DOI 10.1002/mnfr.200800218 Mol. Nutr. Food Res. 2009, *53*, 256 – 265

Review

Tea, Coffee and Prostate Cancer

Andy H. Lee, Michelle L. Fraser and Colin W. Binns

School of Public Health, Curtin University of Technology, Perth, WA, Australia

Worldwide, prostate cancer has the second highest incidence of all cancers in males with incidence and mortality being much higher in affluent developed countries. Risk and progression of the disease may be linked to both genetic and environmental factors, especially dietary factors. Tea and coffee are two of the most popular beverages in the world and have been investigated for possible effects on health outcomes, including cancer. However, very little dietary advice for their consumption exists. The evidence for a relationship between coffee or tea consumption and prostate cancer is reviewed in this paper. While current evidence indicates that coffee is a safe beverage, its consumption probably has no relationship with prostate cancer. Tea, especially green tea, has shown some potential in the prevention of prostate cancer. While evidence from epidemiologic studies is currently inconclusive, strong evidence has emerged from animal and *in vitro* studies. We also consider what level of evidence is required to make recommendations for preventive measures to the public. Although evidence on the relationship between coffee, tea and prostate cancer is not complete, we consider it strong enough to recommend tea as a healthier alternative to coffee.

Keywords: Coffee / Dietary guidelines / Epidemiologic studies / Prostate cancer / Tea

Received: April 30, 2008; revised: June 2, 2008; accepted: June 5, 2008

1 Introduction

Worldwide, prostate cancer has the second highest incidence of all cancers in males [1] and in many developed countries, it is the most common neoplasm in men beyond middle age [2]. Prostate cancer incidence and mortality varies widely between geographic regions, with overall rates in high-income countries such as Australia and USA being nearly six times higher than in middle to low-income countries such as China, Japan, and African countries [1, 2]. However, the reported incidence in countries such as China is increasing rapidly [3]. This variation in incidence suggests that risk and progression of the disease may be linked to both genetic and environmental factors, especially dietary factors. Discovering possible chemopreventive dietary factors is important in the case of prostate cancer due to the aging populations of most Western nations. Prostate cancer is also an ideal candidate disease for chemoprevention because relative survival after diagnosis is high [4] due to its long latency and typical detection in older men who usually have a slower rate of progression [2].

Tea and coffee are two popular beverages that have been investigated for possible effects on health outcomes, including cancer. Coffee was once suspected of increasing the risk of various cancers [5] whereas tea, especially green tea has shown promise in the prevention of cancers including gastrointestinal tract [6 – 8], skin [9, 10], breast [11 – 13], pancreas, esophagus, and lung [14]. Epidemiological studies on tea and prostate cancer have generated inconsistent results [15], however a recent Chinese case-control study reported a significant dose response relationship between green tea consumption and prostate cancer risk [16].

Despite coffee and tea being two of the most commonly consumed beverages all over the world [17], very little dietary advice for their consumption exists. Recently, several reviews have addressed the potential relationship between tea and prostate cancer prevention [18 – 20]. Although they have concluded that tea or tea compounds show promise in prostate cancer prevention, little effort has been made to translate these findings into public health guidelines. This paper therefore, considers whether evidence is currently strong enough to make any dietary recommendations on tea or coffee and prostate cancer prevention by presenting the epidemiologic evidence as well as mechanistic evidence from *in vitro* and animal model studies.

Correspondence: Professor Colin W. Binns, School of Public Health, Curtin University of Technology, GPO Box U 1987, Perth, WA 6845, Australia
E-mail: c.binns@curtin.edu.au
Fax: +61-8-92662958

Abbreviations: CI, confidence interval; **EGCG,** (–)epigallocatechin-3-gallate; **GTC,** green tea catechin; **OR,** odds ratio; **RCT,** randomized controlled trial; **RR,** relative risk

2 Materials and methods

Published articles were located by searching the PubMed, CINAHL, and ProQuest databases with the keywords "tea" and "prostate cancer" and "coffee" and "prostate cancer" without any restriction on publication date. The corresponding reference lists were also searched for relevant articles. The National Health and Medical Research Council's Levels of Evidence for Clinical Practice Guidelines were used to divide and evaluate existing evidence for both coffee and tea [21]. The level of evidence refers to the study design used to minimize bias with the highest level involving a systematic review of randomized controlled trials (RCTs), followed by at least one properly designed RCT, then pseudo- RCTs, then observational studies. Also considered is evidence quality – methods used to minimize bias in the study design and conduct, evidence relevance – extent to which findings can be applied in other settings, and strength of evidence – magnitude and reliability of the treatment effect [21]. In addition, animal model and *in vitro* studies have been included to establish biological plausibility of the observed effects.

3 Results

3.1 Coffee and tea: Patterns of consumption

Tea and coffee are two of the world's most popular beverages and both are consumed in most countries [17]. Worldwide, tea consumption is second only to water and approximately three cups of tea are drunk for every cup of coffee [17]. However, coffee is the preferred drink throughout the majority of Europe and the Americas with 71.5% of coffee consumption taking place in developed countries [17]. Tea consumption dominates in the developing world with 76.6% of consumption taking place in these countries [17]. Tea is also the more popular beverage in liters in Australia [22] and Britain [17]. Of the total tea produced and consumed, 78% is black, 20% green, and less than 2% oolong [23]. Black tea is primarily consumed in Western countries while green tea is mainly consumed in China, Japan, India, and a few countries in North Africa and the Middle East [23].

3.2 The composition of tea and coffee

Coffee is produced by infusing ground, roasted coffee beans, the most popular forms being *Coffea arabica* and *C. canephoria* var. *robusta* [17]. The three most common kinds of tea are green, black, and oolong tea and these are all derived from the *Camellia sinensis* plant [24]. Green tea leaves are steamed when harvested to prevent fermentation whereas black tea is fermented as leaves wither then are rolled and crushed. Oolong tea is partially fermented and considered to be about half as fermented as black tea [24].

Coffee and tea are both complex substances consisting of many compounds. Coffee is reported to contain more than a thousand different chemicals, several of which have been shown to have physiological effects [5]. The stimulatory effects of caffeine [25] and antioxidant activity of chlorogenic acid and caffeic acid have been extensively researched [26] and other micronutrients including magnesium, potassium, niacin, and vitamin E have also been suspected of health effects [5].

Green, oolong, and black teas all contain potentially cancer preventive compounds, however the different manufacturing process changes the profile of these compounds considerably [24]. Polyphenols are the most researched component of tea. Most of the polyphenolic content of green tea is flavanols, know as catechins, including (–)-epicatechin, (–)-epicatechin-3-gallate, (–)epigallocatechin, and (–)epigallocatechin-3-gallate (EGCG) [24]. In black and oolong tea, the fermentation process results in oxidation of simple polyphenols to complex theaflavins and thearubigins and reduces the catechin content of black tea to approximately a third of that of green tea [24].

3.3 Coffee and prostate cancer: Epidemiologic evidence

Coffee has been studied extensively for relationships with various cancers. Early case-control studies indicated a possible positive relationship between coffee consumption and several cancers [27, 28]. It is possible however, that the association between coffee drinking and other unhealthy behaviors such as smoking and lack of exercise generated these observations as subsequent studies have produced little evidence of any significant relationship with cancer [5].

The possible relationship between coffee and prostate cancer has been investigated in epidemiologic studies since the 1980s. We identified seven case-control [29–35] and four cohort studies [36–39] reporting on coffee consumption and prostate cancer risk and two cohort studies examining prostate cancer mortality [40, 41]; see Table 1. Results of these studies were very inconsistent. Overall, no relationship has emerged with almost all studies reporting no association or nonsignificant positive and nonsignificant inverse associations with prostate cancer. No dose-response relationship emerged from any of these studies and only one reported statistically significant results [29]. However, this hospital-based case-control study conducted in Taiwan, only quantified coffee consumption as "yes" or "no" and the number of coffee consumers in the sample was very low consisting of 31 cases (13.1%) and 36 controls (7.5%) [29]. It is also possible that consumption of coffee in this Taiwanese study was associated with other aspects of a Western diet that may increase cancer risk. Although many of the other studies quantified coffee consumption in more detail and were all conducted in North American and European populations where coffee drinking is more common, coffee

Table 1. Summary of epidemiologic studies of coffee and prostate cancer

Country	Study design	Sample size	Coffee consumption level	Results: Adjusted OR, RR (95% CI) or *p* for trend	Reference
Taiwan	Case-control (hospital-based)	237 cases, 481 controls	Coffee drinking *versus* non-drinking	OR: 1.88 (1.07 – 3.30)	[29]
Canada	Case-control (population-based)	399 cases, 476 population controls, 621 cancer controls	>119 drink years *versus* <57 drink years[a)]	OR: 1.1 (0.6 – 2.0) for population controls	[30]
Greece	Case-control (hospital-based)	320 cases, 246 controls	≥3 cups/day *versus* none	*p* for trend: 0.27	[31]
Canada	Case-control (population-based)	1623 cases, 1623 controls	<1 cup/day *versus* none 1 – 3 cups/day *versus* none ≥4 cups/day *versus* none	OR: 0.8 (0.6 – 1.1) OR: 1.0 (0.7 – 1.3) OR: 1.1 (0.8 – 1.5)	[32]
Canada	Case-control (population-based)	617 cases 637 controls	0 – 500 g/day *versus* none >500 g/day *versus* none	OR: 0.84 (0.58 – 1.22) OR: 0.97 (0.65 – 1.44)	[33]
Sweden	Case-control (population-based)	406 cases, 1218 controls	1 – 2 cups/day *versus* none 3 – 5 cups/day *versus* none 6 – 9 cups/day *versus* none	OR: 1.77 (0.65 – 5.09) OR: 1.99 (0.78 – 5.46) OR: 1.91 (0.73 – 5.30)	[34]
USA (Utah)	Case-control (population-based)	326 cases, 685 controls	1 – 20 cups/week *versus* none >20 cups/week *versus* none	OR: 0.99 (0.68 – 1.47) OR: 1.09 (0.75 – 1.60)	[35]
Canada	Cohort (retrospective)	3400 (145 developed prostate cancer)	>250 mL/day *versus* none	RR: 1.4 (0.84 – 2.32)	[36]
USA (Hawaii)	Cohort	20 316 (198 developed prostate cancer)	>2.5 cups/day *versus* none	RR: 1.1 (0.7 – 1.7)	[37]
USA (Hawaii)	Cohort	7999 (174 developed prostate cancer)	2 – 4 cups/week *versus* ≤ 1 cup/week ≥5 cup/week *versus* ≤1 cup/week	RR: 0.96 (0.39 – 2.37) RR: 0.92 (0.59 – 1.44)	[38]
USA (Hawaii)	Cohort	7355 men, 108 prostate cancer	Not stated	Not stated, no significant relationship observed	[39]
USA	Cohort (examined mortality)	17 633 men, 149 died of prostate cancer	3 – 4 cups/day *versus* <3 cups/day ≥5 cups/day *versus* <3 cups/day	RR: 0.8 (0.6 – 1.2) RR: 1.0 (0.6 – 1.6)	[40]
USA (California)	Cohort (examined mortality)	21 295 seventh day adventists, 113000 non adventists	Not stated	Not stated, nonstatistically significant inverse association	[41]

a) Drink years: average number of drinks daily multiplied by duration of drinking in years.

was rarely the main focus of the dietary questionnaire. Hence, exposure misclassification including cup size and caffeine variation of particular coffees [42] as well as confounding may have affected the results of these studies.

3.4 Coffee and prostate cancer: *In vitro* and animal evidence

A vast amount of research in animals and *in vitro* cell cultures has also generated inconsistent findings about the role of coffee and its components in cancer. Coffee contains large number of compounds, some of which have been identified as having potentially chemopreventive effects including caffeine [43], chlorogenic and caffeic acids [44] and the diterpenes cafestol and kahweol [45], and others, having potentially carcinogenic effects also including caffeine and methylglyoxal [46].

Some early evidence from molecular, cellular, and animal studies indicated that coffee could inhibit relevant DNA repair mechanisms, modify the apoptotic response and perturb cell cycle checkpoint integrity [47, 48]. One study reported an association between coffee drinking and mutations in the K-ras gene in exocrine pancreatic cancer [49]. However, the majority of research has reported a wide range of chemopreventive effects [45, 46]. Recent *in vitro* and *in vivo* studies in rats have also shown that coffee can suppress proliferation and invasion, possibly by inducing cell cycle arrest, apoptosis and the invasion by scavenging ROS, and can ameliorate abnormal lipoprotein profiles [50].

It is possible that coffee may possess both mutagenic and antimutagenic potential. In the past there has been concern that coffee consumption may increase the risk of bladder and pancreatic cancer, however, two recent reviews have concluded that it is unlikely to have any substantial effect on risk [1, 51]. For all other cancers, the World Cancer Research Fund reported that evidence is too limited to draw a conclusion [1]. In light of all the evidence, coffee probably has no relationship with the risk of prostate cancer.

Table 2. Summary of epidemiologic studies of tea and prostate cancer

Country	Study design	Sample size	Tea type	Tea consumption level	Results: Adjusted OR, RR (95% CI) or O:E ratio of deaths	Reference
China	Case-control (hospital-based)	130 cases, 274 controls	Green	Tea drinking *versus* nondrinking Tea drinking over 40 years *versus* nondrinking >1.5 kg tea leaves/year *versus* none >3 cups/day *versus* none	OR: 0.28 (0.17 – 0.47) OR: 0.12 (0.06 – 0.26) OR: 0.09 (0.04 – 0.21) OR: 0.27 (0.15 – 0.48)	[16]
Japan	Matched case-control (hospital-based)	140 cases, 140 controls	Green and black	≥10 cups green tea/day *versus* ≤1 cup/day ≥1 cup black tea /day *versus* none	OR: 0.67 (0.27 – 1.64) OR: 1.51 (0.89 – 2.56)	[53]
Canada	Case-control	617 cases, 637 controls	Not specified	>500 g/day (≈2 cups) *versus* none	OR: 0.70 (0.50 – 0.99)	[33]
Canada	Case-control (population-based)	1623 cases, 1623 controls	Not specified	<1 cup/day *versus* none 1 – 3 cups/day *versus* none ≥4 cups/day *versus* none	OR: 1.0 (0.8 – 1.2) OR: 1.2 (0.9 – 1.5) OR: 1.1 (0.8 – 1.5)	[32]
Canada (Montreal)	Case-control (population-based)	399 cases, 476 population controls, 621 cancer controls	Not specified	>107 drink-years *versus* <54 drink years[a)]	OR: 2.0 (1.3 – 3.0) for population controls OR: 1.6 (1.0 – 2.4) for cancer controls	[30]
USA (Utah)	Case-control (population-based)	362 cases, 685 controls	Not specified	>5 cups/week *versus* none	OR: 1.06 (0.72 – 1.52) for subjects ≤ 67 years OR: 0.90 (0.59 – 1.36) for subjects>67 years	[35]
Japan	Prospective cohort	49 920 (404 developed prostate cancer)	Green	Localized prostate cancer ≥5 cups/day *versus* <1 cup/day Advanced prostate cancer 1 – 2 cups/day *versus* <1 cup/day 3 – 4 cups/day *versus* <1 cup/day ≥5 cups/day *versus* <1 cup/day	 RR: 1.04 (0.72–1.52) RR: 1.10 (0.61 - 1.97) RR: 0.83 (0.47 – 1.48) RR: 0.52 (0.28 – 0.96)	[54]
Japan	Cohort	19 561 (110 developed prostate cancer)	Green	5 cups/day *versus* <1 cup/day	HR: 0.85 (0.50 – 1.43)	[58]
USA (Hawaii)	Cohort	7999 (174 developed prostate cancer)	Green and black	Ever *versus* never drank green tea Ever *versus* never drank black tea	RR: 1.47 (0.99 – 2.19) RR: 0.83 (0.61 – 1.13)	[38]
USA (Hawaii)	Prospective cohort	7833 (149 developed prostate cancer)	Black	>once/day *versus* almost never	RR: 0.6 (CI not stated)	[59]
UK (London)	Prospective cohort	14 085 (185 developed prostate cancer)	Not specified	≥10 cups/day *versus* <4 cups/day	O:E 0.60 for <4 cups/ day O:E 0.82 for ≥10 cups/day	[60]
Italy	Retrospective cohort	107 prostate cancer cases	Not specified	≥1 cup/day *versus* nonuse	RR: 0.9 (0.5 – 1.7)	[61]
Canada	Retrospective cohort	3400 (145 developed prostate cancer)	Not specified	>500 mL/day *versus* none	RR: 1.02 (0.62–1.65)	[36]

O:E: observed to expected ratio.

a) Drink years: average number of drinks daily multiplied by duration of drinking in years.

3.5 Tea and prostate cancer: Epidemiologic evidence

Table 2 summarizes epidemiologic studies of tea and prostate cancer from the literature. A hospital-based case-control study in China, where green tea is predominantly consumed provides promising evidence for a role of tea in prostate cancer prevention [16]. A total of 130 cases and 274 hospital inpatients without any malignant disease were interviewed in detail about the type, duration, quantity, and frequency of tea consumption. Compared to nontea drinkers, the odds ratio (OR) was 0.28 (95% confidence interval (CI): 0.17–0.47) for those drinking green tea, 0.12 (95% CI: 0.06–0.26) for drinking tea longer than 40 years, 0.09 (95% CI: 0.04–0.21) for consuming more than 1.5 kg of tea leaves *per* year, and 0.27 (95% CI: 0.15–0.48) for drinking more than three cups (1 L) daily. According to the US Food and Drug Administration, this study received high methodological quality ratings [52]. Another hospital-based case control study of 140 cases and 140 controls in Japan reported an OR for drinking two to ten cups of green tea daily ranging from 0.67 to 0.99 [53], but did not attain statistical significance, probably due to the small sample size [52].

A slight reduction in prostate cancer risk was also reported by a larger Canadian case-control study involving 617 cases and 637 population controls [33]. An OR of 0.70 (95% CI: 0.50–0.99) was reported with consumption of more than 500 g (approximately two cups) of tea *per* day [33]. Another case-control study conducted in Montreal, Canada [30] reported an increased risk and two conducted in Canada [32] and Utah, USA [35] reported no association between tea consumption and prostate cancer, although alternative explanations for the observed effects could not be ruled out [30].

Cohort studies have reported inconsistent results, however a recent prospective cohort study in Japan reported a significant dose-dependant relationship between green tea consumption and reduced risk of advanced prostate cancer but no association with localized prostate cancer [54]. These findings suggest the effects of green tea may vary according to prostate cancer stage and are supported by earlier results of small clinical trials and animal model studies [55–57]. In the cohort study, the multivariate relative risk (RR) for advanced prostate cancer for consumption of five or more cups/day *versus* less than one cup was 0.52 (95% CI: 0.28–0.96) [54]. Another Japanese cohort study of 19 561 men (110 cases) reported a slight but nonsignificant decrease in risk [58]. The hazard ratio for consumption of five cups of green tea/day *versus* < 1/day was 0.85 (95% CI: 0.50–1.43). Another cohort of 7999 men of Japanese ancestry living in Hawaii showed a borderline significant increase in risk for green tea consumption, OR = 1.47 (95% CI: 0.99–2.19), but no association for black tea [38]. However, an earlier cohort study involving 7833 Hawaii men of Japanese ancestry observed a weak albeit significant inverse association between black tea intake and prostate cancer incidence, with RR being 0.6 for consuming more than one cup daily *versus* almost never [59]. Three subsequent cohort studies conducted in the UK [60], Italy [61], and Canada [36] where black tea is predominantly consumed [23], found little association between tea consumption and prostate cancer incidence.

The epidemiologic evidence to date is limited in several aspects. Of the three studies reporting positive results [16, 53, 54] two were relatively small case-control study designs that are open to bias due to their retrospective design [52]. In addition, the majority of studies lacked comprehensive assessment of tea intake. For example, only six specified the type of tea consumed as green [16, 38, 53, 54, 58] or black [38, 53, 59]. Although green tea has produced more promising results, only a small number of studies (5) specifically examined its consumption. Also, many studies did not comprehensively assess level of tea intake, for example, one classified consumption only as "never" or "ever" [38]. In addition, few studies considered duration of tea drinking or the preparation method in their assessment. Various methodological issues including the failure to control for potential confounding factors also could have affected the findings.

The possibly more promising results for green than black tea could be the result of several factors. The higher catechin content and antioxidant activity of green tea is one possibility. Also, tea intake was considerably higher in the Chinese study [16] and prospective study in Japan [54] than any others, suggesting low consumption might explain the lack of significance elsewhere. In addition, confounding factors including Asian-style diets such as the consumption of soy products and certain vegetables, low fat and alcohol intake, as well as the small numbers of studies published may contribute.

3.6 Tea and prostate cancer: Clinical trials

A recent double blind placebo controlled study examined the effect of green tea catechins (GTCs) on high-risk men with high-grade prostate intraepithelial neoplasia [55]. Of the 30 men treated daily with GTC capsules, only one tumor was diagnosed after 1 year as opposed to nine tumors diagnosed in the 30 placebos. Despite the small sample, this study provides the first evidence that GTC may possess potent *in vivo* chemopreventive activity in men prone to prostate cancer. Another small clinical trial reported minimal clinical activity of green tea extract capsules in 15 men already diagnosed with hormone refractory prostate cancer [56].

3.7 Animal model studies on tea and prostate cancer

Consistent evidence has emerged from animal models for a protective effect of tea and its components against prostate

cancer. Studies in the transgenic adenocarcinoma of the mouse prostate model have reported reduction in the development of prostate cancer with feeding of GTCs [57]. Apoptosis and significant inhibition of tumor development and metastasis was also reported with oral infusion of green tea polyphenols at a human dose equivalent to six cups of green tea *per* day [62] and with oral feeding of 0.1% GTC [63]. Injecting EGCG has also been shown to inhibit prostate cancer growth in nude mice [63]. In addition, black tea extract has recently showed a significant protective effect against testosterone induced oxidative injury in Wistar rat prostate [64]. Significant inhibition in growth of implanted prostate tumors in athymic nude mice and reduction in prostate specific antigen was also recently reported with treatment of water extract of black tea, theaflavins as well as green tea polyphenols [65].

3.8 *In vitro* cell culture studies on tea and prostate cancer

In vitro cell culture studies have consistently revealed biologically plausible mechanisms by which tea polyphenols and EGCG may affect the development or progression of prostate and other cancers. These components can inhibit cell growth and induce apoptosis through various pathways and can affect multiple cellular events [66].

3.8.1 Antioxidant properties of green tea

Androgens induce oxidative stress, making them key factors in prostate cancer development [64]. Catechins, especially EGCG, are antioxidants or highly effective scavengers of oxidizing molecules including singlet oxygen and various free radicals that many contribute to DNA damage and tumor promotion [67].

3.8.2 Modulation of cyclin kinase inhibitor

One pathway by which cell growth is inhibited and apoptosis induced is through the modulation of cyclin kinase inhibitor. Cyclins are over expressed in prostate cancer and EGCG has been shown to upregulate cyclin-dependent kinase inhibitors such as $p21^{WAFI/CIPI}$ [68 – 71], $p27^{KIPI}$, $p16^{INK4A}$, and $p15^{INK4B}$ and down modulate cyclin D1, cyclin E, cdk2, cdk4, and cdk6 [72].

3.8.3 Effects on proteasome activity

EGCG has also been reported to be a proteasome inhibitor, capable of inducing growth arrest in tumor cells by inhibiting the system that allows cell – cycle progression and protects tumor cells against apoptosis [73].

3.8.4 Alteration of gene expression

Analysis of gene expression found that 25 genes in LNCaP cells, belonging to different regulatory pathways responded to treatment by EGCG [74]. It induced 16 growth inhibitory genes and repressed nine genes most of which belong to the G-protein signaling network. The most prominent suppression was of the PKC-αgene [74]. Green tea polyphenols can also cause significant inhibition of insulin-like growth factor in mice [62], while EGCG may influence the tumor suppressor gene p53 [70, 71].

3.8.5 Influence on enzymes

EGCG has been shown to inhibit transcription factors including p53 and NF-κB. This leads to the activation of $p21^{WAFI}$ and Bax, changing the ratio of Bax to Bcl-2 and activating capases, enzymes that favor apoptosis [71]. Other enzymes also targeted by green tea polyphenols or EGCG include 5α-reductases [75], fatty acid synthase [76], cyclooxygenase-2 [72], urokinase-like plasminogen activator [68], ornithine decarboxylase [77], nitric-oxide synthase [78], mitogen-activated protein kinase [79], and matrix metalloproteinase [80]. A recent study suggests that activation of ERK1/2 (a member of the mitogen-activated protein kinase family) is partially responsible for the antiproliferative effects of EGCG [81].

4 Discussion

Despite coffee and tea being two of the most commonly consumed beverages in the world [17], very little dietary advice on their consumption exists. In the case of coffee, this review of epidemiologic, animal and *in vitro* evidence indicates that coffee consumption probably has no relationship with the risk of prostate cancer. A recent review from the World Cancer Research Fund/American Institute for Cancer Research also stated the level of evidence for effects of coffee on prostate cancer as "limited- no conclusion" [1]. Research to date agrees that coffee consumption is safe for healthy adults [25] but probably has no preventive effects on chronic diseases including cancers [5] and cardiovascular disease [82 – 84].Tea is also a safe beverage but tea and its components, especially green tea have shown promise in the prevention of prostate cancer in animal and *in vitro* studies, in some epidemiological studies and a small clinical trial. Evidence also exists for a possible preventive role of tea for other cancers [85 – 87] and cardiovascular disease [88 – 90].Current evidence for a role of tea in prostate cancer prevention however, is definitely not conclusive and further studies are warranted [1, 91]. The inverse relationships reported by the Japanese prospective study [54] and Chinese case-control study [16] are promising but have not been replicated. Case-control studies, in particular are subject to bias due to their retrospective design [52]. Consistent results have also been reported in animal and *in vitro* studies but these effects are not always reproducible in humans. Also, different types and brands of tea vary greatly in terms of their polyphenol profiles and content [92] and animal and *in vitro* studies often use very high concentrations of tea compounds that may not reflect the actual levels found in

Table 3. Apparent *per* capita consumption (kg/person) of tea and coffee in Australia [22]

	Average 3 years ended						Current year
Item	1938 – 1939	1948 – 1949	1958 – 1959	1968 – 1969	1978 – 1979	1988 – 1989	1998 – 1998
Coffee	0.3	0.5	0.6	1.2	1.6	2.0	2.4
Tea	3.1	2.9	2.7	2.3	1.7	1.2	0.9

the human body after ingestion [93]. The oral bioavailability of GTCs is low and the effective concentration levels determined in *in vitro* studies are many fold more than the resulting systemic levels in humans meaning *in vitro* effects should be interpreted with caution [19, 94].

The National Health and Medical Research Council's hierarchy of evidence describes a meta-analysis or pooled analysis of data from a number of RCTs as the gold standard for clinical practice guidelines [21]. However, the bulk of evidence on tea and prostate cancer comes from epidemiological as well as animal and *in vitro* studies, meaning the level of evidence cannot rise above level III. Kroke *et al*. [95] acknowledge that reaching this gold standard is usually unrealistic when making recommendations for preventive rather than therapeutic measures. Using RCTs to evaluate the effect of lifetime tea drinking on the prostate cancer risk would be difficult and expensive. It would be difficult to use controls due to the impracticality of blinding and randomizing them and the long latency of prostate cancer. Prostate cancer is usually diagnosed in men aged over 65 [1]. However, these factors also make this cancer an ideal candidate for chemoprevention. Considering this, future research should utilize a variety of observational study designs and strengthen current evidence through shorter-term RCTs that examine the effects of tea consumption on prostate cancer development in men with premalignant lesions.It is clear that current evidence is not nearly strong enough to make recommendations when standards for therapeutic substances are considered. However, if nutritionists are asked to recommend either tea or coffee as the healthier option, we believe evidence is sufficient to recommend tea over coffee. World trends indicate that consumption is moving away from tea toward coffee. This is the case, for example, in Australia [22]; see Table 3. In addition, the aging population of many developed countries means the incidence of prostate cancer and other chronic diseases is likely to increase. Therefore, waiting decades for more complete evidence to emerge before making any dietary guidelines on tea and coffee could result in unnecessary morbidity and mortality. Tea is both a safe and popular beverage, its proposed health effects are biologically plausible and recommending its consumption is not inconsistent with any previous public health advice. These factors make it suitable to create dietary guidelines recommending the consumption of tea as a healthier choice than coffee [96].

Evidence on the dosage of tea required for effect, the efficacy of absorption in the human body and the different chemopreventive effects of green, black, and oolong teas is required before any specific and quantifiable dietary guidelines regarding tea consumption and prevention of prostate and other cancers can be made.

The authors have declared no conflict of interest.

5 References

[1] World Cancer Research Fund/American Institute for Cancer Research, *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*, AICR, Washington DC 2007.

[2] Stewart, B. W., Kleihues, P., *World Cancer Report*, International Agency for Research on Cancer, Lyon 2003.

[3] Li, X. M., Ganmaa, D., Qin, L. Q., Liu, X. F., *et al.*, The effects of estrogen-like products in milk on prostate and testes, *Zhonghua Nan Ke Xue* 2003, *9*, 186 – 90.

[4] Australian Institute of Health and Welfare (AIHW) & Australasian Association of Cancer Registries (AACR), *Cancer in Australia 2001*, AIHW cat. no. CAN 23, AIHW, Canberra 2001.

[5] Higdon, J. V., Frei, B., Coffee and health: A review of recent human research, *Crit. Rev. Food Sci. Nutr.* 2006, *46*, 101 – 123.

[6] Setiawan, V. W., Zhang, Z. F., Yu, G. P., Lu, Q. Y., *et al.*, Protective effect of green tea on the risks of chronic gastritis and stomach cancer, *Int. J. Cancer* 2001, *92*, 600 – 604.

[7] Su, L. J., Arab, L., Tea consumption and the reduced risk of colon cancer – results from a national prospective cohort study, *Public Health Nutr.* 2002, *5*, 419 – 425.

[8] Yuan, J. M., Gao, Y. T., Yang, C. S., Yu, M. C., Urinary biomarkers of tea polyphenols and risk of colorectal cancer in the Shanghai Cohort Study, *Int. J. Cancer* 2007, *120*, 1344 – 1350.

[9] Hakim, I. A., Harris, R. B., Weisgerber, U. M., Tea intake and squamous cell carcinoma of the skin: Influence of type of tea beverages, *Cancer Epidemiol. Biomarkers Prev.* 2000, *9*, 727 – 731.

[10] Rees, J. R., Stukel, T. A., Perry, A. E., Zens, M. S., *et al*., Tea consumption and basal cell and squamous cell skin cancer: Results of a case-control study, *J. Am. Acad. Dermatol.* 2007, *56*, 781 – 785.

[11] Wu, A. H., Yu, M. C., Tseng, C. C., Hankin, J., *et al*., Green tea and risk of breast cancer in Asian Americans, *Int. J. Cancer* 2003, *106*, 574 – 579.

[12] Inoue, M., Tajima, K., Mizutani, M., Iwata, H., *et al*., Regular consumption of green tea and the risk of breast cancer recurrence: Follow-up study from the Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC), Japan, *Cancer Lett.* 2001, *167*, 175 – 182.

[13] Zhang, M., Holman, C. D., Huang, J. P., Xie, X., Green tea and the prevention of breast cancer: A case-control study in southeast China, *Carcinogenesis* 2007, *28*, 1074 – 1078.

[14] Nagano, J., Kono, S., Preston, D. L., Mabuchi, K., A prospective study of green tea consumption and cancer incidence, Hiroshima and Nagasaki (Japan), *Cancer Causes Control* 2001, *12*, 501 – 508.

[15] Lee, A. H., Fraser, M. L., Meng, X., Binns, C. W., Protective effects of green tea against prostate cancer, *Expert Rev. Anticancer Ther.* 2006, *6*, 507 – 513.

[16] Jian, L., Xie, L. P., Lee, A. H., Binns, C. W., Protective effect of green tea against prostate cancer: A case-control study in southeast China, *Int. J. Cancer* 2004, *108*, 130 – 135.

[17] Grigg, D., The worlds of tea and coffee: Patterns of consumption, *Geojournal* 2002, *57*, 283 – 294.

[18] Cheung, E., Wadhera, P., Dorff, T., Pinski, J., Diet and prostate cancer risk reduction, *Expert Rev. Anticancer Ther.* 2008, *8*, 43 – 50.

[19] Syed, D. N., Khan, N., Afaq, F., Mukhtar, H., Chemoprevention of prostate cancer through dietary agents: Progress and promise, *Cancer Epidemiol. Biomarkers Prev.* 2007, *16*, 2193 – 2203.

[20] Gupta, S., Prostate cancer chemoprevention: current status and future prospects, *Toxicol. Appl. Pharmacol.* 2007, *224*, 369 – 376.

[21] National Health and Medical Research Council, *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines*, NHMRC, Canberra 1999.

[22] Australian Bureau of Statistics, *Apparent Consumption of Foodstuffs: Australia*, ABS, Canberra 2000.

[23] Mukhtar, H., Ahmad, N., Tea polyphenols: Prevention of cancer and optimizing health, *Am. J. Clin. Nutr.* 2000, *71*, 1698S – 1702S.

[24] Graham, H. N., Green tea composition, consumption, and polyphenol chemistry, *Prev. Med.* 1992, *21*, 334 – 350.

[25] Nawrot, P., Jordan, S., Eastwood, J., Rotstein, J., *et al*., Effects of caffeine on human health, *Food Addit. Contam.* 2003, *20*, 1 – 30.

[26] Iwai, K., Kishimoto, N., Kakino, Y., Mochida, K., *et al*., In vitro antioxidative effects and tyrosinase inhibitory activities of seven hydroxycinnamoyl derivatives in green coffee beans, *J. Agric. Food Chem.* 2004, *52*, 4893 – 4898.

[27] MacMahon, B., Yen, S., Trichopoulos, D., Warren, K., *et al*., Coffee and cancer of the pancreas, *N. Engl. J. Med.* 1981, *304*, 630 – 633.

[28] Miller, D. R., Rosenberg, L., Kaufman, D. W., Helmrich, S. P., *et al*., Epithelial ovarian cancer and coffee drinking, *Int. J. Epidemiol.* 1987, *16*, 13 – 17.

[29] Chen, Y. C., Chiang, C. I., Lin, R. S., Pu, Y. S., *et al*., Diet, vegetarian food and prostate carcinoma among men in Taiwan, *Br. J. Cancer* 2005, *93*, 1057 – 1061.

[30] Sharpe, C. R., Siemiatycki, J., Consumption of non-alcoholic beverages and prostate cancer risk, *Eur. J. Cancer Prev.* 2002, *11*, 497 – 501.

[31] Hsieh, C. C., Thanos, A., Mitropoulos, D., Deliveliotis, C., *et al*., Risk factors for prostate cancer: A case-control study in Greece, *Int. J. Cancer* 1999, *80*, 699 – 703.

[32] Villeneuve, P. J., Johnson, K. C., Kreiger, N., Mao, Y., Risk factors for prostate cancer: Results from the Canadian National Enhanced Cancer Surveillance System. The Canadian Cancer Registries Epidemiology Research Group, *Cancer Causes Control* 1999, *10*, 355 – 367.

[33] Jain, M. G., Hislop, G. T., Howe, G. R., Burch, J. D., *et al*., Alcohol and other beverage use and prostate cancer risk among Canadian men, *Int. J. Cancer* 1998, *78*, 707 – 711.

[34] Gronberg, H., Damber, L., Damber, J. E., Total food consumption and body mass index in relation to prostate cancer risk: A case-control study in Sweden with prospectively collected exposure data, *J. Urol.* 1996, *155*, 969 – 974.

[35] Slattery, M. L., West, D. W., Smoking, alcohol, coffee, tea, caffeine, and theobromine: Risk of prostate cancer in Utah (United States), *Cancer Causes Control* 1993, *4*, 559 – 563.

[36] Ellison, L. F., Tea and other beverage consumption and prostate cancer risk: A Canadian retrospective cohort study, *Eur. J. Cancer Prev.* 2000, *9*, 125 – 130.

[37] Le Marchand, L., Kolonel, L. N., Wilkens, L. R., Myers, B. C., *et al*., Animal fat consumption and prostate cancer: A prospective study in Hawaii, *Epidemiology* 1994, *5*, 276 – 282.

[38] Severson, R. K., Nomura, A. M., Grove, J. S., Stemmermann, G. N., A prospective study of demographics, diet, and prostate cancer among men of Japanese ancestry in Hawaii, *Cancer Res.* 1989, *49*, 1857 – 1860.

[39] Nomura, A., Heilbrun, L. K., Stemmermann, G. N., Prospective study of coffee consumption and the risk of cancer, *J. Natl. Cancer Inst.* 1986, *76*, 587 – 590.

[40] Hsing, A. W., McLaughlin, J. K., Schuman, L. M., Bjelke, E., *et al*., Diet, tobacco use, and fatal prostate cancer: Results from the Lutheran Brotherhood Cohort Study, *Cancer Res.* 1990, *50*, 6836 – 6840.

[41] Phillips, R. L., Snowdon, D. A., Association of meat and coffee use with cancers of the large bowel, breast, and prostate among Seventh-Day Adventists: Preliminary results, *Cancer Res.* 1983, *43*, 2403s – 2408s.

[42] McCusker, R. R., Goldberger, B. A., Cone, E. J., Caffeine content of specialty coffees, *J. Anal. Toxicol.* 2003, *27*, 520 – 522.

[43] Hashimoto, T., He, Z., Ma, W. Y., Schmid, P. C., *et al*., Caffeine inhibits cell proliferation by G0/G1 phase arrest in JB6 cells, *Cancer Res.* 2004, *64*, 3344 – 3349.

[44] Lee, W. J., Zhu, B. T., Inhibition of DNA methylation by caffeic acid and chlorogenic acid, two common catechol-containing coffee polyphenols, *Carcinogenesis* 2006, *27*, 269 – 277.

[45] Cavin, C., Holzhaeuser, D., Scharf, G., Constable, A., *et al*., Cafestol and kahweol, two coffee specific diterpenes with anticarcinogenic activity, *Food Chem. Toxicol.* 2002, *40*, 1155 – 1163.

[46] Porta, M., Vioque, J., Ayude, D., Alguacil, J., *et al*., Coffee drinking: The rationale for treating it as a potential effect modifier of carcinogenic exposures, *Eur. J. Epidemiol.* 2003, *18*, 289 – 298.

[47] Efferth, T., Fabry, U., Glatte, P., Osieka, R., Expression of apoptosis-related oncoproteins and modulation of apoptosis by caffeine in human leukemic cells, *J. Cancer Res. Clin. Oncol.* 1995, *121*, 648 – 656.

[48] Link, C. J. Jr., Evans, M. K., Cook, J. A., Muldoon, R., *et al*., Caffeine inhibits gene-specific repair of UV-induced DNA damage in hamster cells and in human xeroderma pigmentosum group C cells, *Carcinogenesis* 1995, *16*, 1149 – 1155.

[49] Porta, M., Malats, N., Guarner, L., Carrato, A., *et al*., Association between coffee drinking and K-ras mutations in exocrine pancreatic cancer. PANKRAS II Study Group, *J. Epidemiol. Community Health* 1999, *53*, 702 – 709.

[50] Miura, Y., Ono, K., Okauchi, R., Yagasaki, K., Inhibitory effect of coffee on hepatoma proliferation and invasion in culture and on tumor growth, metastasis and abnormal lipoprotein profiles in hepatoma-bearing rats, *J. Nutr. Sci. Vitaminol. (Tokyo)* 2004, *50*, 38 – 44.

[51] La Vecchia, C., Tavani, A., Coffee and cancer risk: An update, *Eur. J. Cancer Prev.* 2007, *16*, 385 – 389.

[52] US Food and Drug Administration, *Letter responding to health claim petition dated January 27, 2004: Green tea and reduced risk of cancer health claim*, Center for Food Safety and Applied Nutrition, Department of Health and Human Services; http://www.cfsan.fda.gov/~dms/qhc-gtea.html, 2004.

[53] Sonoda, T., Nagata, Y., Mori, M., Miyanaga, N. *et al*., A case-control study of diet and prostate cancer in Japan: Possible protective effect of traditional Japanese diet, *Cancer Sci.* 2004, *95*, 238 – 242.

[54] Kurahashi, N., Sasazuki, S., Iwasaki, M., Inoue, M., *et al*., Green tea consumption and prostate cancer risk in Japanese men: A prospective study, *Am. J. Epidemiol.* 2008, *167*, 71 – 77.

[55] Bettuzzi, S., Brausi, M., Rizzi, F., Castagnetti, G., *et al*., Chemoprevention of human prostate cancer by oral administration of green tea catechins in volunteers with high-grade prostate intraepithelial neoplasia: A preliminary report from a one-year proof-of-principle study, *Cancer Res.* 2006, *66*, 1234 – 1240.

[56] Choan, E., Segal, R., Jonker, D., Malone, S., *et al*., A prospective clinical trial of green tea for hormone refractory prostate cancer: An evaluation of the complementary/alternative therapy approach, *Urol. Oncol.* 2005, *23*, 108 – 113.

[57] Caporali, A., Davalli, P., Astancolle, S., D'Arca, D., *et al*., The chemopreventive action of catechins in the TRAMP mouse model of prostate carcinogenesis is accompanied by clusterin over-expression, *Carcinogenesis* 2004, *25*, 2217 – 2224.

[58] Kikuchi, N., Ohmori, K., Shimazu, T., Nakaya, N., *et al*., No association between green tea and prostate cancer risk in Japanese men: The Ohsaki Cohort Study, *Br. J. Cancer* 2006, *95*, 371 – 373.

[59] Heilbrun, L. K., Nomura, A., Stemmermann, G. N., Black tea consumption and cancer risk: A prospective study, *Br. J. Cancer* 1986, *54*, 677 – 683.

[60] Kinlen, L. J., Willows, A. N., Goldblatt, P., Yudkin, J., Tea consumption and cancer, *Br. J. Cancer* 1988, *58*, 397 – 401.

[61] La Vecchia, C., Negri, E., Franceschi, S., D'Avanzo, B., *et al*., Tea consumption and cancer risk, *Nutr. Cancer* 1992, *17*, 27 – 31.

[62] Gupta, S., Hastak, K., Ahmad, N., Lewin, J. S., *et al*., Inhibition of prostate carcinogenesis in TRAMP mice by oral infusion of green tea polyphenols, *Proc. Natl. Acad. Sci. USA* 2001, *98*, 10350 – 10355.

[63] Saleem, M., Adhami, V. M., Siddiqui, I. A., Mukhtar, H., Tea beverage in chemoprevention of prostate cancer: A mini-review, *Nutr. Cancer* 2003, *47*, 13 – 23.

[64] Siddiqui, I. A., Raisuddin, S., Shukla, Y., Protective effects of black tea extract on testosterone induced oxidative damage in prostate, *Cancer Lett.* 2005, *227*, 125 – 132.

[65] Siddiqui, I. A., Zaman, N., Aziz, M. H., Reagan-Shaw, S. R. *et al*., Inhibition of CWR22Rnu1 tumor growth and PSA secretion in athymic nude mice by green and black teas, *Carcinogenesis* 2006, *27*, 833 – 839.

[66] Adhami, V. M., Mukhtar, H., Polyphenols from green tea and pomegranate for prevention of prostate cancer, *Free Radic. Res.* 2006, *40*, 1095 – 1104.

[67] Anderson, R. F., Fisher, L. J., Hara, Y., Harris, T., *et al*., Green tea catechins partially protect DNA from (.)OH radical-induced strand breaks and base damage through fast chemical repair of DNA radicals, *Carcinogenesis* 2001, *22*, 1189 – 1193.

[68] Adhami, V. M., Ahmad, N., Mukhtar, H., Molecular targets for green tea in prostate cancer prevention, *J. Nutr.* 2003, *133*, 2417S – 2424S.

[69] Gupta, S., Ahmad, N., Nieminen, A. L., Mukhtar, H., Growth inhibition, cell-cycle dysregulation, and induction of apoptosis by green tea constituent (–)-epigallocatechin-3-gallate in androgen-sensitive and androgen-insensitive human prostate carcinoma cells, *Toxicol. Appl. Pharmacol.* 2000, *164*, 82 – 90.

[70] Hastak, K., Agarwal, M. K., Mukhtar, H., Agarwal, M. L., Ablation of either p21 or Bax prevents p53-dependent apoptosis induced by green tea polyphenol epigallocatechin-3-gallate, *FASEB J.* 2005, *19*, 789 – 791.

[71] Hastak, K., Gupta, S., Ahmad, N., Agarwal, M. K., *et al*., Role of p53 and NF-kappaB in epigallocatechin-3-gallate-induced apoptosis of LNCaP cells, *Oncogene* 2003, *22*, 4851 – 4859.

[72] Park, O. J., Surh, Y. J., Chemopreventive potential of epigallocatechin gallate and genistein: Evidence from epidemiological and laboratory studies, *Toxicol. Lett.* 2004, *150*, 43 – 56.

[73] Nam, S., Smith, D. M., Dou, Q. P., Ester bond-containing tea polyphenols potently inhibit proteasome activity in vitro and in vivo, *J. Biol. Chem.* 2001, *276*, 13322 – 13330.

[74] Wang, S. I., Mukhtar, H., Gene expression profile in human prostate LNCaP cancer cells by (–) epigallocatechin-3-gallate, *Cancer Lett.* 2002, *182*, 43 – 51.

[75] Hiipakka, R. A., Zhang, H. Z., Dai, W., Dai, Q., *et al*., Structure-activity relationships for inhibition of human 5alpha-reductases by polyphenols, *Biochem. Pharmacol.* 2002, *63*, 1165 – 1176.

[76] Brusselmans, K., De Schrijver, E., Heyns, W., Verhoeven, G., *et al*., Epigallocatechin-3-gallate is a potent natural inhibitor of fatty acid synthase in intact cells and selectively induces apoptosis in prostate cancer cells, *Int. J. Cancer* 2003, *106*, 856 – 862.

[77] Gupta, S., Ahmad, N., Mohan, R. R., Husain, M. M., *et al*., Prostate cancer chemoprevention by green tea: In vitro and in vivo inhibition of testosterone-mediated induction of ornithine decarboxylase, *Cancer Res.* 1999, *59*, 2115 – 2120.

[78] Lin, Y. L., Lin, J. K., (–)-Epigallocatechin-3-gallate blocks the induction of nitric oxide synthase by down-regulating lipopolysaccharide-induced activity of transcription factor nuclear factor-kappaB, *Mol. Pharmacol.* 1997, *52*, 465 – 472.

[79] Chung, L. Y., Cheung, T. C., Kong, S. K., Fung, K. P., *et al*., Induction of apoptosis by green tea catechins in human prostate cancer DU145 cells, *Life Sci.* 2001, *68*, 1207 – 1214.

[80] Demeule, M., Brossard, M., Page, M., Gingras, D., *et al*., Matrix metalloproteinase inhibition by green tea catechins, *Biochim. Biophys. Acta* 2000, *1478*, 51 – 60.

[81] Albrecht, D. S., Clubbs, E. A., Ferruzzi, M., Bomser, J. A., Epigallocatechin-3-gallate (EGCG) inhibits PC-3 prostate cancer cell proliferation via MEK-independent ERK1/2 activation, *Chem. Biol. Interact.* 2008, *171*, 89 – 95.

[82] Sudano, I., Binggeli, C., Spieker, L., Luscher, T. F., *et al*., Cardiovascular effects of coffee: Is it a risk factor? *Prog. Cardiovasc. Nurs.* 2005, *20*, 65 – 69.

[83] Jee, S. H., He, J., Whelton, P. K., Suh, I., *et al*., The effect of chronic coffee drinking on blood pressure: A meta-analysis of controlled clinical trials, *Hypertension* 1999, *33*, 647 – 652.

[84] Noordzij, M., Uiterwaal, C. S., Arends, L. R., Kok, F. J., *et al*., Blood pressure response to chronic intake of coffee and caffeine: A meta-analysis of randomized controlled trials, *J. Hypertens.* 2005, *23*, 921 – 928.

[85] Borrelli, F., Capasso, R., Russo, A., Ernst, E., Systematic review: Green tea and gastrointestinal cancer risk, *Aliment. Pharmacol. Ther.* 2004, *19*, 497 – 510.

[86] Sun, C. L., Yuan, J. M., Koh, W. P., Yu, M. C., Green tea, black tea and breast cancer risk: A meta-analysis of epidemiological studies, *Carcinogenesis* 2006, *27*, 1310 – 1315.

[87] Seely, D., Mills, E. J., Wu, P., Verma, S., *et al.*, The effects of green tea consumption on incidence of breast cancer and recurrence of breast cancer: A systematic review and meta-analysis, *Integr. Cancer Ther.* 2005, *4*, 144 – 155.

[88] Peters, U., Poole, C., Arab, L., Does tea affect cardiovascular disease? A meta-analysis, *Am. J. Epidemiol.* 2001, *154*, 495 – 503.

[89] Kuriyama, S., Shimazu, T., Ohmori, K., Kikuchi, N., *et al*., Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: The Ohsaki study, *JAMA* 2006, *296*, 1255 – 1265.

[90] Shimazu, T., Kuriyama, S., Hozawa, A., Ohmori, K., *et al*., Dietary patterns and cardiovascular disease mortality in Japan: A prospective cohort study, *Int. J. Epidemiol.* 2007, *36*, 600 – 609.

[91] Fleshner, N., Zlotta, A. R., Prostate cancer prevention: past, present, and future, *Cancer* 2007, *110*, 1889 – 1899.

[92] Henning, S. M., Fajardo-Lira, C., Lee, H. W., Youssefian, A. A., *et al*., Catechin content of 18 teas and a green tea extract supplement correlates with the antioxidant capacity, *Nutr. Cancer* 2003, *45*, 226 – 235.

[93] Crespy, V., Williamson, G., A review of the health effects of green tea catechins in in vivo animal models, *J. Nutr.* 2004, *134*, 3431S – 3440S.

[94] Chow, H. H., Hakim, I. A., Vining, D. R., Crowell, J. A., *et al*., Effects of dosing condition on the oral bioavailability of green tea catechins after single-dose administration of Polyphenon E in healthy individuals, *Clin. Cancer Res.* 2005, *11*, 4627 – 4633.

[95] Kroke, A., Boeing, H., Rossnagel, K., Willich, S. N., History of the concept of "levels of evidence" and their current status in relation to primary prevention through lifestyle interventions, *Public Health Nutr.* 2004, *7*, 279 – 284.

[96] Binns, C. W., Lee, M. K., Translating nutrition science into dietary guidelines: Evidence and benchmarking, *J. Korean Dietetics Assoc.* 2001, *17*, 202 – 207.