Trends in Food Science & Technology 78 (2018) 95–106

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: www.elsevier.com/locate/tifs

Review

Tea consumption and disease correlations

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ARTICLE INFO

Keywords:
Black tea
Green tea
Oolong tea
White tea
Cancer
Obesity
Diabetes mellitus
Cardiovascular diseases
Other diseases

ABSTRACT

Tea is the most widely consumed beverage in the world next to water and is obtained from the leaves *Camellia sinensis*. In recent years, the potential health benefits and effect mechanisms of tea have attracted a lot of interest. The potential health benefits of tea have been attributed to its various phenolic compounds with unique biological properties found in tea. These phenolic compounds are especially catechins and their derivatives, which constitute at most 30% of the dry weight of the tea. Tea is a new and effective strategy for reducing the severity of neurological diseases and for protecting against obesity, cardiovascular disease, type 2 diabetes and certain types of cancer (ovaryum, lung, skin, breast, endometrial, prostate, bladder, oral and colorectal cancers).

Overall, the study that supports the health benefits of tea is increasing. But, the amounts of and the frequency of tea consumption that is associated with potential health benefits vary greatly from work to work and this situation creates difficulty in determining the optimal consumption amount and frequency that tea can exhibit health benefits. For this reason, we aimed to examine the health effect of the tea and how much consumption is to investigate whether it meets the claimed health benefits.

Within that frame, there is a need for more studies on the possible health effects of tea. While studying on that effect, the effects of various doses, forms (in synthetic or natural product matrix), exposure in different periods (short or long term) on health should be studied. However, currently the conducted studies are promising for tea is a bioactive component like polyphenol, theaflavins, thearubigins, caffeine and mineral. In addition, although the fact intake with diet proved to be reliable at the end of the conducted acute and chronic toxicity test is another positive part, safety of bioactive component in tea should be supported through further studies.

1. Introduction

The first documented sources of tea appeared in China in the third century CE (Munday, 2016), but archaeological studies indicate that the tea was first consumed in the early Palaeolithic period (Cooper, 2012). Besides its being the oldest drinks, tea has enormous medical, economic and cultural importance since ancient times (Xia et al., 2017). With the awareness that tea improves health and prevents some diseases, its consumption has been considered as a "health-promoting habit" and modern medical researchers have provided the scientific basis for this belief over time (Chen & Lin, 2015; Feng, Ng, Kua, Lee, & Preedy, 2015; Khan & Mukhtar, 2013; Venkateswara, Sirisha, & Chava, 2011). Because tea has antioxidant, thermogenic, anti-inflammatory, cholesterol-lowering, antimicrobial, neuroprotective, anti-hypertensive and anti-carcinogenic properties (Li & Zhu, 2016), its presence in daily human diet is significantly high (Qi et al., 2017). Studies have shown that tea has beneficial effects on many chronic diseases such as cancer, cardiovascular diseases, obesity, diabetes and neurological diseases (Heber et al., 2014; Lee, Su, Pasalich, & Binns, 2013; Mao et al., 2010; Miller et al., 2016; Tomata et al., 2016; b, Wang, Yang, Zhang, & Wu, 2014).

However, many topics like toxicological effects, doses, amounts, usage in the body, advantages and disadvantages, etc. of these active molecules need to be examined. For these reasons this article was reviewed to evaluate health effects of tea.

2. Tea and its composition

The tea plant has two main types, *Camellia sinensis* and *Camellia assamica*. *Camellia sinensis* is a long-lived and small-leaf plant that can withstand cold weather, while *Camellia assamica* is a short-lived, more sensitive and large-leaf plant that can grow easily in tropical and rainy regions (Üstün & Demirci, 2013). Tea is mainly produced from the leaves of plant Camellia sinensis and it is the most widely consumed beverage worldwide next to water (Tang, Li, Qiu, Zhou, & Ma, 2009b). There are four main types of tea: black tea, green tea, white tea and oolong tea (Butt et al., 2014; Vernarelli & Lambert, 2013). Worldwide,

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https://doi.org/10.1016/j.tifs.2018.05.026
Received 14 November 2017; Received in revised form 13 April 2018; Accepted 31 May 2018
Available online 06 June 2018
0924-2244/

approximately 78% of total tea production account for black tea while 20% of total tea production account for green tea (Yuan, 2011). Although these main types of tea are produced from the same plant, they are obtained from different fermentation processes (Yajima, 2014). Green tea is non-fermented while oolong tea is semi-fermented and black tea is fully fermented (Chan, Soh, Tie, & Law, 2011). In addition degree of fermentation for white tea is approximately 10–20% (Kim, Kim, & Lee, 2012). These differences in the fermentation process lead to important differences in the final polyphenols balance (Matthews, 2010). For example; from white tea toward black tea, theaflavins and thearubigins increase while catechins decrease (Selena Ahmed, 2012). Unlike fermented and semi-fermented teas the major polyphenols of unfermented green tea belong to catechin family (Hintzpeter, Stapelfeld, Loerz, Martin, & Maser, 2014; Jówko, 2014) and these are (−)-epicatechin-3-gallate, (−)-epicatechin, (−)-epigallocatechin and (−)-epigallocatechin-3-gallate (EGCG) (Xiang et al., 2016). Furthermore, most of the chemical changes such as production of oxidized polyphenolic compounds such as theaflavins and thearubigins which are account for the sensory characteristics of black tea are occurred during the fermentation process of black tea (Samanta et al., 2015; Wang & Ho, 2009). Among all tea types, white tea is thought to be the oldest form of tea due to it is the least processed tea (Kim, Choi, & Park, 2015; Mao, 2013) and it contains gamma-amino butyric acid (GABA) and L-theanine (Malongane, McGaw, & Mudau, 2017). The polyphenols found in black and green tea are given in Fig. 1 (Lorenz, 2013; Yong Feng, 2006).

Thearubigins and theaflavins in black tea and catechins in green tea are the substances account for the physiological effects of tea (Lorenz, 2013) including inhibition of cancer cell proliferation, inflammation, platelet aggregation and anti-apoptotic proteins; regulation of glucose and lipid metabolism and DNA repair; stimulation immune function; modulation detoxification enzymes and anti-oxidant, anti-inflammatory and antimicrobial activity (Katiyar, Elmets, & Katiyar, 2007; Serafini, Del Rio, Yao, Bettuzzi, & Peluso, 2011; Tenore, Campiglia, Giannetti, & Novellino, 2015). The antioxidant activities of catechins depend on hydroxyl group at C-3 position in the basic structure or the higher degree of hydroxylation of the B ring (Tenore, Stiuso, Campiglia, & Novellino, 2013). Among green tea catechins, EGCG is the most abundant, most potent and most studied catechins as well as most powerful antioxidant for cancer chemoprevention (Chan et al., 2011; Du et al., 2012; Johnson, Bailey, & Mukhtar, 2010). In a study by Hajiaghaalipour, Kanthimathi, Sanusi, and Rajarajeswaran (2015), demonstrated that the antioxidant, anticancer and DNA protective effects of white tea (*C.sinensis)*. The high antioxidant activities correlated significantly to their phenolic content and white tea extracts showed potential as chemotherapeutic agents. They suggested that regular consumption of white tea could maintain good health and protect the body against colorectal cancer. Besides catechins, caffeine contributes to the stimulating properties of tea and theanine contributes to the relaxing properties of tea and both of these have synergistic physiological effects in developing mental alertness (Selena Ahmed, 2012).

3. Tea consumption and disease correlations

Tea consumption protects against the development of chronic diseases (Mao, 2013) and is associated with reduced risk of cardiovascular diseases, cancer, inflammation, obesity and type 2 diabetes (Gondoin, Grussu, Stewart, & McDougall, 2010). As a result of a study, it has been suggested that tea is safe and cheap drink and that its consumption should be supported due to potential health benefits (Lee et al., 2013).

3.1. Tea consumption and cancer

Tea polyphenols with chemo-preventive properties provide the protection against all stages of carcinogenesis by preventing inflammation and progression of tumor due to its antioxidant properties against free radicals and thus it initiates apoptosis and cell cycle arrest (Lee et al., 2013). Black tea polyphenols protect against different types of cancer through their ability to inhibit carcinogenic activating phase 1 enzymes, activate antioxidant and detoxifying enzymes, modulate xenobiotic-metabolizing enzymes, scavenge free radicals, protect against DNA damage, induce apoptosis and inhibit angiogenesis, cell proliferation, invasion and metastasis (Kumar, Pillare, & Maru, 2010; Nagini & Senthil Murugan, 2013). In addition, green tea polyphenols protect against different types of cancer by inhibition of anti-apoptotic protein expression, induction of pro-apoptotic protein expression, activation of caspase-3 and caspase-9, inhibition of cell proliferation, metastasis and angiogenesis and induction of cell cycle arrest and thus it inhibit uncontrolled cell proliferation, induce apoptosis and reduces the risk of cancer cell formation (Amin, Zhang, & Shin, 2013; Kumar &

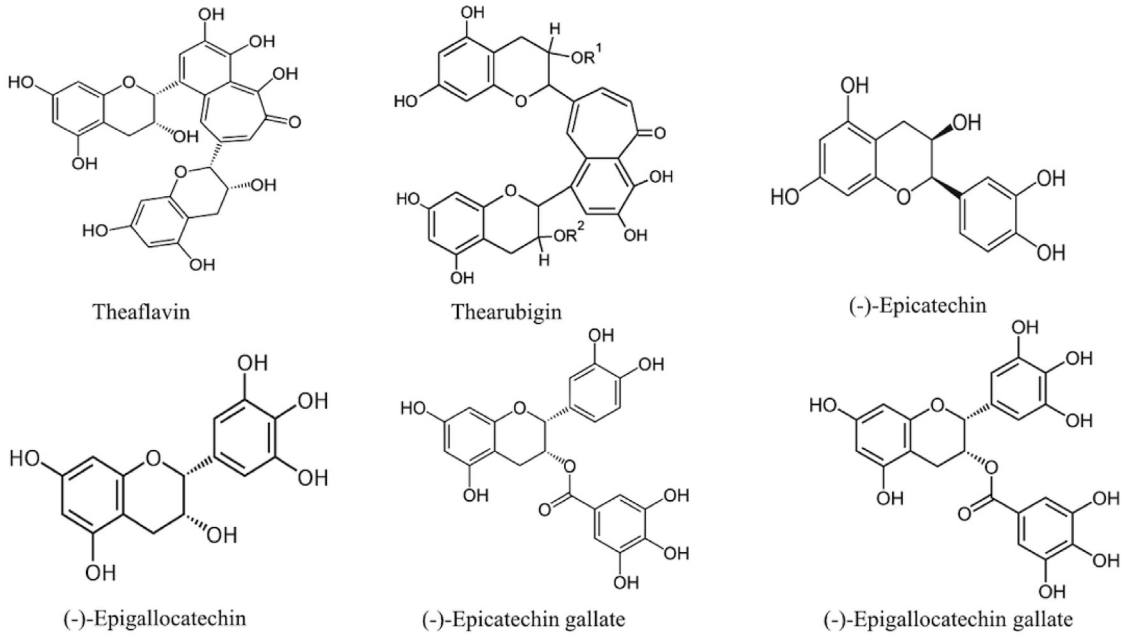

Fig. 1. The polyphenols found in black and green tea.

Table 1
The consumption amounts of EFSA recommended for health effects of tea and its component (EFSA Panel on Dietetic Products & Allergies, 2010,2011, 2012, 2015).

Health effects	Tea components and its mechanism of influence on health	Consumption recommendation for its health benefits
The protection of body weight	Green tea polyphenols/catechins	400–600 mg catechins/day 4 cups green tea/day (800 mL)
	EGCG	115–300 mg EGCG/day 2-5 cups green tea/day
	Caffeine → The regulation of fat metabolism and energy expenditure	Minimum 150 mg caffeine/day
	Caffeine → The promotion of thermogenesis	Minimum 300 mg caffeine/day (at least 3 portions)
	EGCG → Glucose homeostasis	84–386 mg EGCG/day 1,5–8 cups green tea/day
The protection against cardiovascular disease	Green tea extract → The protection from cardiovascular disease	69–657 mg EGCG/day 1-13 cups green tea/day
	Green tea extract → The regulation of levels of cholesterol	616 mg green tea extract/day 277 mg EGCG/day 4,5-5,5 cups green tea/day
	Green tea catechins → Heart health	500–1000 mg catechins 3-10 cups green tea/day
	Green tea extract → The protection the elasticity of capillaries	616 mg green tea extract/day 277 mg EGCG/day 4,5-5,5 cups green tea/day
	Green tea extract → Natural antioxidant property	616 mg green tea extract/day 277 mg EGCG/day 4,5-5,5 cups green tea/day
The protection against cancer	Green tea → The protection from oxidative stress	> 1/2 cup green tea/day
	Green tea catechins → Skin cancer	500–1000 mg catechins/day 3-10 cups green tea/day
	Green tea catechins → Breast and ovarian cancer	500–1000 mg catechins/day 3-10 cups green tea/day
	Green tea catechins → Prostate cancer	500–1000 mg catechins/day 3-10 cups green tea/day
Other health effects	Tea → Mental and cognitive health	3-6 cups green tea/day
	Black tea → Mental stimulant	1 cup green tea/day
	Black tea → Cognitive performance	2-3 cups green tea/day
	Green tea → Cognitive performance	4-6 cups green tea/day
	Caffeine → Cognitive performance	Minimum 32 mg caffeine/day
	Green tea catechins → Colon health	500–1000 mg catechins/day 3-10 cups green tea/day
	Tea → Bone health	1-3 cups green tea/day
	Tea → Oral health	1 cup green tea/day
	Tea → Immune health	1 cup green tea/day

Bhatia, 2014). Especially, green tea polyphenols has recently become the focus of attention due to anticancer activity (Thakur, Gupta, & Gupta, 2012).

3.2. Tea consumption and ovarian cancer

Ovarian cancer is the seventh cause of cancer deaths and the eighth most frequent cancer in the world (White et al., 2014). Although familial, age and genetic factors are the strongest risk factors, dietary and environmental factors and lifestyle can also affect the ethology of ovarian cancer (Doubeni, Doubeni, Myers, & Doubeni, 2016; Lee et al., 2013). A study has demonstrated that the increase in the frequency of green tea consumption can reduce the risk of ovarian cancer. However, again, this study suggests that there is a need for additional works to explain whether black tea is associated with ovarian cancer (Zhang, Binns, & Lee, 2002). Black tea consumption has been found to associate with both a reduction in ovarian cancer risk (Baker et al., 2007) and an increased risk ovarian cancer (Leung et al., 2016). The results are contradictory, but according to the results of a recent meta-analysis, there was an inverse relationship between tea consumption and ovarian cancer (Zhan, Wang, Pan, & Lu, 2017). Green tea polyphenols exhibits beneficial effects on ovarian cancer with the reduction of expression of protein involved in angiogenesis, inflammation, cell motility and cell signalization in epithelial ovarian cancer cells and the induction of apoptosis (Trudel et al., 2012) and black tea polyphenols exhibits beneficial effect by inhibiting ovarian cancer cells (Gao, Rankin, Tu, & Chen, 2016).

Estrogen has been suggested as a risk factor for ovarian cancer (Brown & Hankinson, 2015; Hunn & Rodriguez, 2012). Previous studies have found that green tea polyphenols may modify estrogen metabolism or conjugation (Fuhrman et al., 2013a) and caffeine in tea may alter metabolism and circulating levels of estrogen (Kotsopoulos, Eliassen, Missmer, Hankinson, & Tworoger, 2009; Sisti et al., 2015). Green tea consumption related to decreased level of estrogen in pre- and postmenopausal women while black tea consumption related to increased level of estrogen in postmenopausal women. As a result, the risk of ovarian cancer has been suggested to may be reduced by green tea and may be increased by black tea (Leung et al., 2016).

3.3. Tea consumption and lung cancer

Lung cancer is the main cause of cancer deaths in the world (Cruz, Tanoue, & Matthay, 2011). It has been suggested that dietary factors contribute to the development of lung cancer (Khan, Afaq, & Mukhtar, 2010). Although smoking is major risk factor in the development lung cancer (Mao, Yang, He, & Krasna, 2016), it has been reported that other lifestyle factors such as tea consumption may also affect the risk of lung cancer (Yuan, 2011). Tea polyphenols provides protection against lung cancer by the induction of apoptosis and annexin-1; the inhibition of tumor progression, nitrosation, cell proliferation, cyclooxygenase-2 in lung cancer cells and the activation of transcription factors such as activator protein-1 and nuclear factor kappa beta, which play an important role in the development of lung cancer cells (Li & Zhu, 2016; Tang, Wu, Zhou, Wang, & Yu, 2009a; Wang, Zhang, Liu, Shen, & Li, 2014a). As a result of a dose-response analysis of observational studies, it has been suggested that there are protective effect of green tea against

Table 2
Studies showing the relationship between tea and health.

Diseases	Study types	Tea consumption (min-max)	Health effects of tea consumption	References
Ovarian cancer	Case control	Consumption (−) Consumption (+)	The frequency of tea consumption ↑ ⇒ the risk of ovarian cancer ↓	(Zhang et al., 2002)
Ovarian cancer	Meta analyse	> 1 cup/week > 4 cups/day	Tea consumption ⇒ not associated with the risk of ovarian cancer	(Zhou et al., 2007)
Ovarian cancer	Systematic review	Consumption (−) ≥5 cups/day	High tea consumption ⇒ reduced risk of ovarian cancer (5 studies) and not associated with the risk of ovarian cancer (9 studies)	(Oppeneer & Robien, 2011)
Ovarian cancer	Systematic review	Consumption (−) ≥4 cups/day	Green tea consumption ⇒ reduced risk of ovarian cancer and better prognosis	(Trudel et al., 2012)
Ovarian cancer	Case control	Consumption (−) ≥4 cups/day	Tea consumption ⇒ reduced risk of ovarian cancer	(Lee et al., 2013)
Lung cancer	Meta analyse	–	Tea consumption ⇒ reduced risk of lung cancer	(Wang et al., 2014a)
Lung cancer	In vitro	–	White tea extract ⇒ provides apoptosis in lung cancer	(Mao et al., 2010)
Lung cancer	Review	No consumption > 10 cups/day	High green tea consumption (> 3 cup/day) ⇒ protect against smoking-induced lung cancer	(Liang, Binns, Jian, & Lee, 2007)
Lung cancer	In vitro	–	Green tea extract ⇒ protect against lung cancer	(Lu et al., 2012)
Lung cancer	Meta analyse	Consumption (−) > 7 cups/day	> 2 cups green tea/day ⇒ 18% reduction in risk of lung cancer Black tea consumption ⇒ not associated with the risk of lung cancer	(Tang et al., 2009a)
Skin cancer	Rat study	–	Green tea ⇒ smaller and less tumor formation	(Meeran, Akhtar, & Katiyar, 2009)
Skin cancer	Case control	> 1 cups/day (regular)	Regular tea consumption ⇒ reduced risk of skin cancer	(Rees et al., 2007)
Breast cancer	Case control	Consumption (−) > 3 times/day	Green tea consumption ↑ ⇒ the risk of breast cancer ↓ Black tea consumption ⇒ not associated with the risk of breast cancer	(Wu et al., 2003)
Breast cancer	Meta analyse	–	Green tea consumption ⇒ not associated with the risk of breast cancer	(Wu et al., 2013)
Breast cancer	Case control	–	Green tea consumption ⇒ reduced the risk of breast cancer (weakly)	(Shrubsole et al., 2009)
Breast cancer	Prospective	Consumption (−) > 4 times/day	Black tea consumption ⇒ a positive relationship with breast cancer	(Larsson et al., 2009)
Breast cancer	Case control	< 1 cup/day > 3 cups/day	Tea consum., especially green tea, ⇒ reduced the risk of breast cancer (among premenopausal women) Tea consum., especially green tea, ⇒ increased the risk of breast cancer (among postmenopausal women)	(Li et al., 2016)
Colon cancer	Prospective	1-2 cups/day > 5 cups/day	Green tea ⇒ not associated with lower risk of colorectal cancer	(Suzuki et al., 2005)
Colon cancer	–	–	Regular green tea consumption ⇒ reduced the risk of colorectal cancer (in non-smokers)	(Yang et al., 2011)
Liver cancer	Prospective cohort	< 3 cups/day > 5 cups/day	Green tea consumption ⇒ not significantly associated with the risk of liver cancer	(Inoue et al., 2009)
Liver cancer	Prospective cohort	< 1 cups/day > 5 cups/day	Green tea consumption ↑ ⇒ the risk of liver cancer ↓	(Ui et al., 2009)
Liver cancer	Meta analyse	Consumption (−) > 10 cups/day	Tea consumption ↑ ⇒ the risk of liver cancer ↓	(Sing, Yang, Gao, Gao, & Xiang, 2011)
Prostate cancer	Meta analyse	Consumption (−) > 10 cups/day	Green tea ⇒ a protective effect on prostate cancer but black tea ⇒ no protective effect on prostate cancer	(Zhang et al., 2011)
Oesophagus cancer	Meta analyse	Consumption (−) > 10 cups/day	Green tea ⇒ a protective effect on esophageal cancer but black tea ⇒ no protective effect on esophageal cancer	(Zhang, 2013)
Oral cancer	Meta analyse	–	High tea consumption ⇒ reduced the risk of oral cancer (in green tea consumption but not in black tea)	(Wang et al., 2014)
Endometrial cancer	Meta analyse	–	Tea consumption ⇒ lower the risk of endometrial cancer	(Tang et al., 2009b)
Endometrial cancer	Case control	< 7 times/day > 7 times/day	Tea consump., especially green tea ↑ ⇒ the risk of endometrial cancer ↓ (poorly)	(Gao et al., 2005)
Endometrial cancer	Meta analyse	Consumption (−) > 5 cups/day	Tea consumption ⇒ a protective effect on endometrial cancer	(Je & Park, 2015)
Endometrial cancer	Meta analyse	Consumption (−) > 7 cups/day	Green tea consumption ↑ ⇒ the risk of endometrial cancer ↓ +1 cup/day green tea consumption ⇒ 11% reduction in risk of endometrial cancer	(Zhou, Zhang, Wei, & Wang, 2016)
CVD	Meta analyse	–	3 cups/day tea consumption ⇒ reduced the risk of CVD, cardiac death, total mortality, cerebral infarct and intracerebral hemorrhage	(Zhong et al., 2015)
CVD	Multi ethics	Consumption (−) > 1 cups/day (regular)	Regular tea consumption ⇒ reduced the risk of CVD	(Miller et al., 2016)
CVD	Meta analyse	Consumption (−) > 10 cups/day	Green tea consumption (−) ⇒ the risk of CVD, intracerebral hemorrhage ↑ than < 1 cup/day consumption; < 1 cup/day consumption ⇒ the risk of stroke and myocardial infarction ↑ than 1–3 cups/day consumption; > 10 cups/day consumption ⇒ the levels of LDL cholesterol ↓ than < 3 cups/day consumption	(Pang et al., 2016)
CVD	Prospective	< 1 cups/day > 6 cups/day	Moderate green and oolong tea consumption ⇒ a lower risk of death from CVD	(Mineharu et al., 2011)
CVD	Meta analyse	–	Green tea consumption ⇒ in a significant decrease in systolic blood pressure, total and LDL cholesterol	(Onakpoya, Spencer, Heneghan, & Thompson, 2014)
Obesity	Meta analyse	Caffeine consum. < 300 mg/day > 300 mg/day	EGCG + caffeine ⇒ positive effects on body weight loss and maintaining body weight	(Hursel, Viechtbauer, & Westerterp-Plantenga, 2009)
Obesity	Rat	Green tea polyphenols	Tea polyphenols ⇒ body weight loss	(Heber et al., 2014)

(*continued on next page*)

Table 2 (*continued*)

Diseases	Study types	Tea consumption (min-max)	Health effects of tea consumption	References
Obesity	Rat	Black tea extract	Black tea polyphenols ⇒ anti-obesity effect by inhibiting intestinal lipid absorption	(Uchiyama, Taniguchi, Saka, Yoshida, & Yajima, 2011)
Obesity	In vitro	White tea extract	White tea polyphenols ⇒ reduce triglyceride synthesis during adipogenesis	(Söhle et al., 2009)
Diabetes	Prospective	< 1 cup/day > 5 cups/day	> 3 cups/day tea consumption ⇒ 42% reduction in risk of type 2 diabetes	(Van Dieren et al., 2009)
Diabetes	Meta analyse	Consumption (−) > 6 cups/day	> 3 cups/day tea consumption ⇒ lower the risk of type 2 diabetes	(Yang et al., 2014)
Diabetes	Meta analyse	< 1 cup/day > 4 cups/day	> 4 cups/day tea consumption ⇒ lower the risk of type 2 diabetes	(Jing et al., 2009)
Diabetes	Case control	Consumption (−) > 4 cups/day	> 4 cups/day tea consumption ⇒ 16% reduction in risk of type 2 diabetes	(Consortium, 2012)
Diabetes	Prospective cohort	Consumption (−) > 6 times/day	Black tea consumption ↑ ⇒ the risk of diabetes↓ (in populations at risk of developing type 2 diabetes)	(Odegaard et al., 2008)
Neurological	Prospective cohort	< 1 cup/day > 5 cups/day	Green tea consumption ⇒ significantly lower the risk of dementia	(Tomata et al., 2016)
Neurological	Cohort	–	Regular tea consumption ⇒ lower the risk of cognitive decline and impairment	(Ng, Feng, Niti, Kua, & Yap, 2008)
Neurological	Cross sectional	1 cup/day > 2 cups/day	Higher green tea consumption ⇒ lower the risk of cognitive impairment	(Kuriyama et al., 2006)
Mortality	Prospective	< 1 cup/day > 5 cups/day	> 5 cups/day tea consumption ⇒ 13–17% (men and women, respectively) reduction in risk of death from all causes	(Saito et al., 2015)

lung cancer while there are no important effect of black tea on lung cancer (Wang, Yu, Wu, & Zhang, 2012). In addition, it has also been suggested that there are chemo-preventive effect of white tea on the mechanisms associated with lung tumor formation due to its anti-carcinogenic properties (Mao et al., 2010).

3.4. Tea consumption and skin cancer

Skin cancer is the one of the most alarming increase in incidence worldwide (Pil et al., 2016). Exposure to solar ultraviolet radiation is the major cause of skin cancer (Miura, Hughes, Arovah, van der Pols, & Green, 2015). Depletion of the ozone layer has caused more solar UV-B radiation reaching the Earth's surface (Norval et al., 2011). This situation has been seen as a contributing factor to the increased risk of skin cancer when combined with increased life expectancy and dietary habits and lifestyle changes (Katiyar, 2011). For this reason, effective chemo-preventive agents and strategies are needed to control or reduce the risk of UV-induced skin cancer (Katiyar et al., 2007). Polyphenols in black tea and green tea are thought to be a chemo-preventive agent for skin cancer because they prevent penetration of UV radiation into the skin (Kumar & Bhatia, 2014) and DNA damage by reducing skin inflammation caused by UV radiation with their antioxidant properties (Miura et al., 2015). In addition, green tea has been considered as a skin photo-protection (Katiyar, 2011) since green tea polyphenols prevent photo-carcinogenesis and UVB-induced immune suppression; induce interleukin 12 and thus repair UVB-induced DNA damage; stimulate cytotoxic T cells in skin tumor; inhibit angiogenesis in skin tumor; contribute to the chemoprevention of skin cancer and influence many biomarkers that are involved in UVB-carcinogenesis (Katiyar et al., 2007; Nandakumar, Vaid, & Katiyar, 2011). Furthermore, caffeine in tea induce apoptosis in UVB-damaged keratinocytes (Song, Qureshi, & Han, 2012) and inhibit ATR/Chk1 pathway which is a significant mechanism on UVB-induced carcinogenesis (Conney et al., 2012). A case-control study have suggested that there is no association between tea consumption and the risk of skin cancer (Asgari et al., 2011) while another case-control study have suggested that there is an inverse association between tea consumption and the risk of skin cancer (Rees et al., 2007).

3.5. Tea consumption and breast cancer

Breast cancer, the most frequent cancer in women, is the most frequently diagnosed cancer and the main cause of cancer-related deaths (Donepudi, Kondapalli, Amos, & Venkanteshan, 2014; Shah, Rosso, & Nathanson, 2014; Li et al., 2016). Asian countries have lower incidence of the breast cancer than Western countries (Bhoo-Pathy et al., 2013) and as a result it has been hypothesized that higher green tea consumption have associated with lower breast cancer risk (Iwasaki et al., 2010). This hypothesis is mainly based on the fact that green tea polyphenols can affect the key enzyme involved in estrogen biosynthesis (Fuhrman et al., 2013b; Khan, Zhao, Khan, Walker, & Dasmahapatra, 2011). Estrogen are thought to be significant in breast cancer development in both pre- and postmenopausal women (Chumsri, Howes, Bao, Sabnis, & Brodie, 2011) and high circulating estrogen levels are related to high risk of breast cancer in postmenopausal women (Dai et al., 2010). In addition, since aromatase inhibitors inhibit the conversion of androgens into estrogen, the these inhibitors have been widely used (Files, Ko, & Pruthi, 2010; Hanamura & Hayashi, 2017). Also, tea polyphenols inhibit aromatase that are converted androgens into estrogen (Capellino, Straub, & Cutolo, 2014; Shrubsole et al., 2009) and thus the association between the risk of breast cancer and tea consumption has been widely studied. Additionally, tea polyphenols show anti-breast cancer activity by modulating cell-signalling pathways; inhibiting DNA methylation, angiogenesis and vascular endothelial growth factor (VEGF) expression in stromal cells and ductal tumor cells; suppressing DNA damage; interacting with target proteins that exhibit an inhibitory effect on the breast cancer cell lines; inducing apoptosis and cell cycle arrest and showing anti-metastasis, anti-oxidant and anti-proliferation effect (Leong, Mathur, & Greene, 2008; Rafieian-Kopaei & Movahedi, 2017; Xiang et al., 2016; Yu et al., 2014). Thus, it has been suggested that tea may act as a chemo-preventive agent against the breast cancer development (Wu, Yu, Tseng, Hankin, & Pike, 2003). As a result studies, moderate consumptions of green tea was found to protect against breast cancer (Sinha, Biswas, Nabavi, & Bishayee, 2017). However, there are studies show that there is no relationship between green tea and breast cancer risk or there is a weak relationship between green tea and reduced breast cancer risk or there is a significant positive correlation between black tea and breast cancer risk (Larsson, Bergkvist, & Wolk, 2009; Wu, Zhang, & Kang, 2013, p. 1).

3.6. Tea consumption and colorectal cancer

Colorectal cancer is one of the most frequent cancers worldwide (Fleming, Ravula, Tatishchev, & Wang, 2012) and is the third leading

cause of cancer mortality (Siegel, DeSantis, & Jemal, 2014). It has been recently suggested that dietary and other lifestyle factors may have protective effects on the risk of colorectal cancer (Yang et al., 2011). But the results are contradictory. A study has shown that green tea consumption was not associated with lower risk of colorectal cancer (Suzuki et al., 2005), but several studies have shown that regular tea consumption reduced the risk of colorectal cancer (Liu et al., 2013; Yang et al., 2007, 2011). In addition, prospective and case-control studies have shown that there is no association between tea consumption and the risk of colorectal cancer (Dominianni, Huang, Berndt, Hayes, & Ahn, 2013; Green et al., 2014; Sinha et al., 2012; Wang et al., 2013) and there is a significant inverse association between daily tea consumption and the risk of colon cancer (Su & Arab, 2002). EGCG, a green tea polyphenols, inhibit human epidermal growth factor 3, cyclooxygenase-2, DNA methyltransferases and vascular endothelial growth factor receptors and these mechanisms have a significant role in the development and progression of colon cancer (Moseley, Morris, Knackstedt, & Wargovich, 2013).

3.7. Tea consumption and endometrial cancer

Endometrial cancer is one of the sixth most frequent gynaecological cancer among women in the world (Li & Feng, 2016; Sinreih et al., 2017) and dietary habits can increase or decrease the risk of this cancer by affecting the risk factors of endometrial cancer in the long term (Je & Park, 2015). Estrogen is the major contributing factor to the progression of endometrial cancer (Oh et al., 2017; Yang et al., 2017). Tea contains caffeine that causes changes in hormone levels, such as reducing free estradiol and testosterone and increasing plasma estrogen and sex hormone binding globulin (SHBG). In addition to caffeine, green tea also contains a large amount of the phytoestrogens that are claimed to have protective effects against endometrial cancer due to its anti-estrogenic properties (Tang et al., 2009b). A study shown that there is no or little association between the risk of endometrial cancer and tea consumption (Yang, Crowe, Cairns, Reeves, & Beral, 2015). However another study shown that tea consumption reduces the risk of endometrial cancer (McCann, Yeh, Rodabaugh, & Moysich, 2009). Contrary to the protective effect of green tea, black tea consumption was positively associated with the risk of endometrial cancer (Butler & Wu, 2011).

3.8. Tea consumption and obesity

Obesity is a public health issue that has recently called attention (Chan & Woo, 2010; Hanson, Rutten, Wouters, & Rennard, 2014) because of the dramatic increase in its prevalence (Djalalinia, Qorbani, Peykari, & Kelishadi, 2015) and the association with chronic disease (Bombak, 2014). Lifestyle interventions such as dietary modification form the basis of obesity management (Shukla, Buniak, & Aronne, 2015). Recently there has been growing interest in tea and its polyphenols due to their beneficial effect on obesity (Cheng et al., 2017; Mao, 2013). Black and green tea polyphenols inhibit lipid intake, digestion and absorption (Pan, Gao, & Tu, 2016) and the activity of α-glucosidase, pancreatic lipase and amylase (Glisan, Grove, Yennawar, & Lambert, 2017; Miao, Jiang, Jiang, Zhang, & Li, 2015; Yang & Kong, 2016) and thus inhibit intestinal absorption of nutrients (Unno et al., 2009); stimulate hepatic lipid metabolism (Lee et al., 2015); promote thermogenesis, fat oxidation and faecal lipid excretion (Huang et al., 2014); enhance lipolysis (Chen, Osaki, & Shimotoyodome, 2015); suppress appetite (Lu, Zhu, Shen, & Gao, 2012); decrease the proliferation and differentiation of preadipocytes and lipogenesis (Wang et al., 2014b); prevent the expansion of adipose tissue (Meydani & Hasan, 2010) and thus prevent pathological processes of obesity and exhibit the anti-obesity effect (Gondoin et al., 2010; Pan et al., 2016). Polyphenols in oolong tea also inhibit the activity of α-glucosidase and the formation of small-intestine micelle and regulate lipid metabolism and thus exhibit the anti-obesity effect (He et al., 2009; Tucci, 2010). In addition, it has been suggested that the white tea polyphenols are a natural source that stimulates lipolytic activity in adipocytes and inhibits adipogenesis (Söhle et al., 2009). Besides tea polyphenols, caffeine in tea affect central nervous system activity by inhibiting the phosphodiesterase that rapidly degrades catechol-*O*-methyl-transferase and intracellular cyclic adenosine monophosphate (cAMP) (Rains, Agarwal, & Maki, 2011; Westerterp-Plantenga, 2010) and thus increases energy expenditure (Türközü; Acar Tek, 2017). Furthermore, it has been shown that the consumption of tea polyphenols with regular exercise reduces the risk of obesity (Sharangi, 2009).

3.9. Tea consumption and diabetes mellitus

Diabetes mellitus, is characterized by chronic hyperglycaemia, has recently been growing public health issues worldwide (Asif, 2014; Kharroubi & Darwish, 2015). Lifestyle interventions, such as dietary modification, are among the factors underlying the development of type 2 diabetes (Korat, Willett, & Hu, 2014). One of the dietary factors, tea contains caffeine and polyphenols that possess anti-diabetic effect and thus tea has recently received attention its health effects on diabetes (Fu et al., 2017). Green tea polyphenols affect glucose metabolism and insulin signalization (Khan & Mukhtar, 2013); decrease serum glucose, total cholesterol and triglycerides (Roghani & Baluchnejadmojarad, 2010) and advanced glycation end products formation (Sampath, Rashid, Sang, & Ahmedna, 2017); inhibit the activity of amylase and glucosidase (Fu et al., 2017); modulate insulin secretion, insulin sensitivity and glucose tolerance (Mousavi, Vafa, Neyestani, Khamseh, & Hoseini, 2013) and the gene expression of the phosphoenolpyruvate carboxykinase and glucose-6-phosphatase (Yasui et al., 2010); mitigate cytokine-induced beta cell damage (Chacko, Thambi, Kuttan, & Nishigaki, 2010); increase glucagon like peptide 1 (Liu et al., 2014); mimic the cellular effect of insulin (Suzuki, Miyoshi, & Isemura, 2012); attenuate high glucose induced adverse effects (Yang, Mao, Xu, Ma, & Zeng, 2014); alleviate oxidative stress (Fu et al., 2017); promote tyrosine phosphorylation of insulin receptors (Chacko et al., 2010) and exhibits anti-diabetic effect (Coppock & Dziwenka, 2016, pp. 633–652), so green tea has been considered as a new strategy and supplementary substance for the prevention or treatment of both obesity and diabetes (Kim & Kim, 2013; Rafieian-Kopaei et al., 2014). Besides green tea polyphenols, black tea polyphenols has also been shown to have the potential to prevention of SGLT1 and GLUT2-mediated glucose uptake by inhibiting carbohydrate hydrolysing enzymes such as alpha-glycosidase and alpha-amylase (Satoh, Igarashi, Yamada, Takahashi, & Watanabe, 2015; Striegel, Kang, Pilkenton, Rychlik, & Apostolidis, 2015), the potential to alleviate the oxidative stress parameters associated with diabetes (Kumar & Rizvi, 2015) and the potential to regenerate of damaged pancreas (Yang et al., 2014). In addition, in vitro studies on rats show that green and black tea polyphenols help to prevent hyperglycaemia by inhibiting damage to β-cells and increasing insulin activity (Anderson & Polansky, 2002). However, it has been suggested that green and black tea polyphenols is not hypoglycaemic in individuals with type 2 diabetes (MacKenzie, Leary, & Brooks, 2007). As a result of a study, main mechanism for the anti-diabetic effect of the black tea polyphenols was through insulin secretion while green tea polyphenols was through insulin resistance (Tang, Li, Liu, Huang, & Ho, 2013). Furthermore, it has been found that white tea consumption has improved insulin sensitivity and glucose tolerance in pre-diabetic mice (Alves et al., 2015) and white tea has strong anti-adipogenic and lipolytic effects (Söhle et al., 2009). Therefore, it has been reported that white tea may exhibit anti-diabetic activity by decreasing hyperlipidaemia and oxidative stress following insulin resistance (Islam, 2011).

3.10. Tea consumption and cardiovascular disease

Cardiovascular disease is one of the major causes of morbidity and

mortality in the world (Tarride et al., 2009). Lifestyle factors such as dietary factors are among the factors underlying the aetiology of cardiovascular disease (Eilat-Adar, Sinai, Yosefy, & Henkin, 2013). Recently, there is a growing interest in the protective effects of tea on cardiovascular disease (Deka & Vita, 2011). Tea polyphenols are manifested by their cardioprotective ability to reduce intestinal cholesterol absorption (Zhong, Huan, Cao, & Yang, 2015), blood cholesterol levels, risk of thrombosis, inflammation and oxidative damage (Hodgson, 2008), blood pressure (Arab, Khan, & Lam, 2013) and LDL oxidation (Suzuki-Sugihara et al., 2016); regulate favourably vascular reactivity and plasma lipid profile (Babu, Pon, & Liu, 2008); exhibit anti-thrombotic, anti-oxidant, anti-inflamatuvar and anti-proliferative activity (Deka & Vita, 2011; Jochmann, Baumann, & Stangl, 2008) and beneficial effect on vascular function (Moore, Jackson, & Minihane, 2009); scavenge free radicals (Chan et al., 2011; Hernández, Rodríguez-Rodríguez, & Sanchez-Muniz, 2004); activate anti-oxidant enzymes; inhibit pro-oxidant enzymes (Lambert & Elias, 2010), the proliferation of vascular smooth muscle cells (Babu et al., 2008) and transcription factor nuclear factor kappa beta which mediates the production of cytokines and adhesion molecules (Bhardwaj & Khanna, 2013) and promote nitric oxide release (Miller et al., 2016). In addition, according to literature green tea polyphenols have been reported to prevent cardiovascular diseases such as atherosclerosis, hypertension, endothelial dysfunction, ischemic heart diseases, cardiomyopathy, cardiac hypertrophy and congestive heart failure (Bhardwaj & Khanna, 2013), to improve systolic and diastolic dysfunction (Lustosa et al., 2016), to associated with lower risk of stroke (Arab et al., 2013), to suppress platelet adhesion, to scavenge free radicals and to improve lipid profile by inhibiting key enzymes involved in lipid biosynthesis (Babu et al., 2008). Furthermore, black tea polyphenols have been reported to suppress postprandial hypertriacylglyceremia, to enhance endothelial function and to reduce plasma cholesterol levels, so may show beneficial effect on cardiovascular disease (Dias, Changarath, Damodaran, & Joshi, 2014; Tenore et al., 2013). Consequently tea polyphenols can be an important strategy in reducing the risk of cardiovascular disease (Naito & Yoshikawa, 2009).

3.11. Tea consumption and neurological disease

Neurological diseases, especially Alzheimer's disease and Parkinson disease, are one of the major causes of death worldwide especially in the developed countries (Firoz et al., 2015). Lifestyle factors such as dietary factors affect central nervous system health and disease (Gomez-Pinilla & Gomez, 2011), contribute to the brain's ability to fight against neurological disease (Gomez-Pinilla & Kostenkova, 2008), protect against cognitive decline and dementia (Smith & Blumenthal, 2016), enhance neural repair (Gomez-Pinilla, 2011) and improve cognitive function (Meeusen, 2014). It has been believed that tea consumption has affected cognitive performance for many years and tea traditionally seen as a natural cognitive enhancer (Feng et al., 2015). Studies have shown that regular tea intake is related to better verbal fluency scores, cognitive function (Feng et al., 2012; Shen et al., 2015) and lower the risk of cognitive decline (Noguchi-Shinohara et al., 2014) and cognitive impairment (Ma et al., 2016). Tea polyphenols exhibit anti-inflammation (Ide et al., 2014) and anti-oxidant activity (Schmidt et al., 2014); induce iron-chelating effect (Singh, Mandal, & Khan, 2016); modulate cell survival and cell signalling pathways (Schmidt et al., 2014); regulate the secretion of stress hormone, the levels of L-theanine in brain neurotransmitter system and the production of catecholamine (Feng et al., 2015); reduce oxidative stress associated with age-related brain disorder (Almajano, Vila, & Ginés, 2011); show protective effect on cognitive function and thus tea polyphenols have been proposed as potential neuroprotective agent (Mo et al., 2013). In addition, caffeine in tea has showed protective effects against neurological disease such as Alzheimer's and Parkinson disease by stimulant effects on the central nervous system (Cappelletti, Daria, Sani, & Aromatario, 2015; Prediger, 2010).

Alzheimer's disease, a major cause of dementia, is the most frequent chronic progressive neurodegenerative disease (Crews & Masliah, 2010; Hoshino et al., 2013; Tam & Pasternak, 2017). This disease slowly destroys memory and the ability to think and eventually makes execution of the simplest tasks of everyday life impossible (Cole & Kramer, 2016). Tea polyphenols reduce the risk of Alzheimer's disease by reducing toxic the levels of brain Amyloid β (Aβ) peptide (Dragicevic et al., 2011) and the production of Amyloid β (Aβ) peptide, Alzheimer's disease trigger protein, (Ho, Hung, & Chang, 2013b; Ide et al., 2014); showing their protective effect against diabetes, depression and hypercholesterolemia (Ho, Hung, & Chang, 2013a).

Parkinson disease is the second most frequent chronic progressive neurodegenerative disease (Massano & Bhatia, 2012; Seidl, Santiago, Bilyk, & Potashkin, 2014). Tea polyphenols show neuroprotective effects against Parkinson disease with anti-aggregation, anti-chelating, anti-inflamatuvar and anti-oxidant properties and inhibitory activity on a-synuclein aggregation and modulation of intracellular signalling pathways (Caruana & Vassallo, 2015; Dutta & Mohanakumar, 2015). Tea consumption has shown to protective against Parkinson disease (Li, Ji, & Shen, 2012; Pan, Jankovic, & Le, 2003; Barranco; Quintana, Allam, Del Castillo, & Navajas, 2009), to be associated with lower risk of Parkinson disease (Hu, Bidel, Jousilahti, Antikainen, & Tuomilehto, 2007) and to delay the age of this disease onset (Dutta & Mohanakumar, 2015). Consequently, tea consumption has been suggested as a promising dietary modification that may slow down the formation of age-related neurodegenerative disease (Seidl et al., 2014).

3.12. Tea consumption and infectious disease

Infectious diseases, known as global health problems, are a leading cause of many unexpected and sudden deaths in the world (Kanchan, 2016, pp. 477–487; Seebaluck-Sandoram & Mahomoodally, 2017; Seib & Jennings, 2016, pp. 443–458). Antimicrobial agents is the most important and common strategy used in the treatment of infectious diseases (Leekha, Terrell, & Edson, 2011). Polyphenolic components of tea, especially green tea polyphenols, have been shown to have antimicrobial effect against a wide variety of microorganism (Reygaert & Jusufi, 2013; Taylor, Hamilton-Miller, & Stapleton, 2005). Tea polyphenols exhibit antimicrobial activity by binding to the bacterial lipid bilayer cell membrane, inhibiting bacterial production of toxic metabolites, inhibiting the essential bacterial enzymes (Reygaert, 2014). In addition, green tea polyphenols have revealed to have anti-influenza activity (Lee et al., 2012; Matsumoto, Yamada, Takuma, Niino, & Sagesaka, 2011). EGCG, a green tea polyphenols, adhere to the lipid membranes of microorganism's cell wall and disrupts the lipid membranes; inhibit the folic acid metabolism of microorganism and damage the microorganism particles, so EGCG exhibits antiviral, antifungal and antibacterial activity (Steinmann, Buer, Pietschmann, & Steinmann, 2013). Also, EGCG have been shown to have the therapeutical and antimicrobial effect on Zika virus infections (Carneiro, Batista, Braga, Nogueira, & Rahal, 2016), on herpes simplex virus infections (De Oliveira et al., 2013), on hepatitis B virus infection (Ye et al., 2009), on hepatitis C virus infection (Fukazawa, Suzuki, Wakita, & Murakami, 2012; Wang et al., 2016), on HIV infection (Li, Hattori, & Kodama, 2011) and on anthrax infection caused by Bacillus anthracis which is associated with high mortality (Goel, 2015; Pillai et al., 2015; Falcinelli, Shi, Friedlander, & Chua, 2017).

4. Tea consumption recommendations

EFSA (2015) stated that green tea polyphenols/catechins consumption from all sources between 400 and 600 mg per day (4 cups green tea/day = 800 mL) and EGCG consumption from all sources 115–300 mg (2–5 cups green tea/day) may be safe in healthy adults (EFSA Panel on Dietetic Products & Allergies, 2015).

The consumption amounts of EFSA recommended for health effects of tea and its component are shown in Table 1.

The studies showing the relationship between tea and health are given in Table 2.

5. Conclusions and recommendations

Tea, especially green tea, has recently become the focus of attention due to potential health benefits. The effects of tea on health are generally associated with the compounds in its content. Tea has polyphenol, theaflavins, thearubigins, caffeine and mineral content. These polyphenols have anti-mutagenic, anti-viral, anti-oxidant, anti-inflammatory properties in various biological systems and thus can have a great potential as an alternative strategy for treatment of chronic diseases. Tea also associated with the risk of type 2 diabetes by exhibiting beneficial effect on glucose metabolism and insulin sensitivity. In addition, it has the desired effects by modulating estrogen levels in circulation and thus it is important in the development of hormone-related cancers. The consumption of moderate levels of tea, increases daily energy expenditure and physical performance and reduces fatigue. Polyphenol, theaflavins, thearubigins, caffeine and mineral content in tea also improves motor performance, cognitive performance, a sense of wakefulness and energy, and exhibits its stimulant effect by developing short-term memory and neuroprotective effect as adenosine receptor antagonist. Some individuals have side effects such as headache, nausea, etc., more studies are needed on more subjects worked on more individuals to determine the effective and reliable dose of tea. Therefore, and consumption of 2–5 cups tea per day for adults will be beneficial for adults. Although the fact intake with diet proved reliable at the end of the conducted acute and chronic toxicity test is another positive part, safety of tea should be supported through further studies.

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