over 12 weeks; P<0.01) by 1.6% and reduced insulin resistance by 0.31% (P<0.05), diastolic BP by 1.6 mm Hg and mean arterial BP by 1.2 mm Hg (P<0.05), independent of exercise. Regular exercise increased fat oxidation during exercise by 0.10 g min$^{-1}$ (P<0.01) and reduced abdominal fat by 0.92% (P<0.05). Conclusion: Although HF consumption was shown to improve endothelial function, it did not enhance the effects of exercise on body fat and fat metabolism in obese subjects. However, it may be useful for reducing cardiometabolic risk factors in this population.

**Cardiology in Review**
May-June 2008; 16(3): 109-115
*(Abstract Available)*

**Flavanol-rich cocoa: a cardioprotective nutraceutical.**

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A growing number of epidemiologic studies have shown a link between the ingestion of flavonoid-rich cocoa and cardiovascular health benefits. A particular kind of flavonoid found in cocoa, namely flavan-3-ol (flavanol), has recently received more attention in this context. This review discusses the cardioprotective properties of flavanols, and the mechanisms underlying these beneficial actions.

**Journal of American College of Cardiology**
June 3, 2008; 51(22): 2141-2149
*(Abstract Available)*

**Sustained benefits in vascular function through flavanol-containing cocoa in medicated diabetic patients a double-masked, randomized, controlled trial.**

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OBJECTIVES: Our goal was to test feasibility and efficacy of a dietary intervention based on daily intake of flavanol-containing cocoa for improving vascular function of medicated diabetic patients. BACKGROUND: Even in fully medicated diabetic patients, overall prognosis is unfavorable due to deteriorated cardiovascular function. Based on epidemiological data, diets rich in flavanols are associated with a reduced cardiovascular risk. METHODS: In a feasibility study with 10 diabetic patients, we assessed vascular function as flow-mediated dilation (FMD) of the brachial artery, plasma levels of flavanol metabolites, and tolerability after an acute, single-dose ingestion of cocoa, containing increasing concentrations of flavanols (75, 371, and 963 mg). In a subsequent efficacy study, changes in vascular function in 41 medicated diabetic patients were assessed after a 30-day, thrice-daily dietary intervention with either flavanol-rich cocoa (321 mg flavanols per dose) or a nutrient-matched control (25 mg flavanols per dose). Both studies were undertaken in a randomized, double-masked fashion. Primary and secondary outcome measures included changes in FMD and plasma flavanol metabolites, respectively. RESULTS: A single ingestion of flavanol-containing cocoa was dose-dependently associated with significant acute increases in circulating flavanols and FMD (at 2 h: from 3.7 +/- 0.2% to 5.5 +/- 0.4%, p < 0.001). A 30-day, thrice-daily consumption of flavanol-containing cocoa increased baseline FMD by 30% (p < 0.0001), while acute increases of FMD upon ingestion of flavanol-containing cocoa continued to be manifest throughout the study. Treatment was well tolerated without evidence of tachyphylaxia. Endothelium-independent responses, blood pressure, heart rate, and glycemic control were unaffected. CONCLUSIONS: Diets rich in flavanols reverse vascular dysfunction in diabetes, highlighting therapeutic potentials in cardiovascular disease.

Asia Pacific Journal of Clinical Nutrition
2008; 17 Suppl 1: 284-287
(Article Available)

Effects of cocoa flavanols on risk factors for cardiovascular disease.

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Epidemiologic investigations support the hypothesis that regular consumption of flavonoid-containing foods can reduce the risk of cardiovascular diseases (CVD). While flavonoids are ubiquitous in plants, cocoa can be particularly rich in a sub-class of flavonoids known as flavanols. A number of human dietary intervention trials with flavanol-containing cocoa products have demonstrated improvements in endothelial and platelet function, as well as blood pressure. These studies provide direct evidence for the potential cardiovascular benefits of flavanol-containing foods and help to substantiate the epidemiological data. In this review, results from selective published trials with cocoa and chocolate focused on risk for CVD will be discussed along with a study we recently completed evaluating the effects of the daily consumption of flavanol-containing dark chocolate (CocoaVia?) with and without plant sterol esters on CVD markers in a normotensive population with mild hypercholesterolemia. In this study, the daily consumption of flavanol-containing dark chocolate was associated with a significant mean reduction of 5.8 mmHg in systolic blood pressure. Together the results of these human dietary intervention trials provide scientific evidence of the vascular effects of cocoa flavanols and suggest that the regular consumption of cocoa products containing flavanols may reduce risk of CVD.
Asia Pacific Journal of Clinical Nutrition
2008; 17 Suppl 1: 280-283
(Article Available)

Cocoa flavanols - measurement, bioavailability and bioactivity.

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There has been growing interest in the potential cardiovascular benefits associated with cocoa consumption. As a result of accurate analytical methodologies, there is evidence to support that the flavanols in cocoa can be absorbed, are bioactive, and may be responsible for the cardiovascular benefits associated with regular cocoa consumption. The flavanols in cocoa exist in a multitude of different stereochemical configurations, thus giving rise to a unique and complex mixture of compounds. Given this complexity, the quantitative analysis of cocoa flavanols in foods can be challenging. While there are published methods suitable for the analysis of these compounds, these methods require sophisticated instrumentation and can be challenging to set up. As such, simpler techniques that measure such things as total phenolic content or antioxidant potential have been used as indicators of flavanol content. However, as these simpler assays are prone to interferences and are not specific for flavanols, these methods are not appropriate for use in studies that aim to examine the physiological effects of cocoa flavanols. It is only through the use of methods that can accurately quantify these flavanols that it will be possible to make meaningful dietary recommendations regarding the consumption of cocoa flavanol containing foods.

International Journal of Immunopathology & Pharmacology
(Abstract Available)

Cacao liquor proanthocyanidins inhibit lung injury induced by diesel exhaust particles


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Epidemiological and experimental studies have suggested that diesel exhaust particles (DEPs), which generate reactive oxygen species, may be involved in the recent increase in the prevalence of lung diseases. Cacao liquor proanthocyanidins (CPs) are naturally occurring polyphenols with antioxidative activities. We carried out a study in mice to investigate the effects of dietary supplementation of CPs on lung injury induced by intratracheal administration of DEPs (500 microg/body). Dietary supplementation with 1.0 percent CPs inhibited DEP-induced lung injury, characterized by neutrophil sequestration and edema. Immunohistochemical analyses showed that CPs prevented enhanced expression of vascular cell adhesion molecule-1 and intercellular adhesion molecule-1 caused by DEPs in the lung injury. Numerous adducts of nitrotyrosine, N-(hexanonyl) lysine, 4-hydroxy-2-nonenal, and 8-OHdG were also observed immunohistochemically in the lungs of mice treated with DEPs. However, these indicators of oxidative stress were
barely visible in mice pretreated with CP supplementation. In addition, the level of thiobarbituric acid reactive substances in the lung was decreased by CP supplementation in the presence of DEPs. These results suggest that CPs inhibit DEP-induced lung injury by reducing oxidative stress, in association with a reduction in the expression of adhesion molecules.

Journal of Biological Chemistry
June 2, 2008 (In Press)
(Abstract Available)

Cocoa procyanidins suppress transformation by inhibiting mitogen-activated protein kinase kinase.


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Cocoa was shown to inhibit chemically-induced carcinogenesis in animals and exert antioxidant activity in humans. However, the molecular mechanisms of the chemopreventive potential of cocoa and its active ingredient(s) remain unknown. Here we report that cocoa procyanidins inhibit neoplastic cell transformation by suppressing the kinase activity of mitogen-activated protein kinase kinase (MEK). A cocoa procyanidin fraction (CPF) and procyanidin B2 at 5 microg/ml and 40 microM, respectively, inhibited 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced neoplastic transformation of JB6 P+ mouse epidermal (JB6 P+) cells by 47% and 93%, respectively. The TPA-induced promoter activity and expression of cyclooxygenase-2 (COX-2), which is involved in tumor promotion and inflammation, were dose-dependently inhibited by CPF or procyanidin B2. The activation of activator protein (AP)-1 and nuclear factor (NF)-B induced by TPA was also attenuated by CPF or procyanidin B2. The TPA-induced phosphorylation of MEK, extracellular signal-regulated kinase, and p90 ribosomal s6 kinase was suppressed by CPF or procyanidin B2. In vitro and ex vivo kinase assay data demonstrated that CPF or procyanidin B2 inhibited the kinase activity of MEK1 and directly bound with MEK1. CPF or procyanidin B2 suppressed JB6 P+ cell transformation induced by epidermal growth factor or H-Ras, both of which are known to be involved in MEK/ERK signal activation. In contrast, theobromine (up to 80 microM) had no effect on TPA-induced transformation, COX-2 expression, the transactivation of AP-1 or NF-B, or MEK. Notably, procyanidin B2 exerted stronger inhibitory effects compared to PD098059 (a well-known pharmacological inhibitor of MEK) on MEK1 activity and neoplastic cell transformation.

Age & Ageing
June 5, 2008 (In Press)

Chocolate-induced prolonged angioedema in an elderly patient.

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This report presents a 93-year-old woman with prolonged angioedema associated with diabetic chocolate and chronic angiotensin-converting enzyme inhibitor use.
Expectancy for food or expectancy for chocolate reveals timing systems for metabolism and reward

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The clock gene protein Per 1 (PER1) is expressed in several brain structures and oscillates associated with the suprachiasmatic nucleus (SCN). Restricted feeding schedules (RFS) induce anticipatory activity and impose daily oscillations of c-Fos and clock proteins in brain structures. Daily access to a palatable treat (chocolate) also elicits anticipatory activity and induces c-Fos expression mainly in corticolimbic structures. Here the influence of daily access to food or chocolate was explored by the analysis of the oscillatory patterns of PER1 in hypothalamic and corticolimbic structures. Wistar rats were exposed to RFS or to daily access to chocolate for 3 weeks. Persistence of food or chocolate entrained rhythms was determined 8 days after cessation of the feeding protocols. RFS and chocolate induced a phase shift in PER1 rhythmicity in corticolimbic structures with peak values at zeitgeber time 12 and a higher amplitude in the chocolate group. Both RFS and chocolate groups showed an upregulation of PER1 in the SCN. Food and chocolate entrained rhythms persisted for 8 days in behavior and in PER1 expression in the dorsomedial hypothalamic nucleus, accumbens, prefrontal cortex and central amygdala. The present data demonstrate the existence of different oscillatory systems in the brain that can be activated by entrainment to metabolic stimuli or to reward and suggest the participation of PER1 in both entraining pathways. Persistence and amplification of PER1 oscillations in structures associated with reward suggest that this oscillatory process is fundamental to food addictive behavior.

At a Glance:
Chocolate is used to evaluate the role of the clock gene protein per 1 oscillations in food addictive behavior.

Neuroscience
(Abstract Available)

At a Glance:
Chocolate is used to evaluate the role of the clock gene protein per 1 oscillations in food addictive behavior.

Article Type: Behavioral
Funding Source: Not Stated

Journal of Physiology Heart and Circulatory Physiology
(Abstract Available)

Short and Long Term Effects of (-)-Epicatechin on Myocardial Ischemia Reperfusion Injury.

Yamazaki, K., Romero-Perez, D., Barraza-Hidalgo, M., Cruz, M., Cortez-Gomez, B., Rivas, M., Ceballos, G., Villarreal, F.
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Epidemiological studies have shown a correlation between flavonoid-rich diets and improved cardiovascular prognosis. Cocoa contains large amounts of flavonoids, in particular flavanols (mostly catechins and epicatechins). Flavonoids possess pleiotropic properties that may confer protective effects to tissues during injury. We examined the ability of epicatechin to reduce short and long-term ischemia reperfusion (IR) myocardial injury. Epicatechin (1mg/kg/day) pre-treatment (Tx) was administered daily via oral gavage to male rats for 2 or 10 days. Controls received water. Ischemia was induced via a

At a Glance:
Chocolate is used to evaluate the role of the clock gene protein per 1 oscillations in food addictive behavior.

Article Type: Cardiovascular Health
Funding Source: Not Stated
45 min coronary occlusion. Reperfusion was allowed until 48 h or 3 weeks while Tx continued. We measured infarct (MI) size (%), hemodynamics, myeloperoxidase (MPO) activity, tissue oxidative stress, and matrix metalloproteinase-9 (MMP-9) activity in 48 h groups. Cardiac morphometry was also evaluated in 3 week groups. With 2 days of Tx, no reductions in MI size occurred. After 10 days, a significant ~50% reduction in MI size occurred. Epicatechin rats demonstrated no significant changes in hemodynamics. Tissue oxidative stress was significantly reduced in the epicatechin group vs. controls. MMP-9 activity demonstrated limited increases in the infarct region with epicatechin. By 3 weeks, a significant 32% reduction in infarct size was observed with Tx, accompanied with sustained hemodynamics and preserved chamber morphometry. In conclusion, epicatechin Tx confers cardioprotection in the setting of IR injury. The effects are independent of changes in hemodynamics, are sustained over time, and are accompanied by reduced levels of indicators of tissue injury. Results warrant the evaluation of cocoa flavanols as possible therapeutic agents to limit ischemic injury.

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Chocolate mouth rinse: Effect on plaque accumulation and mutans streptococci counts when used by children.

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Background: Glucosyltransferases (GTF) play an important role in the adherence of bacteria to acquired pellicle. Cocoa bean husk extract (CBHE) has been shown to possess anti-glucosyltransferase and antibacterial activity. Aim: This study aimed to evaluate the effect of CBHE on plaque accumulation and mutans streptococcus count when used as a mouth rinse by children. Materials and Methods: Scaling of the teeth of the selected children was done and the children were instructed to refrain from their routine oral hygiene practices till the morning of the fourth day; they were instead given a placebo mouth rinse for use during this period. On the fourth day, saliva was collected from each subject for microbiological analysis and plaque was disclosed and scored using the modified Quigley and Hein plaque index; later, the teeth were cleaned. After 1 week, scaling of the subjects was done and they were given CBHE mouth rinse to rinse their mouth, following the above protocol. The data was statistically analyzed using Wilcoxon's signed rank test. Results: There was a 20.9% decrease in mutans streptococci counts and a 49.6% decrease in plaque scores in the CBHE group as compared to the placebo group, which was highly significant (P value Conclusion: CBHE is highly effective in reducing mutans streptococci counts and plaque deposition when used as a mouth rinse by children.