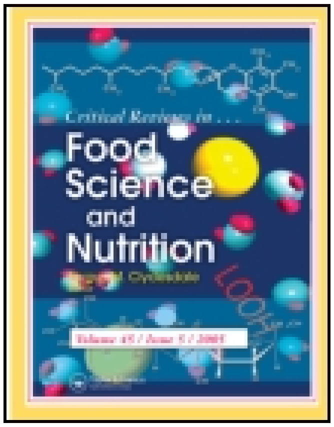

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Epidemiological Evidence Linking Tea Consumption to Human Health: A Review

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Tea has been widely consumed around the world for thousands of years and drinking tea is a daily habit for people of all ages. Tea is a major source of flavanoids, which have become well known as antioxidants. Tea also contains caffeine and theanine, which have been found to associate with health benefits. Many animal and epidemiological studies have been conducted to investigate the link between tea consumption and human health. However, common questions that arise about tea consumption include: whether all teas are the same, why drinking tea is linked with health benefits, how do the different ways of tea preparation impact on availability of tea components, how much and how long a person should consume tea to obtain health benefits, and whether there is any negative health effect associated with drinking tea. To answer these questions, this paper outlines the tea components and their link to human health, discusses major factors affecting availability of tea components in a tea cup, and reviews the latest epidemiological evidence linking tea consumption to human health.

Keywords Antioxidant, caffeine, flavanoids, human health, tea consumption, theanine

INTRODUCTION

Tea (*Camellia sinensis*) was first discovered as a drink and medicine in China around 2737 B.C. Since then tea has been introduced to other countries and is now consumed in every country. Tea has become the second beverage to water in terms of worldwide consumption (Gööck, 1990; Scharbert et al., 2004). Presently, tea has been cultivated in six continents (Scharbert et al., 2004; Vuong et al., 2011b). World tea production in 2006 reached a record of 3.64 million tonnes, of which China, India, and Kenya were the top three biggest producing countries (Vuong et al., 2011c). The world tea production has been continuously increasing; of which black tea production has been projected to grow at 1.9% annually to reach 3.14 million tons by 2017, whereas, the green tea production has been projected to grow at annual rate of 3.8% annually to achieve about 1.57 million tons for the same period (Vuong et al., 2011c).

Tea can be prepared by either brewing fresh or dried tea leaves in hot water. Brewing dried tea leaves is the most popular method to date to prepare a cup of tea (Gööck, 1990; Scharbert et al., 2004). Dried tea is produced from the fresh tea leaf, which contains chlorophyll, carbohydrates, enzymes, protein, caffeine, theanine, flavonoids, and other substances. Flavonoids are the most abundant components in the tea leaf, they are comprised of six catechins and their derivatives (Chu and Juneja, 1997). Carbohydrates and protein also account for a large amount of tea components; however, these components are almost insoluble; whereas, other components are present in small quantities such as caffeine, theanine, volatiles but they are mostly soluble (Chu and Juneja, 1997). The composition of fresh tea leaf varies with the variety, climate conditions, season, position of leaf, soil, cultivation methods, and age of leaf (Graham, 1992; Balentine et al., 1998).

The sensory quality comprising of taste, color and flavor is important parameter of tea beverage and is contributed by flavonoids, caffeine, theanine, and aromatic volatile components (Ninomiya et al., 1997). Among these components, catechins and caffeine contribute the astringency and bitterness, whereas theaflavins (TF) and thearubigins (TR) contribute color and the astringent taste (Graham, 1992). Theanine is responsible for the brothy, sweet, and umami taste (savory taste) of the tea beverage (Wan et al., 2009b). Aromatic volatile components also supplement flavor to the tea infusion (Kato and Shibamoto, 2009).

Numerous studies have investigated the roles of tea constituents in human health and found that the major tea constituents including flavonoids, caffeine, and theanine are linked to the health benefits such as prevention of cancers and

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cardiovascular diseases, reduction the risks of obesity and diabetes, and improvement of immune system (Graham, 1992; Khan and Mukhtar, 2007; Basu et al., 2010). Several epidemiology studies have reported the association between tea consumption and health benefits (Wu et al., 2003; Zaveri, 2006; Zhang et al., 2007). However, the volume of tea required for obtaining health benefits is an area of speculation. This paper outlines the roles of tea constituents in human health, discusses various types of tea and the ways of tea preparation, which generally affect the availability of the tea constituents, and then reviews the recent epidemiological evidences on the link of tea consumption and the health benefits.

TEA CONSTITUENTS AND THEIR LINK TO HUMAN HEALTH

Flavanoids

Flavanoids are the most abundant components in tea and comprise of catechins, TFs, TRs, keamfaron, and quercertin. Keamfaron and quercertin only account for a small amount; whereas, catechins, TFs, and TRs present in a large quantity in tea (Balentine et al., 1998). Flavanoids have been found to inhibit carcinogenesis in humans (Lin, 2009) and the mechanisms are shown in Figure 1.

Catechins

The catechins have the general structure of C6–C3–C6 with two aromatic rings and several hydroxyl groups (Vuong et al., 2010). Catechins can be classified into two groups including epistructured catechins and nonepistructured catechins. Epistrcutured catechins are major catechins in tea and they comprise of Epigallocatechin gallate (EGC), epigallocatechin (EGC), epicatechin gallate, and epicatechin (EC); whereas, nonepistructured catechins only account for small composition in tea including gallocatechin gallate (GCG), gallocatechin (GC), catechin gallate (CG), and catechin (C) (Vuong et al., 2010).

Catechins are rich in green tea and they not only contribute to the beverage quality but also promote health benefits to the consumers. In tea beverage, catechins possess the bitter, astringent, and slight sweet tastes (Balentine et al., 1998). In the body, catechins act as antioxidants because they can donate hydrogen atoms, trap peroxyl radicals, and thus suppress radical chain reactions and terminate lipid peroxidation (Terao et al., 1994). Their scavenging ability is thought to be more powerful than vitamin C, vitamin E, or β-carotene (Vuong et al., 2010). In addition, catechins have been found to chelate transition metal ions, modulate oxidant, and antioxidant enzymes, and affect gene expression (Vuong et al., 2010). However, catechins are unstable and are sensitive to oxidation by enzymes, moisture content, acid, and heat (Balentine et al., 1998; Vuong et al., 2010). In the presence of the enzymes polyphenol oxidase, and peroxidase, catechins are easily oxidized to form TFs and TRs, the reason why the content of catechins is lower in black tea as compared to green tea or oolong tea (Graham, 1992). Catechins are readily degraded when storing dried tea with high moisture content (more than 10%) (Robertson, 1993), brewing tea in alkaline conditions or at high temperature (above 80°C) (Vuong et al., 2010). Therefore, care is needed during storage and preparation process of tea to minimize degradation of the tea catechins.

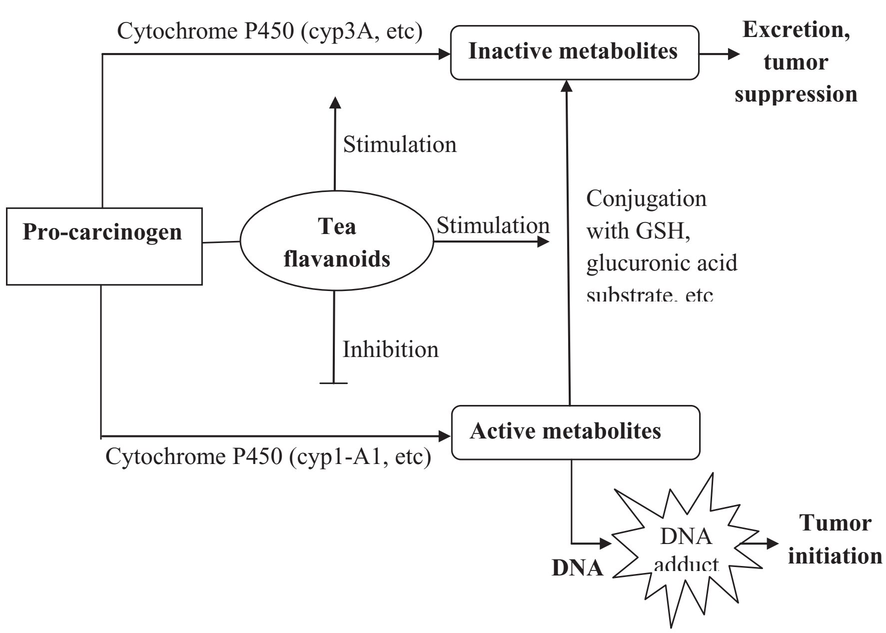

Figure 1 Biochemical mechanisms of anticarcinogenesis by tea flavanoids (Lin, 2009).

Catechins have been linked with cancer prevention. Catechins were found to delay the onset of skin tumor genesis, reduce the cumulative number of skin tumors and increase the tumor-free survival of rats (Roy et al., 2009). Catechins were also found to prevent nitrosamine 4-(methylnitrosamino)-l-(3-pyridyl)-l butanone-induced lung tumorigenesis and inhibit fumonisin B1 promotion in rat liver utilizing diethylnitrosamine as the cancer initiator (Xu et al., 1992; Marnewick et al., 2009). Furthermore, catechins were reported to inhibit cyclin-dependent kinases (cdks) and induce cdk inhibitors p21 and p27 in breast and prostate cancer cells (Gupta et al., 2003; Park and Dong, 2003).

Catechins have been found to lower the level of cholesterol and prevent platelet clumping, increase oxidative stress and dysfunction of the endothelium, all of which are related to the development of coronary artery disease (Sharangi, 2009). Catechins have been associated with reduction of body weight, blood levels of testosterone, insulin, insulin-like growth factor I, glucose, cholesterol, and triglyceride (Kao et al., 2000). Catechins were also found to prevent diet-induce obesity by decreasing energy absorption and increasing fat oxidation (Klaus et al., 2005). In addition, catechins may play a role in preventing microbial diseases, Parkinson's diseases, Alzheimer's diseases, and stroke (Zaveri, 2006; Khan and Mukhtar, 2007).

Catechins have shown synergism with vitamin E, vitamin C, and some organic acids such as citric, malic, and tartaric (Graham, 1992; Hara, 2001); and also have potential in protecting the deterioration of β-carotene, a vitamin A precursor (Hara, 2001). However, catechins can easily form a complex with other components to reduce their availability. For example, catechins can interact with caffeine to form precipitate through π–π interaction and lower their availability (Ishizu et al., 2009). The amount of precipitation is critical to catechin availability and varies with extracting temperatures, precipitate is high when tea is brewed at temperature of over 90°C and low when tea is brewed at temperature of 50°C (Liang et al., 2002).

Catechins can also interact with proteins (Vuong et al., 2010), and may inhibit the absorption of food proteins into the body. In addition, catechins can interact with enzymes such as lipoxygenase, α-amylase, pepsin, trypsin, and lipase and in doing so may inhibit their activities in the body (Sekiya et al., 1984). Catechins also interfere with the emulsification, digestion, and micellar solubilization of lipids (Koo and Noh, 2006). In addition, catechins can bind and form a complex with iron, thus tend to prevent iron absorption in the body (Zijp et al., 2000). Despite these limitations catechins have shown important antioxidant properties.

Theaflavins and Thearubigins

Unlike catechins structured as monomers, TFs and TRs are structured of dimers and polymers, respectively (Zijp et al., 2000; Halder et al., 2006) (Figure 2). TFs and TRs are rich in black tea (Vuong et al., 2010). Typically, black tea contains 10% flavonols, 25% catechins, 30% TFs, and 45% TRs (Zijp et al., 2000). TFs and TRs are astringent compounds which contribute

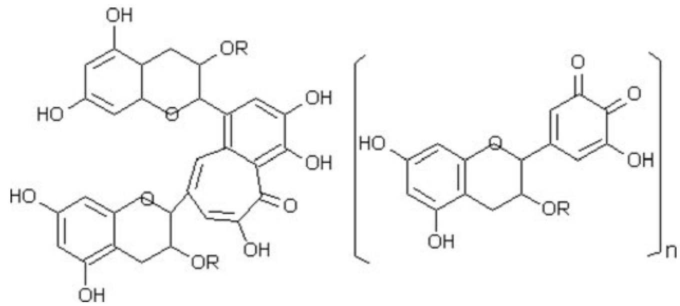

Figure 2 Chemical structure of TFs and TRs. R = Galloyl Group (Zijp et al., 2000).

to the color and taste of the black tea beverage (Halder et al., 2006) and their levels have been found to correlate with black tea quality (Balentine et al., 1998). It is questioned that whether there is any difference in the antioxidative properties between TFs and TRs in comparison with catechins. Studies showed that TFs and TRs in black tea have the same antioxidative properties in comparison with catechins in green tea (Yoshino et al., 1994; Leung et al., 2001). Several studies have linked TFs and TRs with health benefits. For example, both TFs and TRs were reported to inhibit lipid peroxidation *in vivo* (Yoshino et al., 1994). In addition, TFs and TRs were found to have significant anticlastogenic effects in human lymphocytes. However, TFs were found to have more protective effects than TRs (Halder et al., 2006).

Caffeine

There are three methyl xanthines including caffeine, theophylline, and theobromine in tea. However, theophylline and theobromine are only found in small quantities (0.2–0.4% and 0.02% (w/w), respectively) (Chu and Juneja, 1997). Caffeine accounts for a large quantity with its maximum level of about 5% (w/w) (Chu and Juneja, 1997). It is interesting to note that the level of caffeine in tea is higher than that of coffee beans, which actually have only 1.5% (w/w) of caffeine (Chu and Juneja, 1997). Caffeine is a trimethyl derivative of purine 2,6-diol and its level in tea is also influenced by several factors such as season, age of the leaf, variety, and processing methods (Balentine et al., 1998). Caffeine is responsible for the briskness of the black tea beverage because it associates with TFs to give the characteristic black tea flavor (Balentine et al., 1998).

After ingestion in the body, caffeine undergoes demethylation to form paraxanthine, theobromine, and theophylline (Figure 3), which are then broken down in the liver by additional demethylations and oxidation to urates (Safranow and Machoy, 2005; Heckman et al., 2010). Caffeine has been found to link with enhancement of cognitive functioning, improvement of neuromuscular coordination, and elevation of mood and relieves anxiety (Glade, 2010). Caffeine was found to associate with stimulation of the central nervous system and cardiac

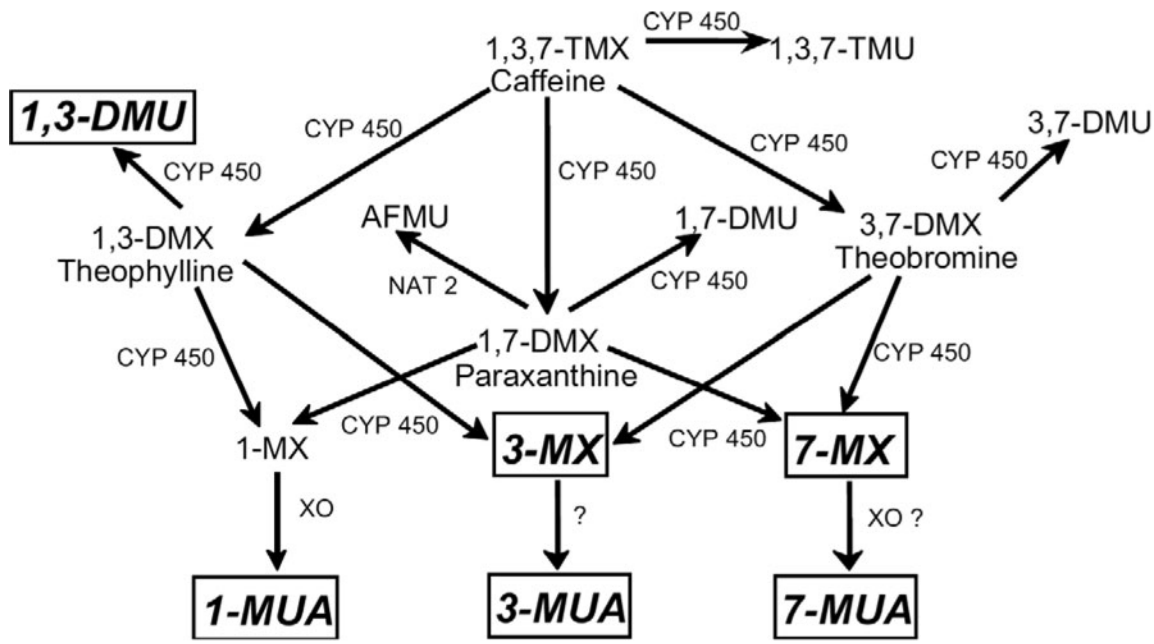

Figure 3 Metabolism of caffeine in humans (Safranow and Machoy, 2005). CYP 450, cytochrome P450; XO, xanthine oxidoreductase; NAT 2, *N*-acetyltransferase 2; MX, DMX, and TMX, mono-, di-, and trimethylxanthines; MUA, DMU, and TMU, mono-, di-, and trimethyluric acids; AFMU, 5-acetylamino-6-formylamino-3-methyluracil.

muscle. Caffeine was also found to elevate plasma free fatty acids and glucose as well as increase peripheral vascular resistance (Harbowy and Balentine, 1997; Griffiths and Woodson, 1998). In addition, caffeine was reported to increase cerebrovascular resistance and increase gastric and other secretions as well as relax smooth muscle (Harbowy and Balentine, 1997; Griffiths and Woodson, 1998). However, it should be noted that caffeine may cause irritation of the gastrointestinal tract and sleeplessness in certain people (Chu and Juneja, 1997). Caffeine may react as a feeble base with acids to form salts, which are very readily hydrolyzed (Stanley et al., 1998). Caffeine may also form the precipitate (cream formation) with TFs and ester-forms of the catechins, thus to reduce their availability (Chao and Chiang, 1999).

Theanine

Theanine is a unique amino acid in nature because, with the exception of being found in the mushroom *Xerocomus badius*, it is occurrence appears to be limited to the *C*. genus, mostly the tea plants *C*. *sinensis var. Sinensis and C*. *scinenisis var. assamica* and some closely related species such as *C*. *japonica* and *C*. *sasanqua* (Juneja et al., 1999; Deng et al., 2008). In tea, theanine accounts for about 50% of the free amino acids, which are involved in producing the distinctive aroma of tea. Theanine has been closely linked with tea's umami taste, the sweet and brothy taste of the tea liquor (Balentine et al., 1998; Juneja et al., 1999). Theanine has been found to correlate highly with tea quality and price (Chu, 1997).

Theanine constitutes between 1% and 3% (w/w) of the dry weight of tea; however, the level of theanine varies in accordance with various factors including growing location and method of cultivation, tea grade, variety, and time of harvest (Chu, 1997, Balentine et al., 1998; Vuong et al., 2011a). Theanine varies with different types of tea. Green tea contains lower or similar levels of theanine as compared to oolong and black teas (Ekborg-Ott et al., 1997). Theanine has been reported to facilitate the generation of alpha brain waves, which are associated with a relaxed but alert mental state and to promote the release of the inhibitory neurotransmitter, γ-aminobutyric acid, which in turn regulates dopamine and serotonin levels in the brain, thus theanine is linked with relaxation and improved learning ability (Mason, 2001; Cooper et al., 2005).

Recent studies have found evidence linking theanine to cancer prevention. Theanine was found to link with the inhibition of the *in vivo* and *in vitro* growth of human non–small cell lung cancer and leukemia cell lines (Liu et al., 2009). Theanine was also found to induce apoptosis in four cancer cell lines including breast, colon, hepatoma, and prostate (Friedman et al., 2007). In the normal cells, theanine was found to convert to glutamate, thus to increase the intracellular glutamate level and lead to increased intracellular glutathione. Therefore, theanine was thought to inhibit doxorubicin-induced toxicity (Figure 4) (Wan et al., 2009b). In addition, theanine was associated with reducing the adverse effects of doxorubicin reactions, providing protection against tissue damage and acting as a biochemical modulator to improve therapeutic efficacy (Sugiyama and Sadzuka, 2004). Theanine has also found to link with providing effective prophylaxis and treatment for Alzheimer's disease,

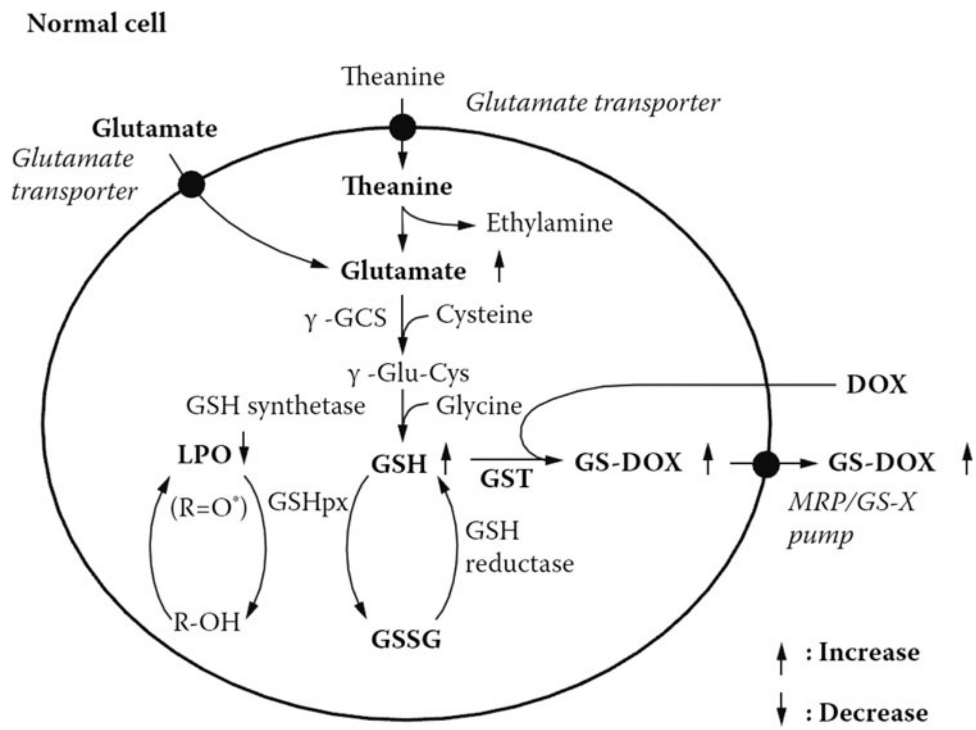

Figure 4 Mechanism of theanine to protect normal tissue from doxorubicin (DOX) toxicity via the changing glutathione (GSH) level (Wan et al., 2009b).

regulating blood pressure, promoting the weight loss and improving the immune system (Yokogoshi and Kobayashi, 1998; Rogers et al., 2007; Di et al., 2010; Takagi et al., 2010).

Other Tea Constituents

Tea contains a high content of carbohydrates which accounts for about 40% of dry weight and one third of it is cellulosic fiber. However, most of the carbohydrates are insoluble and therefore are not present in tea beverage after brewing (Chu and Juneja, 1997; Balentine et al., 1998). Although there is only a small amount of starch in the tea leaf; however, it contributes to the quality of tea. The synthesis of starch occurs at dawn and at sunset and thus leaf harvested in the morning normally contains more starch and is considered of better quality than tea picked later on in the same day (Chu and Juneja, 1997).

Tea also contains several vitamins, of which vitamin C is dominant with about 280 mg per 100 g dried green tea. Green tea has more vitamin C than oolong and black tea because vitamin C is decomposed during the fermentation process (Chu and Juneja, 1997). Tea also contains enzymes like polyphenol oxidase and peroxidase and some inorganic elements such as calcium, potassium, magnesium, and copper. These enzymes and inorganic elements influence the quality of the tea infusion (Balentine et al., 1998). In addition, tea contains some carotenoids and a large number of volatile substances, which contribute to its flavor (Balentine et al., 1998). Tea also contains chlorophyll, which is high in fresh leaves. However, dried green, oolong, and black teas contain less chlorophyll because it is degraded during withering and drying (Jiang, 2009).

MAJOR FACTORS AFFECTING AVAILABILITY OF TEA CONSTITUENTS IN A TEA CUP

There are two major factors which directly affect the availability of tea constituents in a tea cup including the types of tea and the way of preparing a tea cup. This section describes differences among various types of tea and how the different ways of making tea influence the availability of tea components in a tea cup, thus is consequently related to promotion of human health.

Tea Types

There are eight different types of tea, which can be produced from same fresh tea leaves (Cheng, 2006) (Figure 5). However, for each type of tea, the biochemical quality and sensory can vary due to the variety, climatic conditions, nutrition of the tea plant, cultivation method, and the type of leaf (Vuong et al., 2010). For example, *Thea Camellia var. assamica* has higher catechins than *Thea Camellia var. sinensis* (Chu, 1997). The level of catechins in tea leaves is higher when tea is grown in an area with more sunlight or higher temperature (Hara, 2001). Summer leaves have higher levels of catechins than those in

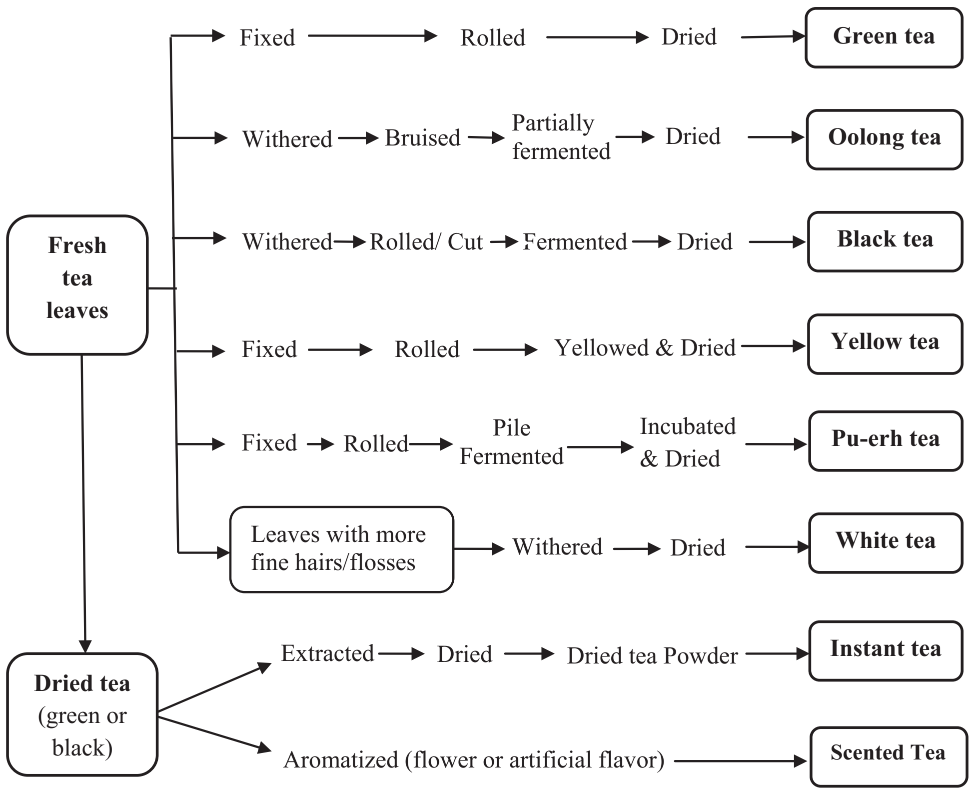

Figure 5 Processing techniques of dried teas (Balentine et al., 1998; Wan et al., 2009a).

spring leaves (Lin et al., 1996; Hara, 2001). Tea, which is fertilized with potassium, has higher catechins and theanine in the leaves than those without fertilization (Venkatesan et al., 2004). Tea grown in shade has higher content of theanine and lower level of catechins than the tea exposing to high levels of sunlight (Hara, 2001). Tea produced from coarse leaves has lower catechins than tea produced from young leaves (apical bud and the two youngest leaves) because the young leaves are richer (2.7-fold) in catechins than old leaves (from the 10th to the 5th leaf) (Chu, 1997; Hara, 2001).

Green, oolong, and black teas are the major types of tea (Vuong et al., 2010). In terms of world tea consumption, black tea accounts for 78% of total consumed tea in the world, while 20% is green tea and less than 2% is oolong tea (Cheng, 2006). Green tea is known as nonfermented tea; whereas, oolong tea and black tea refer to semifermented tea and fermented tea, in which aerobic oxidation of the tea polyphenols, called catechins, is partially and fully promoted and the catechins are enzymatically catalyzed to form TFs and TRs. Therefore, green tea has highest content of catechins, followed by oolong tea and black tea has the lowest content of catechins (Vuong et al., 2011b). In contrast, black tea has higher level of TFs and TRs than oolong tea, and green tea has the lowest level of these components (Vuong et al., 2011b).

Green tea is mostly consumed in Asian countries and North Africa (Mukhtar and Ahmad, 2000). Green tea contains up to 30% (w/w) catechins of its dry weight. It also contains high amount of caffeine and theanine, which account for up to 5% and 3% (w/w) dry weight, respectively (Graham, 1992; Balentine et al., 1998). When brewing with boiling water, green tea produces a green–yellow solution with a fresh and grassy flavor (Wan et al., 2009a). Green tea is more astringent than black and oolong tea (Balentine et al., 1998). There is a strong association between sensory quality and tea composition. Green tea with acceptable sensory quality normally contains a higher amount of theanine, which produces brothy, umamy taste. Lower amounts of caffeine and catechins are associated with bitter and astringent tastes (Chu and Juneja, 1997).

Unlike green tea, black tea is mostly consumed in Western countries and some Asian countries (Mukhtar and Ahmad, 2000). Black tea has a low content of catechins with about 9% (w/w) dry weight; however, it comprises up to 23% (w/w) dry weight of TFs and TRs (Graham, 1992; Balentine et al., 1998). When brewing in boiling water, black tea produces an orange–red solution with distinct fragrance and flavor (Wan et al., 2009a). TFs are considered to be the major compounds which are associated with color and taste of the black tea solution (Graham, 1992). Oolong tea is mainly consumed in Asian countries such as China and Taiwan (Mukhtar and Ahmad, 2000). As it is a partially fermented tea, the chemical composition and the sensory quality are somewhat intermediate between those of green and black teas (Balentine et al., 1998). Oolong tea contains up to 20% (w/w) catechins of its dry matter. Unlike black tea or green tea, oolong tea has a unique combination of the freshness of green tea and the fragrance of black tea (Wan et al., 2009a).

The Ways of Tea Preparation

Quality of a tea serving varies with quantity of tea, volume and temperature of water, length of brewing time, application of agitation, and additional ingredients such as sugar, lime, and milk (Astill et al., 2001). Preparation of tea differs between countries and individuals within a country. In Asia, green tea is generally prepared by brewing dried tea with boiling water in a tea pot. The first infusion is normally discarded and the subsequent infusions are consumed (Su et al., 2006). Recently, green tea has been ground and packed in the filter bags (2–4 g/bag) and tea liquor has been prepared by infusing a tea bag in a tea pot or a cup/mug for a period of time (three minutes). This method of preparation has become popular, even in the Western countries, because of its convenience. Oolong tea is generally prepared by infusing tea in a tea pot following by stirring and steeping for a period of time (three to five minutes) (Su et al., 2007). In some parts of China, oolong tea is prepared by first quick washing with hot water, then brewing with hot water for a certain of time (three minutes) (Su et al., 2006).

Black tea is prepared by infusing a quantity of tea (in a tea bag) with boiling water in a pot or a cup/mug with a period of less than three minutes. Black tea is usually consumed when it is hot, with or without milk and/or sugar (Astill et al., 2001). In India, Pakistan, and some Middle Eastern countries, black tea is prepared by boiling a quantity of tea in a pan with water for several minutes before consumption (Astill et al., 2001).

The weight of tea in a tea bag varies from 1.5 to 3.25 g. Package instruction for brewing time is three minutes with the recommended volume of water varying between 200 and 235 mL (Astill et al., 2001). Previous studies have demonstrated that conditions for effectively extracting catechins and caffeine from tea with water were: 80°C after 20 minutes, 90°C after 15 minutes, and 95°C after 10 minutes of brewing (Bond et al., 2003; Perva-Uzunalić et al., 2006). For efficient extraction of theanine, a recent study found that most theanine was extracted after brewing tea in water at 80°C after five minutes (Keenan et al., 2010). It appears that household preparation of tea is not efficient for optimal extraction of tea bioactive components and this is the reason why a large volume of tea (several cups) was required for obtaining health benefits.

Recent studies have found that microwave-assisted extraction of bioactive components was very effective (Pan et al., 2003; Spigno and Faveria, 2009), because it disrupts the structure of the cells and thus more tea components are extracted into the beverage (Vuong et al., 2010). It appears that the use of microwaves for 30 seconds to 1 minute after infusing tea in the hot water may help to improve extraction efficiency of tea components. However, further study is needed to provide conclusive evidence.

It is common in Western countries to consume black tea with lime, milk, or sugar (Gööck, 1990). There is no evidence showing an interaction between tea and sugar constituents; however, care is needed when adding sugar because of the correlation between sugar consumption and atherosclerosis, heart problems, dermatosis, neoplasms, obesity, acidosis, hypoglycemia, and dental caries (Wright et al., 2007; Gyntelberg et al., 2009). On the contrary, addition of lime is thought to benefit human health because it not only additionally provides vitamin C but also helps protect tea components from degradation, tea components are more stable at low pH (Vuong et al., 2010).

It is questionable whether addition of milk reduces activity of flavonoids in the tea solution. Findings from a study of nine healthy volunteers showed that the addition of milk reduced antioxidant power (Langley-Evans, 2000), another study of 16 healthy female volunteers also found that addition of milk prevented vascular protective effect of black tea (Lorenz et al., 2007). Evidence on the contrary showed a slightly larger study of 21 healthy volunteers found that addition of milk into tea did not affect its antioxidant properties (Leenen et al., 2000). Other studies ($n = 9$ and $n = 18$) also found that addition of milk into tea did not affect its antioxidant power (Hollman et al., 2001; Reddy et al., 2005). Therefore, it can be tentatively concluded that the addition of milk is unlikely to decrease tea antioxidant power.

TEA CONSUMPTION AND HUMAN HEALTH

Many animal studies have linked tea components with various health benefits as mentioned previously. However, the impacts of these tea components might not be the same in human body because of species differences in the bioavailability and actions of these active components involved (Chen et al., 1997). The bioavailability between individual tea components might be also different in humans. For example, Yang et al. (1998) found that EC and EGC have higher bioavailability than that of EGCG. Therefore, it is complex in determining the mechanism as well as association between tea consumption and health benefits.

Many epidemiological studies have been conducted to investigate the link between tea consumption and human health. This section reviews results from previous epidemiological studies published over the last 10 years to provide information relating to the link between tea consumption and health benefits.

Cancers

Numerous epidemiological studies have investigated the association between tea consumption and prevention of cancers. Findings were inconsistent and contradictory (Table 1). Findings from studies have shown that consumption of green tea (three cups per day or more) significantly lowered the risk of lung cancer among nonsmoking women, but not for smoking women (Zhong et al., 2001). Intake of tea was found not to be associated with prevention of lung cancer among smokers for both men and women (Baker et al., 2005). Further results from studies reported that daily tea consumption was not significantly associated with reduction of the lung cancer risk (Bonner et al., 2005; Li et al., 2008). Overall, the results show that it is

Table 1 The link between tea consumption and human health

Disease	Subjects/population and location	Method for information of tea intake	Volume of tea consumed	Outcomes	Ref.
Lung cancer	Study for two years; 649 women with primary lung cancer and 675 controls aged 35–69 years; Shanghai, China	In-person interview	≥3 cups/week for at least one year	Green tea intake lowered the risk of lung cancer among nonsmoking women (odds ratios (OR) = 0.65; 95% CI, 0.45–0.93)	(Zhong et al., 2001)
	Study for seven years; $n = 41{,}440$ aged 40–79 years, Northeastern Japan	Food frequency questionnaire (FFQ)	≥5 cups/day	Green tea intake was not associated with reduction of lung cancer (The multivariable-adjusted HRs as compared to ≤1 cup/day: 1.17 (95% CI: 0.85–1.61)	(Li et al., 2008)
Skin cancer	Study 1: 2 years; study 2: 3 years; 770 with basal cell (BCC), 696 with SCC and 715 controls subjects aged 25–74 years, New Hampshire	In-person interview	≥2 cups/day	Tea intake was associated with a significantly lower risk of SCC (OR = 0.65; 95% CI 0.44-0.96), but not with BCC (OR = 0.79; 95% CI, 0.63–0.98)	(Rees et al., 2007)
	Study on 300 participants with incidence of esophageal SCC and 571 controls; Golestan province, Iran	In-person interview	≥1 L/day (four cups)	Hot tea (60–64°C) and very hot tea (≥65°C) intake was associated with an increased risk of esophageal cancer (OR = 2.07; 95% CI, 1.28–3.35; and OR = 8.16; 95% CI, 3.93–16.9, respectively)	(Islami et al., 2009)
Liver cancer	Hospital-based study for 3.5 years; 185 incidents of hepatocellular carcinoma (HCC) and 412 controls aged 43–84 years, Italy	FFQ	≥1 cup/week	No association was found between tea intake and reduction of HCC risk (OR = 1.43; 95% CI, 0.76–2.66)	(Montella et al., 2007)
	Study for nine years; $n = 41{,}761$ aged 40–79 years, Northeastern Japan	FFQ	≥5 cups/day	Drinking green tea had a significantly lower risk of liver cancer among men (HRs = 0.63; 95% CI, 0.41–0.98), and women (HRs = 0.50; 95% CI, 0.27–0.90)	(Ui et al., 2009)
Gastrointestinal tract cancer	Study for four years; 627 with biliary tract cancer, 1,037 with biliary stones and 959 controls, Shanghai, China	In-person interview	≥3 cups/week for at least six months	Tea in take significantly reduced risks of biliary stones (OR = 0.73; 95% CI, 0.54–0.98) and gallbladder cancer (OR = 0.56; 95% CI, 0.38–0.83)	(Zhang et al., 2006)
Breast cancer	Study for five years; 297 breast cancer and 665 controls aged 45–74 years, Singapore	24-hour food recalls	≥1 cups/week	There was no association between intake of black tea and breast cancer. Intake of green tea was not associated with decrease of breast cancer among women with low-activity ACE but was strongly associated for women with high-activity ACE (OR = 0.29; 95% CI, 0.10–0.79)	(Yuan et al., 2005)
	Study for 9.6 years; $n = 27{,}323$ participants, Netherlands	FFQ	≥1 cups/day	No association between tea intake and breast cancer in women	(Pathy et al., 2010)
	Study for three years; 501 breast cancer and 594 controls aged 25–74 years, Los Angeles County	In-person interview	≥85.7 mL/day (1/2 cups)	Risk of breast cancer was not statistically associated with black tea intake but with green tea consumption (OR = 0.53; 95% CI, 0.35–0.78)	(Wu et al., 2003)
	Study for one year; $n = 1{,}009$ aged 20–87 years, Southeast China	FFQ	≥2 cups/day	Green tea consumption was associated with a reduced risk of breast cancer (OR = 0.57; 95% CI, 0.47–0.69)	(Zhang et al., 2007)
Pancreatic cancer	Study for 11 years; $n = 102{,}137$, Japan		≥1 cup/day	Tea intake was not associated with reducing the risks of pancreatic cancer	(Luo et al., 2007)
Bladder cancer	Study for two years; 927 bladder cancer and 2,118 controls, Canada	Telephone interview	≥1 cup/day	Tea intake had no association with bladder cancer	(Bianchi et al., 2000)
Prostate cancer	Study for one year; 130 prostate cancer and 274 controls, Hangzhou, China	In-person interview	≥3 cups/day	Green tea intake lowered the risks of prostate cancer (OR = 0.27; 95% CI, 0.15–0.48)	(Jian et al., 2004)

likely that consumption of tea might be linked to prevention of lung cancer for healthy people but not for the smokers. Further epidemiological study in this area is needed.

Squamous cell carcinomas (SCC) are a carcinomatous cancer that occurs in many different organs. A study found that regular drinking tea (at least one cup per day for more than 1 month) was associated with a significantly lower risk of SCC (Rees et al., 2007). It is important to note that tea should not be drunk when it is hot (more than 60°C) because drinking hot tea was found to strongly associate with a higher risk of esophageal SCC cancer development (Islami et al., 2009).

In vivo studies have linked tea flavanoids with prevention of liver cancer. Conversely, an epidemiological study found that frequent drinking tea did not decrease the risk of hepatocellular carcinoma (Montella et al., 2007). Another study found no association between regular tea intake and prevention of liver risks or hepatitis C and B virus status (Inoue et al., 2009). Contrary evidence from a larger population based study ($n = 41761$, nine years follow-up) found that daily consumption of five cups or more could significantly lower the risks of liver cancer (Ui et al., 2009). A meta-analysis conducted recently by Sing et al. (2011) provided more evidence for the link between tea consumption and prevention of the development of primary liver cancer.

Findings have shown that consumption of more than three cups of tea a day for at least three months could significantly lower the risk of breast cancer (Zhang et al., 2007; Shrubsole et al., 2009). However, findings of a study conducted in the US have shown an association between reduction of the breast cancer risks and green tea consumption, but not for black tea intake (Wu et al., 2003). Another study confirmed that black tea consumption did not reduce the risk of breast cancer and drinking green tea could lower the risk of breast cancer among women with high-activity angiotensin-converting enzyme (ACE) but not for those with low-activity ACE (Yuan et al., 2005). A study conducted in the Netherlands found that regular drinking tea has no link with the reduction of breast cancer (Pathy et al., 2010). The results from studies in this area have not been consistent but there is an association between green tea consumption and prevention of breast cancer.

Several reviews have summarized findings from previous *in vivo* studies, which reported that tea catechins could prevent pancreatic, bladder, gastrointestinal, and prostate cancers (Zaveri, 2006; Khan and Mukhtar, 2007; Sharangi, 2009). Recent epidemiological studies found that regular tea intake has no association with reducing the risks of pancreatic cancer (Luo et al., 2007; Lin et al., 2008). No link was found between drinking tea and decreasing the risks of bladder cancer (Bianchi et al., 2000; Woolcott et al., 2002). Studies showed that tea consumption was significantly associated with reduction in the risks of gastrointestinal and prostate cancers (Jian et al., 2004; Bettuzzi et al., 2006; Zhang et al., 2006; Kurahashi et al., 2008). Zhang et al. (2006) revealed that consumption of at least 1 cup of tea daily for at least six months significantly reduced biliary tract cancer. Jian et al. (2004) reported that prostate cancer risk decreased with increasing frequency, duration, and quantity of green tea intake. Green tea consumption was also found to limit an antineoplastic activity, as defined by a decline in prostate specific antigen levels, among patients with androgen independent prostate carcinoma (Jatoi et al., 2003).

Overall, results from epidemiological studies were inconsistent and conflicting. In most of these studies, the data on the tea intake were obtained from the dietary questionnaires to recall the information (Table 1). This is a major limitation of the epidemiological studies inferring the relationship of the tea intake and cancers. The inevitable question that needs to be answered is how much of tea should a person drink daily and for how long to prevent certain types of cancer? In most studies, the tea consumption was recorded in milliliter or cups per day, week, or month for a certain time. Therefore, there are many biases which influence the results and conclusions drawn. For example, the volume of the tea cup was varied among the studies. Furthermore, important parameters such as the type of tea, quantity of tea, volume of water, temperature of water, and the length of brewing time, all of which directly affect the availability of the tea constituents and antioxidant power of the tea beverage have been neglected. Therefore, consumption of five cups might provide lower levels of tea constituents compared to three cups. It is recommended that future epidemiological studies should consider these issues when designing the methods to minimize bias of the results.

Coronary Cardiovascular Disease

A population based-control study in Japan of patients with significant coronary stenosis ($n = 109$, six months) found that consumption of at least six cups of tea a day could lower incidence of coronary artery disease (Sano et al., 2004). Another larger study in Japan ($n = 13{,}916$, one year) showed that daily consumption of at least 10 cups of tea significantly decreased levels of serum total cholesterol in both men and women (Tokunaga et al., 2002). Daily consumption of three cups of tea or more could reduce the risks of coronary cardiovascular disease (CVD) mortality (Gans et al., 2010). The similar findings were observed in a large study ($n = 40530$, 11 years), where the volume of tea required was higher with at least five cups a day (Kuriyama et al., 2006). The volume of tea intake for obtaining benefits is clearly inconsistent.

Overall, tea consumption has been linked with reducing the risks of CVD, but it should be noted that tea might interact with cardiovascular medication (Izzo et al., 2005). One study showed that tea intake could antagonize the effect of warfarin, which produces anticoagulation by inhibiting production of the vitamin K-dependent clotting factors and thus drinking tea might reduce the patient's degree of anticoagulation (Taylor and Wilt, 1999). Another clinical trial found that tea consumption of at least three cups a day may augment drug therapy (Bahorun et al., 2010).

Obesity and Diabetes

Tea is thought to be associated with prevention of obesity and diabetes. Although the mechanism for this association is complex, bioactive components of tea are thought to play a role in modulation of energy balance, endocrine systems, food intake, lipid and carbohydrate metabolism, the redox status, and activities of different types of cells (Kao et al., 2006). In addition, tea components may affect the sympathetic nervous system activity, increase energy expenditure, and promote the oxidation of fat (Rains et al., 2011). However, findings from recent studies are conflicting. A study on obese Chinese women (BMI $\geq$ 28 kg/m^2) with polycystic ovary syndrome ($n = 34$, 3 months) reported that daily consumption of two capsules containing 90 mg EGCG (equivalent to 1.5 cups of tea) did not significantly reduce body weight and did not alter the glucose or lipid metabolism (Chan et al., 2006). On the contrary, a study on obese people in Thailand (BMI $>$ 25 kg/m^2) ($n = 60$, three months) found that consumption of a 250 mg green tea capsule after breakfast, lunch, and dinner could reduce body weight (Auvichayapat et al., 2008). A study in Oklahoma ($n = 41$, two months) with metabolic syndrome found that daily consumption of four cups (928 mg catechins) of tea or two capsules (870 mg catechins) significantly decreased body weight and BMI and lowered lipid peroxidation (Basu et al., 2010). The positive affect of tea intake and obesity was obtained when higher amount of tea extract was taken daily by the participants (750 mg, 870 mg per four cups) in comparison with low amount (180 mg per 1.5 cups) in the study which found no link between tea intake and obesity.

In a large study on African American women ($n = 46$ 906, 12 years), results showed that tea consumption was not associated with reducing the risk of diabetes (Boggs et al., 2010). Results from another study ($n = 36$ 908, five years) also revealed that green tea intake did not associate with prevention of type 2 diabetes; however, daily consumption of 1 cup of black tea showed a reduction of 14% in the risk of diabetes in Asian men and Singaporean women (Odegaard et al., 2008). On the contrary, results from a study in Japan ($n = 17{,}413$) aged 40–65 years and had no history of type 2 diabetes for five years, showed that there was no association between consumption of black or oolong teas and diabetes. However, daily consumption of at least six cups of green tea was associated with a reduced risk for type 2 diabetes (Iso et al., 2006). A meta-analysis also revealed that tea consumption of more than four cups per day (RR, 0.8; 95% CI, 0.7–0.93) may play a role in the prevention of type 2 diabetes (Jing et al., 2009). Consumption of 1500 mL (six cups) of oolong tea a day significantly lowered concentrations of plasma glucose and fructosamine, thus drinking oolong tea might be an effective adjunct to oral hypoglycemic drugs in the treatment of type 2 diabetes (Hosoda et al., 2003). Again from the findings, it is difficult to draw a conclusion on what kind of tea, how much and how long a person should consume tea to obtain the health benefits. However, epidemiological evidence showed that tea consumption was likely to prevent the risk of obesity and diabetes. It should be noted that consumption of tea with sugar is associated with weight control and diabetes (Gyntelberg et al., 2009), thus the amount of sugar added in tea should be minimized.

Other Impacts of Tea Intake on Health

In animal studies, tea bioactive components have been found to improve the immune system, oral health, and inflammatory processes (Hamer, 2007). Bioactive components have been found to prevent microbial diseases and oral health (Zaveri, 2006; Khan and Mukhtar, 2007), but there is no epidemiological evidence in human studies to confirm these health benefits.

Tea intake has been reported to improve bone health. Daily consumption of two to three cups of tea has been found to associate with higher spinal bone mineral density and daily intake of four cups or more was found to increase total body bone mineral density (Chen et al., 2003). In addition, bone mineral density was found higher in the old women who drank tea in comparison with whom did not drink tea. The inference is that tea consumption might protect against osteoporosis in older women (Hegarty et al., 2000). Tea has been found to affect the mood and cognitive performance in humans. Intake of tea caffeine (250 mg) could increase alertness, jitteriness, and blood pressure, whereas, intake of theanine (200 mg) was found to antagonize the effect of caffeine on blood pressure but did not significantly affect jitteriness, alertness, or other aspects of mood (Rogers et al., 2008). Results from another study found that intake of two cups of black tea (400 mL) for 24 hours could positively affect human mood (Scott et al., 2004).

Tea consumption has been found to associate with various positive health impacts; however, it is questionable whether there is any negative impact of consuming tea. Tea flavanoids interact with proteins and major digestive enzymes such as α-amylase, pepsin, trypsin, and lipase (Sekiya et al., 1984; He et al., 2007), thus it is thought that tea intake may inhibit absorption and digestibility of the dietary proteins and foods but there is limited epidemiological evidence confirming this link. Results from a study showed that addition of the tea extract to the diet did not change protein digestibility of weaning male rats (Chang et al., 1994). Another study also found that polyphenols in tea waste incorporated in the diet did not affect the food digestibility of goats (Kondo et al., 2004). Therefore, the absorption and digestibility of the dietary proteins and foods might not be affected by the tea consumption. Further animal and human studies are needed to investigate this association.

Iron deficient and iron deficiency anemia are major problems, especially for young women with approximately two billion and one billion people worldwide affected, respectively (Thankachan et al., 2008). Tea polyphenols were found to bind with iron (Zijp et al., 2000), and therefore tea consumption might decrease the iron absorption and increase risk of iron deficiency especially in vulnerable group. However, findings from one study found that consumption of decaffeinated black tea and green tea (four cups per day) during or immediately following the meals did not affect on the absorption of iron and other minerals such as calcium, copper, magnesium, and zinc among young adults (Prystai et al., 1999). Another study also found that tea intake had no association with the risks of iron depletion among healthy adults (Mennen et al., 2007). Tea intake was also not found to be related to iron status in vulnerable group who is at risk of iron deficiency (Hogenkamp et al., 2008). Conversely, findings from a study revealed that intake of black tea at one or two cups per day decreased iron absorption by 49% ($P < .05$) or 66% ($P < .01$), respectively (Thankachan et al., 2008). Further study defining the link between tea intake and iron absorption is necessary. To minimize the negative impact of tea intake and iron absorption, tea should not be consumed during meals (Johnson, 2006).

CONCLUSIONS

Tea is a rich source of bioactive constituents such as flavanoids, caffeine, and theanine which have been found to link with various health benefits such as prevention of cancers, CVD, obesities, and diabetes. However, availability of these components in a tea cup varies and depends on the types of tea and the ways of preparation. Eight major types of tea can be produced from the fresh leaves of *C. Sinensis* and these teas are different in terms of biochemical quality and sensory attributes. Preparing tea with milk or lime with/without sugar does not affect the antioxidant properties of the tea constituents. However, amount of sugar addition should be controlled if large volume of tea is consumed daily.

Results from epidemiological studies were inconsistent and thus it is difficult to conclude how much of tea a day and how long a person should consume tea to obtain the health benefits. Most studies confirmed that there is no harm in drinking too much tea and tea consumption has associated positive health impacts, and yet, drinking several cups of tea daily can keep the doctor away.

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