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To cite this article: Masood Sadiq Butt & M. Tauseef Sultan (2011) Coffee and its Consumption: Benefits and Risks, Critical Reviews in Food Science and Nutrition, 51:4, 363-373, DOI: [10.1080/10408390903586412](https://doi.org/10.1080/10408390903586412)

To link to this article: <https://doi.org/10.1080/10408390903586412>



Published online: 22 Mar 2011.



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# Coffee and its Consumption: Benefits and Risks

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*Coffee is the leading worldwide beverage after water and its trade exceeds US \$10 billion worldwide. Controversies regarding its benefits and risks still exist as reliable evidence is becoming available supporting its health promoting potential; however, some researchers have argued about the association of coffee consumption with cardiovascular complications and cancer insurgence. The health-promoting properties of coffee are often attributed to its rich phytochemistry, including caffeine, chlorogenic acid, caffeic acid, hydroxyhydroquinone (HHQ), etc. Many research investigations, epidemiological studies, and meta-analyses regarding coffee consumption revealed its inverse correlation with that of diabetes mellitus, various cancer lines, Parkinsonism, and Alzheimer's disease. Moreover, it ameliorates oxidative stress because of its ability to induce mRNA and protein expression, and mediates Nrf2-ARE pathway stimulation. Furthermore, caffeine and its metabolites help in proper cognitive functionality. Coffee lipid fraction containing cafestol and kahweol act as a safeguard against some malignant cells by modulating the detoxifying enzymes. On the other hand, their higher levels raise serum cholesterol, posing a possible threat to coronary health, for example, myocardial and cerebral infarction, insomnia, and cardiovascular complications. Caffeine also affects adenosine receptors and its withdrawal is accompanied with muscle fatigue and allied problems in those addicted to coffee. An array of evidence showed that pregnant women or those with postmenopausal problems should avoid excessive consumption of coffee because of its interference with oral contraceptives or postmenopausal hormones. This review article is an attempt to disseminate general information, health claims, and obviously the risk factors associated with coffee consumption to scientists, allied stakeholders, and certainly readers.*

**Keywords** coffee, caffeine, cardiovascular, diabetes mellitus, chemoprevention, Parkinsonism

## INTRODUCTION

In the present century nutrition is focused on meeting the challenges arising due to growing awareness among masses regarding the health-promoting properties of their diets. During recent times, the exploration of diet and health linkages diverted consumers towards nature (Butt and Sultan, 2009; Butt et al., 2009). Beverages are an important component of our daily diet and they are categorized into two broader horizons, namely alcoholics and non-alcoholics. A number of options are available among non-alcoholic beverages including coffee, tea, fruit juices, carbonated beverages, etc. However, coffee holds second position in consumption among all beverages after water, and people from all over the world consume approximately 500 billion cups annually (Prakash et al., 2002; Clarke and Vitzthum, 2001).

Coffee has a long-lasting history but was introduced as an economic crop during the fifteenth century. Now it has become the second largest traded commodity worldwide after petroleum and it accounts for US\$10 billion annually. More than 70 countries cultivate this plant, but Brazil, Colombia, Ethiopia, and India are the leading producers. Brazil and Colombia are the major players and account for 39% of the world share (ICO, 2004).

Often, coffee is consumed for its stimulatory effects owing to its rich phytochemistry among which caffeine is the most prominent. Coffee is the richest source of caffeine and 240-mL of instant coffee contains approximately 100 mg of caffeine (Belay et al., 2008). Considering the importance of this active alkaloid, Frary et al. (2005) conducted a survey regarding caffeine intake from different sources and reported that 70% of caffeine comes from coffee while soft drinks and tea contribute 16 and 12% respectively. Caffeine (*1,3,7-trimethyl xanthine*) is white crystalline powder having a bitter taste. It was first isolated from coffee in 1820 (Matijasevich et al., 2005; Mazzafera et al., 1991). Processing techniques such as green bean

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dewaxing and wet processing reduce caffeine contents but generally its concentration remains in the range of 0.65 to 2.30% (Ranheim and Halvorsen, 2005; McCusker et al., 2003). Some other components also played a pivotal role in health care, i.e., chlorogenic acid (3-3,4-Dihydroxycinnamoyl quinic acid), caffeic acid (3,4-Dihydroconnamic acid), and hydroxyhydroquinone (1,2,4-Trihydroxybenzene). These components are potent antioxidants and impart several health benefits like protecting the body from the hazardous effects of free radicals. Their effectiveness against diabetes mellitus and cardiovascular disparities is well understood (Brezová et al., 2009; Suzuki et al., 2008; Farah and Donangelo, 2006; Ky et al., 2001).

Debate still persists whether coffee is beneficial or troublesome for human health. Its consumption has been associated with a momentous decrease in chronic diseases such as Parkinsonism, diabetes mellitus, and several cancer lines (Cavin et al., 2008). On the contrary, evidence pertaining to its role in cardiovascular disorders and some forms of cancer has been presented in a number of research studies (Mukamal et al., 2009). Moreover, coffee consumption tends to reduce the efficacy of some cardioprotective medicines like atorvastatin (Riksen et al., 2009; Ye et al., 2008; Taylor and Demmig-Adams, 2007). No doubt, health claims associated with coffee consumption are broad enough to recommend it as a table drink; nevertheless, some contradictions still demand further research on the subject. The consumption of coffee is increasing all over the globe and its sale is on the rise in developing economies, especially in India and Pakistan. Considering the amount of coffee consumption particularly in the Western world, North American regions, and some Asian countries, this review article can act as a comprehensive treatise regarding its benefits and risks.

## COFFEE PLANT: AN OVERVIEW

The coffee plant belongs to the family *Rubiaceae* and genera *Coffea*. It is usually a woody perennial tree which grows at higher altitudes; 70 different species of genera *Coffea* are being reported but most important are *Coffea Arabica* (arabica coffee) and *Coffea canephora*, (robusta coffee). These two varieties differ in their taste, appearance, and between caffeine contents. A hedonic trend of consumers falls in favor of arabica coffee as compared to robusta coffee (CTA, 2003). Arabica accounts for 75–80% of the world production while the rest of the 20% market share has been captured by robusta coffee. Robusta coffee produces an inferior tasting beverage with some higher caffeine contents. The tocopherols contents of *Arabica* are also higher than robusta coffee (Alves et al., 2009). Processing of coffee involves picking of the bean, drying, roasting, grinding, and brewing to yield the final coffee. Decaffeination and filtration is carried out some times to remove components such as caffeine and lipid fraction. In this entire process the coffee beans undergo several physical and chemical changes like flavor and antioxidant properties (Sacchetti et al., 2009; Parras et al., 2007).

## BOTANICAL CLASSIFICATION

Kingdom: *Plantae*  
Division: *Magnoliophyta*  
Class: *magnoliopsida*  
Order: *Gentianales*  
Family: *Rubiaceae*  
Genus: *Coffea*  
Species: *Arabica*; *Canephora*



As far as the composition of coffee is concerned, caffeine is no doubt considered as its major and active ingredient. Caffeine is metabolized in the liver by enzymes known as 1A2 (or CYP1A2) that include dimethylxanthines, paraxanthine, theobromine, and theophylline. These metabolites produce some distinctive functions in the body ranging from enhancing the sense of sensation to improving attention (Pardo-Lozano et al., 2007). Some genetic factors also influence the speed and fate of caffeine as effects are more pronounced in subjects showing slow caffeine metabolism (Cornelis et al., 2006). Safe limits for caffeine intake have been described in Table 1. Additionally, coffee contains polyphenols including hydroxyhydroquinone (HHQ) and chlorogenic acids (Fig. 1).

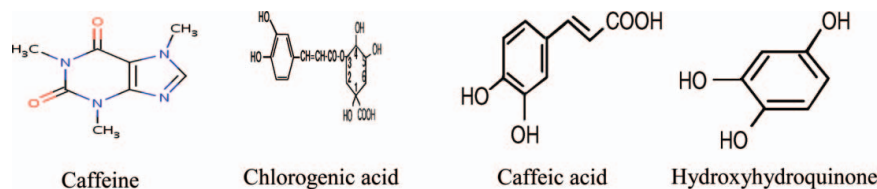
The health benefits of decaffeinated coffee are often attributed to chlorogenic acid. Likewise, its lignans and some mineral components also possess therapeutic potential (Celik et al., 2009; Suzuki et al., 2008; Farah and Donangelo, 2006; Ky et al., 2001). It provides protection against cardiovascular diseases, diabetes mellitus, Parkinson's disease, Alzheimer's disease, DNA damage, and improves the antioxidant status of the body (Conney et al., 2007). It produces alertness through stimulating functions and effective treatment for sleepy people. Some contradiction still persists that its high consumption results in high intakes of caffeine which is addiction and leaving this habit brings some discomfort in the form of headache, muscle pain, etc. (Lee et al., 2007).

Some of the components of coffee like caffeine interact with some xenobiotics, especially in women taking hormones to cure postmenopausal problems. It is a risk factor for breast cancer and some reports suggested a positive hazard ratio for its association with prostate cancer. Risks for development of rheumatoid arthritis and osteoporosis increase with increased consumption of coffee on a regular basis. Cafestol and kahweol has equivocal actions as cholesterol raising potential on one hand and the on other hand possessing chemopreventive potential (Pardo-Lozano et al., 2007; Matijasevich et al., 2005).

**Table 1** Safe limits for caffeine

Age group	Caffeine (mg/day)
Healthy adults	400–450
Pregnant Women	300
Children (4–6 years)	45

Source: Nawrot et al., 2003

**Figure 1** Chemical structures of components.**COFFEE AND ITS CHEMOPREVENTIVE POTENTIAL**

Lifestyle factors play an important role in cancer insurgence and its progression all over the world. Civilizations consuming traditional diets rich in bioactive components are at lower risk of various maladies, for example, the consumption of antioxidants or antioxidants rich foods and lower risk of cancer (Butt et al., 2009; Ohishi et al., 2008; Divisi et al., 2006). Many meta-analyses highlighted the benefits of coffee consumption, inferred to be associated with the lower risk of colorectal, liver, renal, ovarian, pancreas, esophagus, endometrial, and pharyngeal cancer (Friberg et al., 2009; Hu et al., 2009; Ramos, 2008). Several lines of action have been presented (Table 2) in this

regard but the most important among them are the rich phytochemistry of coffee (Huber et al., 2008; Song et al., 2008).

An inverse association between coffee consumption and the risk of colorectal cancer, one of the most frequently occurring cancers in the western world, has been reported in several case-control studies (Naganuma et al., 2007). In this regard, Oba et al. (2006) observed declines in colorectal cancer among individuals consuming two or more cups of decaffeinated coffee daily. However, Huber et al. (2008) further suggested that coffee consumers are at lower risk of colon cancer and attributed reduction to high content of the diterpenes, Kahweol, and Cafestol (George et al., 2008; Tao et al., 2008). Their findings support that coffee and its components are responsible for chemopreventive poten-

**Table 2** Coffee consumption and cancer

Cancer type	Research Group	Relationship with coffee
Bladder cancer	Villanueva et al., 2009 Demirel et al., 2008 Altwein et al., 2007 De Stefani et al., 2007	Modest increased bladder cancer risk among coffee drinkers No association Showed no significant association Inverse relationship for $3 \leq$ cups/day
Breast cancer	Tang et al., 2009 Ganmaa et al., 2008  Kotsopoulos et al., 2007 Lee et al., 2007 Naganuma et al., 2007 Oba et al., 2006	Increased risk of cancer No positive association of breast cancer; Higher consumption increase risk 64% reduction in breast cancer risk for daily users Inverse association with colon cancer among women. Coffee consumption was not associated with colorectal cancer. daily coffee drinkers reduced risk; RR=0.43
Gastric cancer	Botelho et al., 2006	Positive association; OR: 0.97
Liver cancer (Hepatocellular carcinoma)	Ohishi et al., 2008 Huber et al., 2008 Larsson et al., 2008 Montella et al., 2007	Decrease HCC risk Induction of phase II detoxifying enzymes 2 cups of coffee/day; 43% reduced risk of liver cancer Inverse relationship; 14 cups/week of coffee (OR = 0.4)
Laryngeal cancer	Zvrko et al., 2008	Inverse relationship for 5 cups/day
Lung Cancer	Tang et al., 2010	Increased risk of cancer Reduced risk with decaffeinated coffee
Non-melanoma skin cancer	Abel et al., 2007	10.8% lower prevalence; 6 <cups/day reduces by 36%
Ovarian cancer	Song et al., 2008 Tworoger et al., 2008 Steevens et al., 2007  Baker et al., 2007 Silvera et al., 2007	No relationship with coffee consumption Modest inverse association No significant association; Multivariable rate ratios 0.94 No association and risk of ovarian cancer Positive association; >4 cups coffee/day
Pancreatic cancer	Luo et al., 2008 Larsson et al., 2008 Porta et al., 2007	Reduced risk Lower the chances of onset of cancer Increase with high consumption
Prostate cancer	Wigle et al., 2008 Gallus et al., 2007	Increased risk Increased risk (OR = 1.9)
Renal cell cancer	Hu et al., 2009 Lee et al., 2007	No association has been found Lower risk of renal cell cancer; $3 \leq$ cups/daily
Stomach cancer	Larsson et al., 2006	Coffee consumption; Positively associated

tial. More recently, Je et al. (2009) also supported the inverse association of coffee consumption with that of colorectal cancer.

The role of coffee in the etiology of hepatocellular carcinoma (HCC) has generated great interest (Montella et al., 2007; Cadden et al., 2007). Coffee may protect against the development of HCC and it is inversely associated with HCC (Gelatti et al., 2005). Inoue et al. (2005) arrived at the same conclusion while studying the same in the Japanese population. However, this matter needs further clarification and should be addressed in well-planned cohort studies to corroborate the findings (Tanaka et al., 2007; Shimazu et al., 2005). Recently, Hussain and El-Serag (2009) further highlighted the positive role of coffee and its active ingredient caffeine for the control of liver cancer.

Ovarian cancer is not associated with either caffeinated or decaffeinated coffees. Some studies reported that ingredients present in coffee hold potential against ovarian cancer but the presence of caffeine mitigates their effect (Song et al., 2008; Baker et al., 2007). Caffeine, a major ingredient of coffee, has been proposed to have a favorable affect on the modulation of circulating estrogen levels and therefore might be important in the development of hormone-related cancers (Friberg et al., 2009; Hirose et al., 2007). On the contrary, a modest inverse association exists between caffeine intake and ovarian cancer risk for women who have never used either oral contraceptives or postmenopausal hormones (Tworoger et al., 2008). Ganmaa et al. (2008) observed no substantial association between caffeinated and decaffeinated coffee with the onset or progression of breast cancer. However, their results suggested a weak inverse association between caffeine-containing beverages and risk of postmenopausal breast cancer (Tworoger et al., 2008). The debate between the association of breast cancer and coffee consumption still needs to be settled.

Pancreatic cancer kills more than 250,000 people each year worldwide and has a poor prognosis. There was no evidence linking alcohol or coffee consumption with an increased risk of pancreatic cancer. Such work is important for reducing the incidence of this fatal disease (Hart et al., 2008). No association was found between bladder cancer and drinking coffee (Demirel et al., 2008). Topical applications of caffeine to mice previously treated with UVB for 20 weeks (high risk mice without tumors) inhibited the formation of tumors and stimulated apoptosis in the tumors (Conney et al., 2007). Consumption of six or more cups of caffeinated coffee/day resulted in 36% reduction in nonmelanoma skin cancer (Abel et al., 2007).

Contrary to its chemopreventive potential, some positive association has been reported between coffee consumption and breast and laryngeal cancer (Tang et al., 2009; Zvrko et al., 2008). Likewise, Tang et al. (2010) reported a positive association of coffee consumption with that of lung cancer even at a dose of 2 cups/day. However, they reported that the consumption of decaffeinated coffee holds an inverse relationship with lung cancer. Furthermore, Wigle et al. (2008) and Gallus et al. (2007) reported that coffee consumption increased the risk of prostate cancer, while Larsson et al. (2006) highlighted the inverse association of coffee with that of stomach cancer.

The mechanism behind the anticancer perspectives varied with the component of interest, e.g., caffeine, chlorogenic acids, cafestol, and kahweol. In this regard there is evidence supporting the anticancer perspectives of cafestol and kahweol. The mode of action includes inhibition of phase I activating enzyme expression and its activity, induction of phase II detoxifying enzymes, and regulation of Nrf2/ARE signaling pathways, all of which are of significant importance (Cavin et al., 2002; Huber et al., 2008). In addition, Cavin et al. (2008) suggested that coffee-mediated stimulation of the Nrf2-ARE pathway results in increased endogenous defense mechanisms against oxidative damage that may be associated with a protection against various types of chemical stresses (Higgins et al., 2008).

Overall, it can be concluded that coffee consumption is associated with a reduced risk of liver, kidney, and to a lesser extent, premenopausal breast cancers as well as colorectal cancers. It is not well correlated with prostate, pancreatic, and ovarian cancers (Nkondjock et al., 2009). Moreover, the role of caffeine is controversial as the decaffeination of coffee has shown some positive influences in all risk groups. Conflicting issues pertaining to the chemopreventive prospects of coffee demands collaborative research across different countries and civilizations to find the exact mechanism, as varying statements hinder its utilization in chemopreventive strategies.

## **DIABETES MELLITUS AND COFFEE CONSUMPTION**

Diabetes mellitus is one of the leading causes of mortality in both the developed and developing world. According to estimates worldwide, 376 millions peoples will be affected by the year 2030 (Wild et al., 2004). Rational planning and allocation of resources is necessary to combat this disorder. Quantification of the associated risks/factors like aging, lack of physical activity, lifestyle changes, and obesity must be undertaken. In this regard, diet-based strategies should be devised to control diabetes mellitus and the pathogenesis of diabetes mellitus can be prevented by slight modification in our daily diet. For this purpose utilization of natural compounds is gaining wide popularity (Steyn et al., 2004). In this era, much emphasis has been paid to these natural compounds and a lot of evidence has been generated supporting this viewpoint (van Dam, 2003; Hu et al., 2006).

Coffee consumption has been negatively correlated with the incidence of metabolic syndromes and diabetes mellitus. These effects are due to its nutritional profile as its components act as antioxidants and enhance insulin sensitivity, etc. It has been reported in some studies that caffeine intake decreases insulin sensitivity that results in decreased glucose storage (Keijzers et al., 2002; Greer et al., 2001). Efficacy studies in animal modeling have given some clues about the mechanisms of coffee action. Caffeine exerts beneficial effects on glucose metabolism through increased uncoupling protein expression and lipid oxidation. These further lead to decreased glucose storage capacity

**Table 3** Benefits of coffee and its components against diabetes mellitus

Sr. #	Coffee and Functional Component	Health Benefits
1	Coffee	<ul style="list-style-type: none"> <li>• Inverse relationships with diabetes mellitus</li> <li>• Improves antioxidant potential of the body</li> <li>• Better glucose tolerance</li> </ul>
2	Decaffeinated coffee	<ul style="list-style-type: none"> <li>• Delays intestinal absorption of glucose</li> <li>• Increased glucagon-like peptide-1 (Glucose-induced insulin secretion and insulin action)</li> </ul>
3	Caffeine	<ul style="list-style-type: none"> <li>• Lower risk of diabetes mellitus</li> <li>• Reduces glucose storage</li> </ul>
4	Chlorogenic acid	<ul style="list-style-type: none"> <li>• Improves glucose metabolisms</li> <li>• Reduced early glucose</li> <li>• Reduce insulin responses</li> <li>• Antioxidant effects</li> <li>• Inhibiting glucose-6-phosphatase</li> <li>• Improves mineral distribution</li> </ul>
5	Quinides	<ul style="list-style-type: none"> <li>• Increases insulin sensitivity</li> </ul>
6	Quinic acid	<ul style="list-style-type: none"> <li>• Improves glucose metabolism</li> </ul>
7	Trigonelline	<ul style="list-style-type: none"> <li>• Improves glucose metabolism</li> </ul>
8	Lignan secoisolariciresinol	<ul style="list-style-type: none"> <li>• Improves glucose metabolism</li> </ul>

\*Sources: (van Dijk et al., 2009; Zhang et al., 2009; Shearer et al., 2007; Rodriguez de Sotillo et al., 2002; van Dam et al., 2002; Johnston et al., 2003; Yoshioka et al., 2003)

which in turn reduces the extent of diabetes mellitus (van Dijk et al., 2009). Decaffeinated coffee consumption is also associated with lower fasting C-peptide concentrations and this association was not weaker than caffeinated coffee (Wu et al., 2005). The explanation in Table 3 illustrates the action of coffee and its ingredients for their possible effects to improve the glucose metabolism and depicts an inverse relationship of coffee consumption with diabetes mellitus. Evidence is available that caffeine is not mainly responsible for the hypoglycemic potential but the cumulative effect of components including chlorogenic acid play the key role (Zhang et al., 2009; Shearer et al., 2007). The mode of action of coffee and its active ingredients include improvement of glucose and insulin metabolisms with some positive modulating effects on enzymes (van Dijk et al., 2009; Shearer et al., 2007; Greenberg et al., 2006; Rodriguez de Sotillo et al., 2002). Moreover, the Pan American Health Organization also recommended the consumption of coffee (3–4 cups/day) to improve general public health and to avoid chronic diseases.

The aforesaid discussion can be helpful in arguing that coffee holds hypoglycemic potential and caffeine is not fully responsible but some other components also play an important role (Kato et al., 2009; Greenberg et al., 2006). Moreover, coffee can be useful in reducing the extent of complications from diabetes like cardiovascular disorders, etc. (Zhang et al., 2009; Hong et al., 2008; Campos and Baylin, 2007). Research investigations support the potential use of coffee against diabetes/hyperglycemia but further studies are still urgently required for greater precision and elaboration of the exact mechanism of action.

## CARDIOVASCULAR HEALTH AND COFFEE

Cardiovascular disparities are the leading cause of death all over the world. Several intrinsic and extrinsic factors play an important role in the onset and pathogenesis of such maladies. The American Heart Association has categorized several risk factors that include high cholesterol, high homocysteine level, atherosclerosis, arterial calcification, and several others (Ramaa et al., 2006). A slight modification in the diet plan can be useful in preventing such maladies. As far as coffee is concerned, the debate is still continues on its role in heart health.

The antioxidants present in coffee are useful in lowering the risk of coronary heart disease. Chlorogenic acid improves the antioxidative status of the body and reduces LDL oxidation (Cornelis and El-Sohehy, 2007). A cohort study conducted by Bidel et al. (2006) revealed that coffee intake is associated with reduced total coronary heart disease (CHD) mortality. Cardiovascular diseases are an important cause of mortality in patients diagnosed with diabetes mellitus and evidence provides support to the proposed hypothesis that coffee consumption is inversely correlated with the CHD in diabetes mellitus (Zhang et al., 2009). Moreover, Lopez-Garcia et al. (2008) suggested that coffee consumption is inversely associated with markers of inflammation that in return provide protection against endothelial dysfunction. Additionally, moderate consumption of coffee may reduce the risk of cerebral infarction among men (Larsson et al., 2008).

Ingredients other than caffeine such as chlorogenic acid and caffeic acid are antioxidant in nature and their presence slows down the process of inflammation, thereby providing protection from the hazardous effect of free radicals and against endothelial damage, etc. (Sudano et al., 2005). Consumption of coffee may inhibit inflammation and thus reduce the risk of cardiovascular and other inflammatory diseases in postmenopausal women (Anderson et al., 2006). Coffee consumption was reported in several studies to be associated with reduction in coronary calcification particularly in women. Some components of coffee vary in their response and interfere with each other as chlorogenic acid and HHQ in their action to increase blood pressure, as HHQ led down the CQA-induced improvement in blood pressure and endothelial function (Suzuki et al., 2008). Chronic coffee consumption reduces platelet activation and plasma C-reactive protein in healthy men. These effects may contribute to sustained cardiovascular health (Steptoe et al., 2007).

Generally, several mechanisms of action exist for coffee regarding its impact on the cardiovascular system. One generalized mechanism shares the effects of caffeine consumption on blood pressure as it enhances the arterial stiffness resulting in increased blood pressure (Sudano et al., 2006). Likewise, some components present in unfiltered coffee like cafestol and kahweol, etc. raise serum lipids and enhance the risk of cardiovascular disorders. In this case there is still some confusion, as to whether these components are involved in the deposition of LDL cholesterol but the oxidation of this lipid fraction is

not reported to occur revealing that the negative effects of coffee are not as high as they are hypothesized in the literature (Suzuki et al., 2008). Usually, consumption of 3–4 cups/day led to a small increase in both LDL and HDL cholesterol which cannot be regarded as a major risk factor for coronary heart disease (de-Ross et al., 1997). The resistance of LDL to oxidative modification increased significantly after coffee drinking, but the LDL(–) concentration did not increase. The concentration into LDL of conjugated forms of caffeic, p-coumaric, and ferulic acids increased significantly after coffee consumption. Drinking 200 mL (1 cup) of coffee induces an increase in the resistance of LDL to oxidative modification, probably as a result of the incorporation of the phenolic acids in coffee into LDL (van Woudenberg et al., 2008; Yukawa et al., 2004). However, further research is needed to confirm these findings and to clarify the possible interactive effect of gender and smoking with coffee consumption.

On the contrary, Riksen et al. (2009) concluded that coffee drinking may have an acute effect in triggering coronary events and increasing infarct size in selected patient groups (Greenberg et al., 2007; Rosner et al., 2007). Myocardial infarction is not associated with the consumption of coffee as reported by Corti et al. (2005). However, coffee in excess of 8 cups per day may aggravate cardiac arrhythmias and raise plasma homocysteine (Verhoef et al., 2002). Excessive coffee intake was related to coronary heart disease owing to the presence of cholesterol raising agents (Tverdal et al., 1990). Moreover, studies suggested that coffee is not a risk factor alone but associated habits such as smoking and alcohol consumption are other important causes of this widespread risk of CHD or death. In men, slightly increased mortality from CHD and all causes in heavy coffee drinkers is largely explained by the effects of smoking and a high serum cholesterol level (Kleemola et al., 2000). Caffeine causes an acute increase in the arterial wave reflection which can increase the pulsatile load of the heart. Higher homocysteine levels have been detected in Norwegian men and women who take more than nine cups of coffee per day (Kamimori et al., 2000; Nygard et al., 1997).

Cardiovascular malformations (CVM's) are not well correlated with coffee or caffeine consumption (Mineharu et al., 2010; Celik et al., 2009; Greenberg et al., 2008; Klatsky et al., 2008; Browne et al., 2007). Silletta et al. (2007) and Wu et al. (2009) also supported this hypothesis as they also concluded that there is no association between cardiovascular health disparities and coffee consumption (Ahmed et al., 2009). For the determination of exact conditions researchers should conduct meta-analysis, and the relation between coffee consumption and cardiovascular disease should be well explored. Previous studies did not justify completely that coffee consumption is associated with cardiovascular threats (Silletta et al., 2007; Riksen et al., 2009; Wu et al., 2009). In a nut shell, it can be concluded that coffee has some positive influences on heart health although evidence exists that coffee exerts its role in causing cardiovascular disorders. Moderate consumption of coffee could be effective in lowering the cardiovascular maladies by following the recommendation of

the Pan American Health Organization of consuming 3–4 cups coffee daily for maintaining adequate health.

### **COFFEE AND PARKINSONISM**

Parkinson's disease (PD) is a brain disorder involving inactivation of motor neurons, etc. The cause of PD is likely multi-dimensional but generally the process of aging, heavy metal toxicity such as from lead, and other chronic diseases such as diabetes mellitus are of important consideration (D'Amelio et al., 2009). Excessive intake of dietary lipids and milk consumption, a high caloric diet, and head trauma may also increase the incidence (Hu et al., 2007; Chade et al., 2006; Coon et al., 2006). There are many dietary components that result in lowering the risk of PD, such as the use of coffee/caffeine and tea. Although cigarette smoking and non-steroidal anti-inflammatory drugs (NSAIDs) also lower the risks but the associated health hazards are large enough to restrict their applications (Chade et al., 2006; Ross and Petrovitch, 2001).

Epidemiological studies have consistently demonstrated an inverse association between coffee consumption and PD (Cavin et al., 2008; Joghataie et al., 2004). Coffee intensifies the antioxidant defense mechanism of the immune system by inducing the expression of mRNA and enzymes mitigating the negative effects of free radical on neurodegeneration. It also inhibits CYP1A1/2, the receptor molecule involved actively in the detoxification mechanism (Cavin et al., 2008; Higgins et al., 2008).

Coffee or its important constituents act primarily by the direct action of blocking adenosine receptors and by the indirect action on neurotransmitter receptors. Stimulation of Nrf2-ARE pathway results in increase in endogenous mechanism against electrophilic and oxidative damage that further supports its neuroprotective potential (Ascherio et al., 2004; Fredholm, 2004; Schwarzschild et al., 2002). In addition, Cavin et al. (2008) suggested that coffee-mediated stimulation of the Nrf2-ARE pathway results in increased endogenous defense mechanisms. All these lines of actions adopted by coffee or caffeine eventually help in controlling the path leading to Parkinsonism. Some other health problems are also associated with Parkinson's disease such as type-2 diabetes. Diabetes mellitus enhances the chances of Parkinsonism and the mechanism behind this increase involves neurodegeneration (D'Amelio et al., 2009; Hu et al., 2007).

The effectiveness of coffee and caffeine to reduce the risk of Parkinson's disease is gender dependent. Gender difference may be due to an interaction between caffeine and use of postmenopausal estrogens. Ascherio et al. (2004) suggested that caffeine reduces the risk of PD but this hypothetical beneficial effect may be overdone by estrogen replacement therapy. Metabolic differences due to genetic variation also lower the efficiency of caffeine as slow and fast caffeine metabolizers differ significantly from each other. Overall, the association between caffeine intake and risk of PD was observed in both fast and



slow caffeine metabolizers but remedial action was painstaking in slow metabolizers. Animal models studies provide experimental evidence that both caffeine and its metabolite are neuro-protective (Tan et al., 2007). Mechanisms behind its protective actions have been well illustrated in different studies as major hypotheses but a great deal of consideration has been paid to its sensation-seeking traits which might underlie the Parkinsonian personality (Evans et al., 2006). Excessive daytime sleepiness (EDS) can also be a module for predicting future pathogenesis of PD (Abbott et al., 2005). Some other proposed mechanisms highlight the importance of water intake as it seems essential to add water in the diet to reduce the occurrence of PD (Ueki and Otsuka, 2004).

The hypothesis of the association of Parkinsonism cure with coffee containing caffeine validated the preceding discussion but its dosage needs to be further refined.

### **COFFEE AND ALZHEIMER'S DISEASE**

Alzheimer's disease (AD) is also a form of brain disorder. Increasing age, neurodegeneration, and the apolipoprotein E epsilon4 allele are the significant associated risks for the pathogenesis of Alzheimer's disease (Lindsay et al., 2002). A recent epidemiological study suggested that higher caffeine intake over decades reduces the risk of Alzheimer's disease (AD). Arendash et al. (2006) demonstrated that moderate daily intake of caffeine may delay or reduce the risk of AD. They proposed mechanisms that caffeine is associated with decrease in Abeta production as a result of reduced expression of Presenilin 1 (PS1) and  $\beta$ -secretase (BACE). These enzymes play a significant role in amyloid formation and their inhibition or reduced expression could provoke new channels in Alzheimer's therapies (Fujimoto et al., 2008). Brain disorders are often attributed to tissue damage/neurodegeneration characterized with loss of neurons in brain tissues. Trigonelline, a constituent of coffee beans, demonstrated the regeneration of dendrites and axons, in addition to memory improvement (Tohda et al., 2005). Improvement in memory and mechanism of action need attention in patients diagnosed with Alzheimer's disease although defined coffee consumption is associated with a reduced risk of Alzheimer's disease (Lindsay et al., 2002).

Some other benefits associated with coffee consumption are due to the antioxidants present in coffee. It improves the overall antioxidant capacity of the body and thus could contribute to ameliorating oxidative stress, inflammation, and carcinogenesis (Butt et al., 2008). Lee and Jeong, (2007) suggested that kahweol and cafestol are effective in ameliorating  $H_2O_2$ -induced oxidative stress and DNA damage, probably via scavenging free oxygen radicals. Later, Lee et al. (2007) suggested the protective effects for the above-mentioned components against the  $CCl_4$  induced hepatotoxicity. They further highlighted the possible mechanisms—blockage of CYP2E1-mediated  $CCl_4$  bioactivation and free radical scavenging effects. There is some evidence that supports the fact that coffee may be helpful in managing

asthma, stopping headache, boosting mood, and even preventing cavities when medication is unavailable (Naygard et al., 2003).

### **LACKLUSTER OF COFFEE CONSUMPTION**

No doubt, the benefits associated with the consumption of coffee are greater in numbers but still need attention in order to explain its detrimental effects on human health. It has long been a suspected cause of hypertension but there are ambiguities in the results. Coffee abstinence is associated with a lower hypertension risk than coffee consumption. An inverse U-shaped relation between coffee intake and risk of hypertension was observed in women (Noordzij et al., 2005).

Bonilha and Li (2004) have observed risks of excessive coffee intake on epilepsy control through antiepileptic drugs (AED's). Experimental studies indicated that chronic caffeine exposure may progressively reduce the protective potential of AEDs (Schmidt and Löscher, 2005). Kaufman and Sachdeo (2003) have reported that a large intake of caffeinated beverages dramatically decreased seizure control. Isolated clinical data has also provided evidence that epileptic patients should avoid caffeinated beverages (Kaufman and Sachdeo, 2003; Bonilha and Li, 2004; Zagnoni and Albano, 2002).

People facing the problem of sleep loss should avoid coffee consumption (Salín-Pascual et al., 2006; Tiffin et al., 1995). Caffeine contains adenine base and this structural resemblance with adenosine results in binding of adenosine receptors produces harmful effects like addiction, etc. Adenosine is used in emergency medicine to treat supraventricular arrhythmias and caffeine in such special cases may interfere with the patient's recovery (Johnson-Kozlow et al., 2002). Coffee/caffeine intake enhances the sense of sensation; people feel active and become habitual and withdrawal is accompanied with headache, fatigue, etc. (Salín-Pascual et al., 2006).

Recent reports suggest little association between the consumption of coffee/decaffeinated coffee with the risk of rheumatoid arthritis (RA) and osteoporosis. Coffee consumption could be considered as a possible threat for the onset of such maladies although evidence generated from studies has been unable to predict some strong correlation (Karlson et al., 2003). Cerebral infarction, an important health problem, is also significantly associated with increased consumption of coffee (Larsson et al., 2008). Pregnant women consuming more than 6 cups/day of coffee are more vulnerable to abortion and lower fetal weight (Fernandes et al., 1998). Females facing postmenopausal problems should also avoid coffee intake as it interferes with metabolism and affects the proper outcome of the treatments (Kotsopoulos et al., 2009; Santos et al., 1998).

### **CONCLUSIONS**

Debate still persists as to whether coffee is beneficial or somewhat troublesome for human health. The Pan American



Health Organization recommended coffee consumption for fitness but advised pregnant and postmenopausal women to avoid its excessive consumption. Intake of 2–3 cups/daily of coffee can improve cognitive functioning, the sense of sensation, as well as digestion. Moreover, the same dosage could be effective against coronary heart diseases, diabetes mellitus, cancer lines, Parkinsonism, and Alzheimer's disease. Risks associated with its excessive consumption involve insomnia, coronary complexities, and some others. Health disparities related to coffee consumption are often attributed to the consumption of an excess amount of caffeine or allied components present in its lipid fraction. Different processing techniques could be applied to remove such challenging components in order to minimize the associated risks. Probing for the detrimental effects of coffee should be focused on further to draw a conclusive approach for endusers to eliminate the ambiguities.

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