

# CAFFEINE IN TEA *CAMELLIA SINENSIS* – CONTENT, ABSORPTION, BENEFITS AND RISKS OF CONSUMPTION

A. GRAMZA-MICHAŁOWSKA

Corresponding author: Faculty of Food Science and Nutrition, Poznań University of Life Sciences, Wojska Polskiego 31, 60-624 Poznań, Poland, Tel. +48(61)8487331, Fax +48(61)8487430, E-mail: angramza@up.poznan.pl

**Abstract:** Therapeutic properties of tea *Camellia sinensis* are of particular interest since it has been consumed for ages and was always regarded as safe beverage. Tea is most popular beverage in the world because of its attractive aroma, exceptional taste, health promoting and pharmaceutical potential. Current results showed that antioxidative, antibacterial and other health effects are attributed to its caffeine content and caffeine – polyphenols interactions. An overview is given on caffeine content in different tea leaves beverage. Special attention is drawn to caffeine physiological effect on human organism. Controversies concerning the possible caffeine influence on human physical and psychological health are briefly summarized and presented.

**Key words:** Tea, *Camellia sinensis*, caffeine, health effect, physiological effect, thermogenesis, health risk.

## Introduction

Therapeutic properties of tea *Camellia sinensis* are of particular interest since it has been consumed for ages and was always regarded as safe beverage. Tea is most popular beverage in the world because of its attractive aroma, exceptional taste, health promoting and pharmaceutical potential. Recent research proved that bioactive value of tea is related to its antioxidative properties, playing protective role against free radical mediated diseases, mentioning cardiovascular diseases, cancer and Alzheimer's disease (44, 69, 97, 100, 104, 117). Current results showed that antioxidative, antibacterial and other health effects are attributed to its caffeine content and caffeine – polyphenols interactions (30). Dullo et al. (33) indicated that green tea rich in both catechin and caffeine are more effective sympathetically mediated thermogenesis potentiators than caffeine itself, therefore allowing better obesity management.

The aim of this paper is to provide information on the caffeine content in different tea leaves beverage. Special attention is drawn to caffeine physiological effect on human organism, its benefits and risk of consumption.

## Caffeine in tea

Tea leaves (*Camellia sinensis* L.) are rich in constituents that contribute to the majority of its health benefits (42, 43). Major tea constituents are catechins, alkaloids however are one of formative tea quality factors including: caffeine, theophylline and theobromine (103). Caffeine, was firstly discovered in coffee, however similar component isolated from tea leaves was named theine (23). Chemical composition of tea leaves and their infusion depends on such essential factors like tea cultivar, species of tea shrub or tree, season of collecting, leaves age, climate, geochemical composition of the soil and cultivating method, environmental pollution, drying conditions and technological production processes (35, 111). Because brewing techniques do vary according to cultural customs all

around the world it is very difficult to estimate the caffeine intake from tea or coffee. Main consequences of tea fermentation process are gradual lowering of catechins level in tea leaves and gallic acid content increasing (102), however the content of alkaloids becomes altered to a small degree (103). Theaflavins and thearubigins levels decrease also gradually, while the level of caffeine increases in the process of 85 % fermentation from 8,69 to 16,03 mg / 100mg of leaf dry weight (72).

Muthumani and Kumar examined tea leaves fermentation time on the caffeine concentration and found that it remained unchanged during 15 - 180 minutes of the process (82). Next to polyphenols, methylxanthines are very important biologically active compounds, where caffeine is major component of tea beverage. Horzic et al. evaluated the caffeine content in different teas extracted with use of household conditions (water temperature ranged from 80 - 100°C). Results showed increased caffeine content in following order: oolong tea (156 mg/l) < black tea (184 mg/l) < white tea (198 mg/l) < green tea (297 mg/l) (55). Second brewing resulted in 50% lower caffeine content than in the first brew, third brew lead to further 50% caffeine content decrease. No caffeine was found in herbal teas of linden and chamomile.

There are many investigations on catechins and caffeine quantities extracted during brewing of tea leaves. Chen, Shi and Chen studied the influence of temperature and time of extraction on oolong tea brewing composition (22). Results showed considerable chemical composition changes with increase in the pH of tea leaves infusion. A significant decrease of theaflavins and catechins (EGCG, ECG and EGC) content was noted. However, the increase in caffeine, gallic acid and epicatechins content was observed. The rise in caffeine content was linked with disintegration of the caffeine – theaflavins aggregate, as a result of alkaline medium influence (70). Caffeine higher content however was found in fermented teas: up to 4,8 % of dry weight and about 3,8% in green tea (35). Results of Cloughley (26) showed that caffeine decomplexation

## CAFFEINE IN TEA *CAMELLIA SINENSIS* – CONTENT, ABSORPTION, BENEFITS AND RISKS OF CONSUMPTION

from theaflavins as the latter decrease, and extractable caffeine levels increase with the storage time. It was stated that the differences in substance levels result from tea kind and leaf structure, influencing further leaching kinetics (65). Results of Yang, Hwang and Lin showed that higher caffeine amounts could be released from bag teas as hotter water was used (119). It was also found that caffeine in tea infused with cold water also increased with increasing duration. Jaganyi and Ndlovu (58) showed that caffeine infusion rate from tea leaves increased significantly with an increase in tea bag size. It was also found that the tea bag membrane offered some hindrance to caffeine infusion. Yao et al. (120) examined tea constituents of teas in Australian and international markets and found that tea leaves contained slightly higher or similar amounts of caffeine than tea bags. Black and green tea leaves consisted of 3,89 and 3,71% of caffeine respectively, respective ranges for tea bags were similar. It was found that lower caffeine content in Australian teas due to late harvesting of more mature leaves than those of imported ones (90). Results of Owuor and Chavanji (89) showed that changing caffeine content due to the tea leaves maturity (differences from 20 - 40%), and it is higher in young leaves than older ones. Also tea form (leaves or bags) had significant influence on caffeine extraction level. It was found that caffeine was extracted in stable amounts from tea leaves, variably however from tea bags due to tea bags paper quality affecting beverage quality (120). Other factor influencing caffeine extraction was found to be water temperature. Lin, Liu and Mau (73) found that hot water was more effective in extracting caffeine than cold water, also higher ratios of tea leaves to water extracted more caffeine than lower ratios. Similarly to caffeine also tea catechins were extracted in higher amounts in hot water.

Tea contains more caffeine than coffee, but brewing process dilutes tea more than coffee, resulting in 30% less caffeine per cup (10). The caffeine contents are differentiated according to tea kind. It was found that with increase in fermentation step also the caffeine content in brewing increases (74). Fully fermented black tea has the highest caffeine content, white and green teas however, are not fermented and they contain lower levels of caffeine. Hilal and Engelhardt (53) evaluated caffeine content in different fermentation degree tea leaves and showed, that white tea contained nearly two times higher level of caffeine than green tea and 30% higher level than black tea. Also the brewing method is a very important factor. Broken leaves have higher caffeine yield than the whole ones. Also brewing temperature and time influences the caffeine content (41). The results of Astill et al. study show that the variety, growing environment, manufacturing conditions, and grade of tea leaf influence final infusion compositions (6). Major determinant of tea beverages component concentrations was the preparation method, including the amounts of tea and water used, infusion time, and amount of agitation.

Wang, Hu, Wan and Pan (112) showed that the caffeine content in tea leaves increased reasonably after treating with

microorganisms (orthodox pile-fermentation), and the amount of caffeine content increase varied significantly between black and green teas (27.57% and 86.41%). The authors suggested that caffeine content changes in tea leaves during the pile-fermentation depended on the growth and reproduction of microorganisms, as well as on the tea composition.

Caffeine is widely consumed nervous system stimulant, although it is occurring naturally in some foods it is also used as food additive or drug and pharmaceuticals components. Consumption of caffeine occurs in a variety forms like tea beverage, coffee, mate, cocoa products, cola nuts, energy drinks and pain relief or slimming products (5).

Barone and Roberts (9) have suggested average caffeine consumption varying from 2,4 mg/kg in North America to 7,0 mg/kg in Scandinavia, and daily caffeine intake of 4 mg/kg body weight for U.S. adult consumers, and 1 mg/kg for children younger than 18 years of age. Today's youth major sources of caffeine became energy drinks, similar to soft drinks except large amounts of stimulant drugs in addition to caffeine (content range from 30mg/250mL to 150 mg/250 mL) (107). Chou and Bell (24) have investigated the caffeine content in USA beverages from different stores and found, that most store-brand carbonated beverages contained less caffeine than their national-brand counterparts.

### Absorption and metabolism of caffeine

Caffeine consumed with beverages is absorbed rapidly from the gastrointestinal tract and distributed throughout all body organs in proportion to body water (71). More rapid consumption is with oral mucosa, achieved by chewing caffeine containing products. It was found, that absorption mainly goes by small intestine, although approximately 90% of caffeine is absorbed from stomach within 20 minutes, with peak plasma concentrations occurring an hour later (25, 76). Caffeine is eliminated through liver biotransformation to dimethylxanthines, dimethyl and monomethyl uric acids, trimethyl and dimethylallantoin and uracil derivatives (4). Transformation of caffeine occurs in liver microsomes, excluding the C-8 oxidation of 1-methylxanthine into 1-methyluric acid, mediated by the xanthine oxidase (3).

According to Busto et al. (18) mean caffeine half-life in human plasma is 5 hours, however total plasma clearance is estimated to be 0,078 L/h/kg. Variations in caffeine absorption could be influenced by administration route, form, and the presence of other dietary constituents, including fiber, also by smoking and consumer's age (3, 48, 57). Consumed caffeine is absorbed by no hepatic effect, as evidenced no differences in plasma concentration after oral or intravenous administration had been found. Caffeine binds reversibly with proteins of plasma. The distribution volume within the body suggests its hydrophilic orientation, freely distributed into intracellular tissue (3). Caffeine is rapidly absorbed throughout body water; however it is also sufficiently lipophilic to pass through

biological membranes and therefore crossing the blood – brain barrier (57). Renal tubules readily reabsorb caffeine, which is why after glomerulus's filtration only percentage is unchanged excreted in urine. Caffeine limited appearance indicates that its metabolism is rate limiting factor in the plasma clearance (4).

Caffeine metabolism primary occurs in the liver, through N-methylation, acetylation and oxidation catalyzed by hepatic microsomal enzyme systems (45). Major enzyme responsible for the caffeine N-methylation leading to paraxanthine is CYP450-1A2 isosyme. Caffeine acetylation is genetically controlled by an autosomal dominant gene, leading to slow clearance and higher blood levels (105). Moffat et al., (79) results showed that caffeine is excreted in the urine within 48 hours, with only 1% as unchanged drug. It was found that repeated caffeine ingestion does not alter its absorption or metabolism (38). The primary metabolism route is 3-ethyl demethylation, accounting to 75-80 percent of caffeine and involves cytochrome P4501A2 (4). Dominant metabolite in human body is paraxanthine, rising in plasma to concentration 10 x higher than of theophiline and theobromine. Caffeine is actually cleared faster than paraxanthine. Fact, that human organism converts caffeine into paraxanthine with no apparent toxic effect suggests paraxanthine's low toxicological potency (108, 109). Paraxanthine formation and its excretion in the urine is to be major caffeine metabolism pathway. Hetzler et al. (51) found that paraxanthine is an equipotent adenosine antagonist to caffeine in vitro. Other research demonstrated that both significantly increased diastolic blood pressure, plasma epinephrine and free fatty acids (13). Extent conversion of caffeine to paraxanthine would be a factor in determining individual response to caffeine.

### **Physiological effect of tea**

Food and beverages amounts of caffeine administration have measurable impact on human performance in wide range of physiological effects. Most common of caffeine ingestion effects are cardiovascular and renal, others like memory, alertness and cognitive performances are also well known (52). Human cognitive functions after caffeine consumption are performed via several mechanisms. Most significant mechanisms are: antagonism of adenosine receptors and phosphodiesterases inhibition, respecting physiological and behavioral effect. Other mechanisms like calcium release from intracellular stores and antagonism of benzodiazepine receptors are also very important (83). A number of studies have demonstrated that caffeine enhances cognitive performance independent of its ability to reverse symptoms of withdrawal and sleep deprivation (57).

Ferre et al. (36) found that caffeine appears to stimulate synthesis and release of catecholamines like noradrenaline, as well as enhance the actions of dopamine agonists. It was suggested that those interactions could explain the stimulant caffeine effect, perhaps clarifying self-mutilation behavior such

as found in Lesh-Nyhan syndrome and possible lower incidence of Parkinson's disease related to caffeine consumption (99). It was also noted that caffeine suppresses REM sleep and decreases total sleep time, in a opposition to adenosine (96). El Yacoubi and coworkers (34) have shown to reduce the ethanol-induced hypnotic effects in mammals caused by adenosine A2A receptors activation. It was found that caffeine dose dependent kinetics has been shown even after very low doses consumption (29). Kerr et al. (63) found that cigarettes and caffeine facilitated memory and motor function in a variety of psychomotor tasks. No significant caffeine effect was found across phases of menstrual cycle in healthy, nonsmoking women (60), decreased caffeine metabolic rate however was noticed in healthy postmenopausal women on estrogen replacement therapy (95). It is also proved that oral contraceptive use could double the caffeine half-life (1).

It was proven that caffeine reduced reaction time and enhanced the accuracy on vigilance tasks in dose dependent manner. Research results showed that the effective caffeine dose varies from individuals and other factors like time, caffeine consumption habits and body relaxation (85). It was proven that caffeine stimulates central nervous system, is a diuretic, accelerates extraction of toxic substances from organism and stimulates myocardium (54, 92, 118). However, is not accumulated in organism and few hours are needed to remove it after consumption (40). Reasonable caffeine consumption does not cause growth of heart disease incidence, and consumption of 3-4 cups of tea leaves infusion daily is considered as safe (84).

Summarizing, pharmacological impacts of caffeine include stimulation, intellectual activity sustainment and reaction time decrease. The maximum caffeine oral dose for human was evaluated as approximately 150-200 mg/kg of body weight (57). High doses of caffeine cause convulsions and vomiting, with complete recovery in six hours, other effects are nervousness, irritability and restlessness. Several controlled trials have examined the effect of caffeine on serum glucose and insulin levels. Results showed that acute administration of caffeine could impair glucose tolerance and decrease insulin sensitivity (62, 93).

### **Caffeine and behavior**

Caffeine is well known for its stimulant properties, being constituent of beverages, foods and plenty of drugs available on the market. It is the most widely consumed of psychotropic drugs (12), however its popularity is attributed to its stimulant effects and slowing habituation (28). Increased scientific attention was directed on caffeine because of its detrimental physiological (cardiovascular function) and psychological effects (cafeinism) (75, 94). However, the health risk of moderate caffeine consumption is relatively small (50). It was found that caffeine withdrawal is followed by clear physiological changes like headaches. It is a result of high

## CAFFEINE IN TEA *CAMELLIA SINENSIS* – CONTENT, ABSORPTION, BENEFITS AND RISKS OF CONSUMPTION

caffeine consumption, meeting the criteria for typical psychoactive substance of dependence, manifested by drug-seeking behavior born in mind (46). Caffeine effect on human health is mainly based on arousal effect on cardiovascular system (11, 61), heart rate variability (121), ischemic stroke as a result of arrhythmias (77), arterial stiffness, further elevating the arterial pressure (110), and miscarriages (39). Besides the bad caffeine influence there are results of its beneficial impact. It may have ergogenic effect on exercise (16, 78). It is also improving the duration, performance and perception of exercise in young and elderly people (88).

Several mechanisms of action have been proposed for the caffeine properties. Action mechanism has been attempted in many types of cells, including cardiac muscle, hepatocytes, tracheal cells (47) and skeletal muscle cells (15). Well known mechanism of caffeine action is the release of ACh from neuronal cells. Other discoveries involved the mobilization of intracellular calcium (56, 101), phosphodiesterase inhibition (17), and antagonism of benzodiazepine and adenosine receptors (113). Caffeine is neurotransmission modulator, which action can be characterized by effects on presynaptic and postsynaptic receptors, release and turn-over of neurotransmitters (83). Caffeine affects a range of neurotransmitters like acetylcholine (21), serotonin (49), catecholamines (8) and amino acids (27).

It was found that caffeine has strong impact on cerebral energy metabolism and blood flow (86, 87). From the other research it is known that high caffeine consumption (250 mg) leads to fatigue decreasing, sleepiness, drowsiness, this same time also increased alertness or more vigor, but caffeine could also have beneficial effect on performance and reflect faster encoding of new information (106). It was found that caffeine helps to improve the performance of high impulsives (presumably less aroused persons in the morning) (98). Also the caffeine overdose cases have been reported (64). Although caffeine intoxications are rare, they prove the toxic potential of this common constituent, resulting the tachycardia, atrial arrhythmias, convulsions or even coma (19). Caffeine toxic effect is increased when taken with other medicines, because it is metabolized through the cytochrome P450 system – primarily by the isoenzyme CYP1A2. This enzyme is inhibited also by antipsychotics and antiarrhythmic drugs, which could become toxic in presence of caffeine (20). Research on caffeine interactions with alcohol and nicotine did not show significant results (116).

### Thermogenesis and caffeine

Scientists suggest that tea components may promote body weight and fat loss by thermogenesis stimulation (2, 14, 32, 67). First thermogenic effect of green tea was attributed to its caffeine content (7). Alkaloids such as caffeine inhibit phosphodiesterases resulting in an increased and more sustained effect of norepinephrine on thermogenesis (31).

Research on tea and weight loss suggests that higher thermogenic effect is generally attributed to caffeine content (33). It was found that individuals, consuming the tea extract containing 90 mg EGCG, three times daily, burned 266 kcal per day more than the group without addition of catechins. However caffeine ingested in equivalent amount that is found in green tea did not show significantly higher energy expenditure, suggesting that thermogenic properties of tea may be due to interactions between caffeine and polyphenols. It was reported that green tea extract stimulates brown adipose tissue thermogenesis to a much greater extent than that which can be attributed to its caffeine content per se in rats (33). Muroyama and coworkers (80, 81) used mixture of thiamine, arginine, caffeine and citric acid to monitor the anti-obesity effect in non-insulin dependent diabetic mice and lipid metabolism in healthy subjects and found reduced adipose tissue mass and disorders in lipid metabolism.

The relative importance of the mechanisms by which caffeine exerts its various effects is not fully clarified (115). Other research suggests that the metabolic response to caffeine may result from an effect on adipocyte phosphodiesterase and lipolysis, independently of catecholamines. Long-term research showed no caffeine influence on energy expenditure in caffeinated compared to decaffeinated coffee consumption (91). Thus caffeine may influence both energy expenditure and energy intake (115). Tea extract showed also strong inhibition of lipases "in vitro", causing reduced triacylglycerols lipolysis (59).

### Potential health risks of caffeine

Tea beverage is generally considered as safe for human, however epidemiological research have raised concerns about association between health and continued consumption of caffeine. Cross sectional study investigated the link between tea and coffee consumption, and serum uric acid level. Results showed an inverse association in coffee, no association was found with tea consumption (66). These findings were in agreement with results of Choi and Curhan (23), who showed no significant association between tea consumption with lower serum uric acid level and hyperuricemia frequency, suggesting associations via components other than caffeine. Results of many researchers have proven that caffeine is major factor influencing heart and cardiovascular activity. It was suggested that occasional caffeine consumption will have stronger impact on hypertension of individuals who do not consume caffeine routinely at this same dose level. Other research showed caffeine influence on reproduction, it was suggested that caffeine causes menstrual cycle shortening, delayed implantation, spontaneous abortion, low infant birth weight, premature birth and congenital malformations. Human studies research suggests a correlation between caffeine and teratogenicity, which might be explained by confounding factors such as cigarette smoking and alcohol drinking (37).



Caffeine is playing major part in fluid homeostasis, as it is a well-known diuretic. However the risk of water deficit might be increased in high (desert) or very low temperature conditions (57). Concerning caffeine behavioral influence, it was suggested that caffeine plays role in adverse affecting of mental performance and decrement of mental functions. Caffeine could be preventing factor in senile dementia. It was proven, that tea caffeine can improve memory, thinking, judgment and ability to learn from the experience (68). Other research suggested that caffeine possibly alters the degree of responsiveness of stressors to stressful stimuli, varying according to previous caffeine consumption (57).

## Conclusion

Considering tea bioactive compound such as caffeine, which among food ingredients that are not nutritive, has potentially high impact on human organism. In conclusion, present review shows that tea beverage caffeine has significant physiological abilities, like to increase alertness, energy, mental fatigue, but also rejuvenates human body. The ability to scavenge reactive oxygen species showed new promising light for research on tea beverage caffeine application as a significant biological activity constituent.

**Acknowledgment:** The Faculty of Land and Food Systems, University of British Columbia, Vancouver, Canada and EU project POIG 01.01.02-00-061/09 support is gratefully acknowledged. No conflict of interest related to the content of the guidelines was detected.

## References

- Abernethy D R, Todd EL (1985) Impairment of caffeine clearance by chronic use of low-dose oestrogen-containing oral contraceptives. *Eur J Clin Pharmacol* 28:425-428.
- Acheson KJ, Gremaud G, Meirim I, Montigon F, Krebs Y, Fay LB, Gay LJ, Schneider P, Schindler C, Tappy L (2004) Metabolic effects of caffeine in humans: lipid oxidation or futile cycling? *Am J Clin Nutr* 79(1):40-46.
- Arnaud MJ (1987) The pharmacology of caffeine. *Progress in Drug Research* 31:273-313.
- Arnaud MJ (1993) Metabolism of caffeine and other components of coffee. In S. Garattini (Ed.), *Caffeine, coffee, and health* (pp. 43-96). Raven Press, New York.
- Ashihara H, Crozier A (2001) Caffeine: A well known but little mentioned compound in plant science. *Trends Plant Sci* 6:407-413.
- Astill C, Birch MR, Dacombe C, Humphrey PG, Martin PT (2001) Factors Affecting the Caffeine and Polyphenol Contents of Black and Green Tea Infusions. *J Agric Food Chem* 49:5340-5347.
- Astrup A, Toubro S, Cannon S, Hein P, Breum L, Madsen J (1990) Caffeine: a double-blind, placebo-controlled study of its thermogenic, metabolic, and cardiovascular effects in healthy volunteers. *Am J Clin Nutr* 51(5):759-767.
- Atkinson J, Enslen M (1976) Self-administration of caffeine by the rat. *Arzneimittelforsch* 26:2059.
- Barone JJ, Roberts HR (1996) Caffeine consumption. *Food Chem Toxicol* 34:119-129.
- Barone JJ, Roberts HR (1984) Human consumption of caffeine. In P.B. Dews (Ed.), *Caffeine: perspectives from recent research* (pp. 59-73). Berlin Springer-Verlag.
- Barry RJ, Rushby JA, Wallace MJ, Clarke AR, Johnstone SJ, Zlojutro I (2005) Caffeine effects on resting –state arousal. *Clin Neurophysiology* 116:2693-2700.
- Benowitz NL (1990) Clinical pharmacology of caffeine. *Annu Rev Med* 41:277.
- Benowitz NL, Jacob P, Mayan H, Denaro C (1995) Sympathometic effects of paraxanthine and caffeine in humans. *Clin Pharm Ther* 58:684-691.
- Berube-Parent S, Pelletier C, Dore J, Tremblay A (2005) Effects of encapsulated green tea and Guarana extracts containing a mixture of epigallocatechin-3-gallate and caffeine on 24 h energy expenditure and fat oxidation in men. *Brit J Nutr* 94(3):432-436.
- Bianchi CP (1961) The effect of caffeine on radiocalcium movement in frog sartorius. *J Gen Phys* 44:845-858.
- Birnbaum LJ, Herbst JD (2004) Physiologic effects of caffeine on cross-country runners. *J Strength Cond Res* 18:463-465.
- Burg AW, Warner E (1975) Effect of orally administered caffeine and theophylline on tissue concentrations of 3,5 – cyclic AMP and phosphodiesterase. *Federation Proc* 34:332.
- Busto U, Bendayan R, Sellers EM (1989) Clinical pharmacokinetics of non-opiate abused drugs. *Clin Pharmacokinet* 16:1-26.
- Cannon ME, Cooke CT, McCarthy JS (2001) Caffeine – induced cardiac arrhythmia: an unrecognized danger of health food products. *Med J Australia* 174:520-521.
- Carrillo JA, Benitez J (2000). Clinically significant pharmacokinetic interactions between dietary caffeine and medications. *Clin Pharmacokinet* 39:127-153.
- Carter AJ, O'Connor WT, Carter MJ, Ungersted, U (1995) Caffeine enhances acetylcholine release in the hippocampus in vivo by a selective interaction with adenosine A1 receptors. *J Pharm Exper Therap* 273:637.
- Chen CC, Shi LL, Chen CC (1996) Effect of extraction temperature and time on polyphenol contents and composition and sensory quality of oolong tea infusion. *Food Sci Taiwan* 23:285-298.
- Choi HK, Curhan G (2007) Coffee, tea, and caffeine consumption and serum uric acid level: the third national health and nutrition examination survey. *Arthritis Rheum* 57(5):816-821.
- Chou KH, Bell LN (2007) Caffeine Content of Prepackaged National-Brand and Private-Label Carbonated Beverages. *J Food Sci* 72(6):C337-C342.
- Chvasta TE, Cook AR. (1971) Emptying and absorption of caffeine from the human stomach. *Gastroenterology* 61:838-843.
- Cloughley JB (1981). Storage deterioration in Central African tea: changes in chemical composition, sensory characteristics and price evaluation. *J Food Sci Agric* 32:1213-1223.
- Colombato S, Fasulo L, Mondarini A, Malabaila A, Grillo MA (1989) Effect of caffeine of ornithine metabolism in rat brain, liver and kidney. *Ital J Biochem* 28:75.
- Davidson R, Smith B (1989) Arousal and habituation: differential effects of caffeine, sensation seeking and task difficulty. *Pers Indiv Differ* 10:111.
- Denaro CP, Brown CR, Wilson M, Jacob P, Benowitz NL (1990) Dose-dependency of caffeine metabolism with repeated dosing. *Clin Pharm Therap* 48:277-285.
- Devasagayam TPA, Kamat JP, Mohan H, Kesavan PC (1996) Caffeine as an antioxidant: inhibition of lipid peroxidation induced by reactive oxygen species. *Biochim Biophys Acta* 1282:63-67.
- Dreher HM (2003) Measuring health status in HIV disease: challenges from a sleep study. *Holis Nurs Pract* 17:81-90.
- Dulloo AG, Duret C, Rohrer D, Girardier L, Mensi N, Fathi M, Chantre P, Vandermander J (1999) Efficiency of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr* 70(6):1040-1045.
- Dulloo AG, Seydoux J, Girardier L, Chantre P, Vandermander J (2000) Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine and sympathetic activity. *Intl J Obes Rel Metab Dis* 24:252-258.
- El Yacoubi M, Ledent C, Parmentier M, Costentin J, Vaugeois JM (2003) Caffeine reduces hypnotic effects of alcohol through adenosine A2A receptor blockade. *Neuropharmacol* 45:977-985.
- Fernandez PL, Pablos F, Martin MJ, Gonzales AG (2002) Study of catechin and xanthine tea profiles as geographical tracers. *J Agric Food Chem* 50:1833-1839.
- Ferre S, Fuxe K, Von Euler G, Johansson B, Fredholm BB (1992) Adenosine-dopamine interactions in the brain. *Neurosci* 51:501-512.
- Fredholm BB, Battig K, Holmen J, Nehlig A, Zvartau EE (1999) Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. *Pharm Rev* 51:83-133.
- George J, Murphy T, Roberts R, Cooksley WGE, Halliday KW, Powell LW (1986) Influence of alcohol and caffeine consumption on caffeine elimination. *Clin Exp Pharm Phys* 13:731-736.
- Giannelli M, Doyle P, Roman E, Pelerin M, Hermon C (2003) The effect of caffeine consumption and nausea on the risk of miscarriage. *Paediatr Perinat Epidemiol* 17:316-323.
- Graham TE (1997) The possible actions of methylxanthines on various tissues. In T. Reilly, M. Orme (Eds.), *The clinical pharmacology of sports and exercise* (pp. 257-270). Elsevier, Amsterdam.
- Gramza A, Korczak J (2005) Tea constituents (Camellia sinensis L.) as antioxidants in lipid systems. *Trends Food Sci Tech* 16:351-358.
- Gramza A, Korczak J, Amarowicz R (2005) Tea polyphenols – their antioxidant properties and biological activity - a review. *Pol J Food Nutr Sci* 14(55):3:219-235.
- Gramza-Michałowska A, Bąjerska-Jarzębowska J (2007) Leaves of Camellia sinensis: Ordinary Brewing Plant or Super Antioxidant Source? *Food* 1:56-64.
- Gramza-Michałowska A, Hęś M, Korczak J (2008) Tea extracts antioxidative potential in emulsified lipid systems. *Acta Sci Pol, Technol Aliment* 7(3):29-34.
- Grant DM, Campbell ME, Tang BK, Kalow W (1987) Biotransformation of caffeine by microsomes from human liver. Kinetics and inhibition studies. *Biochem Pharmacol* 36:1251-1260.

# CAFFEINE IN TEA CAMELLIA SINENSIS – CONTENT, ABSORPTION, BENEFITS AND RISKS OF CONSUMPTION

46. Griffiths RR, Evans SM, Heishman SJ, Preston KL, Sannerud A, Wolf B, Woodson PP (1990) Low dose physical dependence in humans. *J Pharmacol Exp Therap* 255:1123.
47. Guthrie JR, Nayler WG (1967) Interaction between caffeine and adenosine on calcium exchangeability in mammalian atria. *Arch Intern Pharmacodyn Ther* 170:323.
48. Haddad LM, Winchester JF (1983) Clinical management of poisoning and drug overdose. Philadelphia: WB. Saunders Company.
49. Haleem DJ, Yasmeen A, Haleem MA, Zafar A (1995) 24-hour withdrawal following repeated administration of caffeine attenuates brain serotonin but not tryptophan in rat brain: implications for caffeine-induced depression. *Life Sci* 57:PL285.
50. Heishman SJ, Henningfield JE (1999) Is caffeine a drug of dependence? Criteria and comparisons. In B.S. Gupta, U. Gupta (Eds.), *Caffeine and behavior: current views and research trends* (pp. 31-43). CRC Press Washington, DC.
51. Hetzler RK, Knowlton RG, Somani SM, Brown DD, Perkins RM (1990) Effect of parazantine on FFA mobilization after intravenous caffeine administration in humans. *J Appl Physiol* 68:44-47.
52. Higdon JV, Frei B (2006) Coffee and Health: A Review of Recent Human Research. *Crit Rev Food Sci Nutr* 46(2):101-123.
53. Hilal Y, Engelhardt U (2007) Characterization of white tea – comparison to green and black tea. *J Verbr Lebensm* 2:414-421.
54. Hindmarch I, Rigney U, Stanley N, Quinlan P, Rycroft J, Lane J (2000) A naturalistic investigation of the effects of day-long consumption of tea, coffee and water on alertness, sleep onset and sleep quality. *Psychopharmacol* 149:203-216.
55. Horzic D, Komes D, Belscak A, Kovacevic Ganic K, Iverkovic D, Karlovic D (2009) The composition of polyphenols and methylxanthines in teas and herbal infusions. *Food Chem* 115:441-448.
56. Hughes AD, Herring S, Bolton TB (1990) The action of caffeine on inward barium current through voltage dependent calcium channels in single rabbit ear artery cells. *Pfluegers Arch* 416:462.
57. Institute of Medicine. Caffeine for the sustainment of mental task performance: formulations for military operations (2001) Institute of Medicine (U.S), Committee on Military Nutrition Research, Food and Nutrition Board. National Academy Press, Washington.
58. Jaganyi D, Ndlovu T (2001) Kinetics of tea infusion. Part 3: the effect of tea bag size and shape on the rate of caffeine extraction from Ceylon orange pekoe tea. *Food Chem* 75:63-66.
59. Juhel C, Armand M, Pafumi Y (2000) Green tea extract (AR25) inhibits lipolysis of triglycerides in gastric and duodenal medium in vitro. *J Nutr Biochem* 11:45-51.
60. Kamimori GH, Joubert A, Otterstetter R, Santaromana M, Eddington ND (1999) The effect of the menstrual cycle on the pharmacokinetics of caffeine in normal, healthy eumenorrheic females. *Eur J Clin Pharmacol* 55:45-49.
61. Kaufman KR, Sachdeo RC (2003) Caffeinated beverages and decreased seizure control. *Seizures Eur J Epilepsy* 12:519-521.
62. Keijzers GB, De Galan BE, Tack CJ, Smits P (2001) Caffeine can decrease insulin sensitivity in humans. *Diabetes Care* 25:364-369.
63. Kerr JS, Sherwod N, Hindmarch I (1999) Separate and combined effects of the social drugs on psychomotor performance. In B.S. Gupta, U. Gupta (Eds.), *Caffeine and behavior: current views and research trends* (pp. 77). Boca Raton, FL, CRC Press.
64. Kerrigan S, Lindsey T (2005) Fatal caffeine overdose: two case reports. *Forensic Sci Intl* 153:67-69.
65. Khokhar S, Magnusdottir SGM (2002) Total phenol, catechin and caffeine contents of teas commonly consumed in the United Kingdom. *J Agric Food Chem* 50:565-570.
66. Kiyohara C, Kono S, Honjo S, Todoroki I, Sakurai Y, Nishiwaki M, Hamada H, Nishikawa H, Koga H, Ogawa S, Nakagawa K (1999) Inverse association between coffee drinking and serum uric acid concentrations in middle-aged Japanese males. *Brit J Nutr* 82:125-130.
67. Komatsu T, Nakamori M, Komatsu K, Hosoda K, Okamura M, Toyama K, Ishikura Y, Sakai T, Kunii D, Yamamoto S (2003) Oolong tea increases energy metabolism in Japanese females. *J Med Invest* 50:170-175.
68. Kuroda Y, Hara Y (2004) Age related diseases and tea. In *Health effects of tea and its catechins* (pp. 56). Kluwer Academic, New York.
69. Leon-Carmona JR, Galano A (2011) Is caffeine a good scavenger of oxygenated free radicals? *J Phys Chem B* 4538-4546.
70. Liang Y, Xu Y (2001) Effect of pH on cream particle formation and solids extraction yield of black tea. *Food Chem* 74:155-160.
71. Liguori A, Huges JR, Grass JA (1997) Absorption and subjective effects of caffeine from coffee, cola, and capsules. *Pharmacol Biochem Behav* 58:721-726.
72. Lin JK, Lin CL, Liang YC, Lin-Shiau SY, Juan IM (1998) Survey of catechins, gallic acid and methylxanthines in green, oolong, pu-erh and black teas. *J Agric Food Chem* 46:3635-3642.
73. Lin S-D, Liu E-H, Mau J-L (2008) Effect of different brewing methods on antioxidant properties of steaming green tea. *LWT – Food Sci Technol* 41:1616-1623.
74. Lin YS, Tsai YJ, Tsai JS, Lin JK (2003) Factors affecting the levels of tea polyphenols and caffeine in tea leaves. *J Agric Food Chem* 51:1864-1873.
75. Mackay DC, Rollings JW (2005) Caffeine and caffeinism. *J Royal Naval Med Serv* 75:65.
76. Marks V, Kelly JF (1973) Absorption of caffeine from tea, coffee and coca cola. *Lancet* 1:827.
77. Mattioli AV, Bonatti S, Monopol D, Zennaro M, Mattioli G (2005) Influences of regression of left ventricular hypertrophy on left atrial size and function in patients with moderate hypertension. *Blood Pressure* 14:273-344.
78. McLellan TM, Bell DG, Kamunori GH (2004) Caffeine improves physical performance during the 24h of active wakefulness. *Aviat Space Environ Med* 75:666-672.
79. Moffat AC, Osselson MD, Widdop B, Galichet LY (2004) Clarke's analysis of drugs and poisons in pharmaceuticals, body fluids and postmortem material (pp. 736-738), 3rd edition, London: Pharmaceutical Press, Vol. II.
80. Muroyama K, Murosaki S, Yamamoto Y, Ishijima A, Toh Y (2003 a) Effect of intake of a mixture of thiamin, arginine, caffeine and citric acid on adiposity in healthy subjects with high percent body fat. *Biosci Biotech Biochem* 67:2325-2333.
81. Muroyama K, Murosaki S, Yamamoto Y, Odaka H, Chung HC, Miyoshi M (2003 b) Anti-obesity effects of mixture of thiamin, arginine, caffeine and citric acid in non-insulin dependent diabetic KK mice. *J Nutr Sci Vit* 49 :56-63.
82. Muthumani T, Kumar RSS (2007) Influence of fermentation time on the development of compounds responsible for quality in black tea. *Food Chem* 101:98-102.
83. Myers JP, Johnson DA, McVey DE (1999) Caffeine in the modulation of brain function. In B.S. Gupta, U. Gupta (Eds.), *Caffeine and behavior: current views and research trends* (pp. 17-25). CRC Press Washington, DC.
84. Myers MG (1991) Caffeine and cardiac arrhythmias. *Annals Int Med* 114:147-150.
85. Nawrot P, Jordan S, Eastwood J, Rotstein J, Hugenholtz A, Feeley M (2003) Effects of caffeine on human health. *Food Add Contam* 20(1):1-30.
86. Nehling A (1999) Cerebral energy metabolism and blood flow: useful tools for the understanding of the behavioral effects of caffeine. In B.S. Gupta, U. Gupta (Eds.), *Caffeine and behavior: current views and research trends* (pp. 31-34). CRC Press Washington, DC.
87. Nehling A, Daval JL, Debry G (1992) Caffeine and the central nervous system: Mechanism of action, biochemical, metabolic and psycho stimulant effects. *Brain Res Rev* 17:139- 170.
88. Norager CB, Jensen MD, Madsen MR, Laurberg S (2005) Caffeine improves endurance in 75-year-old citizens: a randomized, double-blind, placebo-controlled cross over study. *J Appl Physiol* 99:2302-2306.
89. Owuor PO, Chavanji AM (1986) Caffeine contents of clonal tea, seasonal variations and effects of plucking standards under Kenyan conditions. *Food Chem* 20:225-233.
90. Owuor PO, Obanda AM, Tsushida T, Murai T (1986) Comparison of the chemical composition of black teas from main black tea producing parts of the world. *Tea* 7:71-78.
91. Pasman WJ, Westerterp-Plantenga MS, Saris WHM (1997) The effectiveness of long-term supplementation of carbohydrate, chromium, fiber and caffeine on weight maintenance. *Intl J Obes* 21:1143-1151.
92. Passmore AP, Kondowe GB, Johnston GD (1987) Renal and cardiovascular effects of caffeine: a dose response study. *Clin Sci* 72:749-756.
93. Petrie HJ, Chown SE, Belfie LM, Duncan AM, McLaren DH, Conquer JA, Graham TE (2004) Caffeine ingestion increases the insulin response to an oral-glucose-tolerance test in obese men before and after weight loss. *Am J Clin Nutr* 80:22-28.
94. Pirich C, O-Grady J, Sininger H (1993) Coffee, lipoproteins and cardiovascular disease. *Wien Klinische Wochenschr* 105:3.
95. Pollock BG, Wylie M, Stack JA, Sorisio DA, Thompson DS, Kirshner MA, Folan MM, Condifier KA (1999) Inhibition of caffeine metabolism by estrogen replacement therapy in postmenopausal women. *J Clin Pharm* 39:936-940.
96. Porkka-Heiskanen T, Strecker RE, Thakkar M, Bjorkum AA, Greene RW, McCarley RW (1997) Adenosine: a mediator of the sleep-inducing effects of prolonged wakefulness. *Science* 276:1265-1268.
97. Prasanthi JR, Dasari B, Marwarha G, Larson T, Chen X, Geiger JD, Ghribi O (2010) Caffeine protects against oxidative stress and Alzheimer's disease-like pathology in rabbit hippocampus induced by cholesterol-enriched diet. *Free Rad Biol Med* 49:1212-1220.
98. Revelle W, Humphreys MS, Simon L, Gilliland K (1980) The interactive effects of personality, time of day, and caffeine: a test of arousal model. *J Exp Psychol [Gen]* 109:1.
99. Ross GW, Abbot RD, Petrovitch H, Morens DM, Grandinetti A, Tung KH, Tanner CM, Masaki KH, Blanchette PL, Curb JD, Popper JS, White LR (2000) Association of coffee and caffeine intake with the risk of Parkinson' disease. *JAMA* 283:2674-2679.
100. Rosso A, Mossey J, Lippa CF (2008) Caffeine: neuroprotective functions in cognition and Alzheimer's disease. *Am J Alzheimers Dis Other Demen* 23:417-422.
101. Sandow A, Burst M (1996) Caffeine potentiation of twitch tension of sartorius muscle. *Biochem* 345:232.
102. Sava VM, Yang SM, Hong MY, Yang PC, Huang GS (2001) Isolation and characterization of melanic pigments derived from tea and tea polyphenols. *Food Chem* 73:177-184.

*JNHA: NUTRITION*

103. Schulz H, Engelhardt UH, Wegent A, Drews HH, Lapczynski S (1999) Application of near-infrared reflectance spectroscopy to the simultaneous prediction of alkaloids and phenolic substances in green tea leaves. *J Agric Food Chem* 47:5064-5067.
104. Shankar S, Ganapathy S, Srivastava R (2007) Green tea polyphenols : biology and therapeutic implications in cancer. *Front Biosci* 12:4881-4889.
105. Shils ME, Olson JA, Shike M, Ross AC (1999) *Modern nutrition in health and disease*, 9th Edition, Baltimore: Lipincott Williams & Wilkins.
106. Smith BD, Osborne A, Mann M, Jones H, White T (2004) Arousal and behavior: biopsychological effects of caffeine. In A. Nehling (Ed.), *Coffee, tea, chocolate, and the brain* (pp. 35-52). Boca Ranton, CRC Press.
107. Smith BD, White T, Shapiro R (2007) The arousal drug of choice: sources and consumption of caffeine. In B.D. Smith, U. Gupta, B.S. Gupta (Eds.), *Caffeine and activation theory. Effects on health and behavior* (pp. 10-40). Boca Ranton, CRC Press.
108. Stavric B (1988a) Methylxanthines: toxicity in humans. 3. Theobromine, paraxanthine and the combined effects of methylxanthines. *Food Chem Toxicol* 26:725-733.
109. Stavric B (1988b) Methylxanthines: toxicity to humans. 2. Caffeine. *Food Chem Toxicol* 26:645-662.
110. Vlachopoulos C, Kosmopoulou F, Panagiotakos D, Ioakeimidis N, Alexopoulos Pistavos C (2004) Smoking and caffeine have a synergistic detrimental effect on aortic stiffness and wave reflections. *J Am College Cardiol* 44:1911-1917.
111. Wang LF, Kim DM, Lee CY (2000) Effects of heat processing and storage on flavanols and sensory qualities of green tea beverage. *J Agric Food Chem* 48:4227-4232.
112. Wang X, Hu S, Wan X, Pan C (2005) Effect of microbial fermentation on caffeine content of tea leaves. *J Agric Food Chem* 53:7238-7242.
113. Weir RL, Hruska RE (1983) Interaction between methylxanthines and the benzodiazepine receptor. *Arch Intern Pharmacodyn Ther* 265:42.
114. Westerterp-Plantenga M, Diepvens K, Joosen AMCP, Bérubé-Parent S, Tremblay A (2006) Metabolic effects of spices, teas, and caffeine. *Physiol Behav* 89:85-91.
115. Westerterp-Plantenga MS, Lejeune MP, Kovacs EM (2005) Body weight loss and weight maintenance in relation to habitual caffeine intake and green tea supplementation. *Obesity Res* 13:1195-1204.
116. White JM (1999) Behavioral effects of caffeine co-administered with nicotine, benzodiazepines, and alcohol. In B.S. Gupta, U. Gupta (Eds.), *Caffeine and behavior: current views and research trends* (pp. 76-83). CRC Press Washington, DC.
117. Wójciak KM, Dolatowski ZJ, Okoń A (2011) The effect of water plant extracts addition on the oxidative stability of meat products. *Acta Sci Pol Technol Aliment* 10(2):175-188.
118. Woodward M, Tunstall-Pedoe H (1999) Coffee and tea consumption in the Scottish Heart Health Study follow-up: conflicting relations with coronary risk factors, coronary heart disease and all-cause mortality. *J Epidem Com Health* 53:481-487.
119. Yang DJ, Hwang LS, Lin JT (2007) Effects of different steeping methods and storage on caffeine, catechins and gallic acid in bag tea infusions. *J Chromatogr A*, 1156:312-320.
120. Yao L, Liu X, Jing Y, Caffin N, D'Arcy B, Singanusong R, Datta N, Xu Y (2006) Compositional analysis of teas from Australian supermarkets. *Food Chem* 94:115-122.
121. Yeragani VK, Krishnan S, Engles HJ, Gretebeck R (2005) Effects of caffeine on linear and nonlinear measures of heart rate variability before and after exercise. *Depress Anxiety* 21:130-134.