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

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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. Resent 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 thearubigens 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 leafs 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

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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 leafs contained slightly higher or similar amounts of caffeine than tea bags. Black and green tea leafs 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 leafs than those of imported ones (90). Results of Owuor and Chavanji (89) showed that changing caffeine content due to the tea leafs maturity (differences from 20 - 40%), and it is higher in young leafs than older ones. Also tea form (leafs or bags) had significant influence on caffeine extraction level. It was found that caffeine was extracted in stable amounts from tea leafs, 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 (caffeinism) (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 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), aerial 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, trachel 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 triacyloglycerols lipolise (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.

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