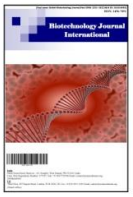

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Coffee: Constituents and Health Benefits

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Authors' contributions

This work was carried out in collaboration between both authors. Author SS designed the study, performed literature searches and wrote the first draft of the manuscript. Author AK designed and supervised the study, gave instructions to the co-author, contributed in adding recent references and finalized the manuscript. Both authors read and approved the final manuscript.

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ABSTRACT

Since ancient times, coffee has been one of the widely consumed beverages all over the world. It is renowned for its refreshing, body stimulating effect and unique taste. It belongs to the genus *Coffea*, class *Dicotyledoneae*, order *Rubiales* and family *Rubiaceae*. Coffee is a natural complex chemical mixture constituted of several compounds. It is accountable for numerous bioactivities and a number of compounds exhibit these effects. Some of the significant bioactivities documented are anti-oxidant, anti-mutagenic, anti-carcinogenic and anti-obesity properties. The varying constituents of coffee responsible for the chemo-protective effects are mainly polyphenols including chlorogenic acids and their degradation products. Others include caffeine, diterpenoid alcohols such as kahweol, cafestol and other phenolics. Coffee has been reported to exhibit both protective and adverse effects on various body systems such as skeletal (bone), reproductive, nervous and cardiovascular systems; homocysteine and cholesterol levels and so on. The present review provides an overview of the coffee and its constituents; and their relationship with various diseases. Recent investigations on its health benefits, with focus on their anti-cancer, anti-obesity properties and effect on cardiovascular diseases have also been discussed.

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Keywords: Coffee; caffeine; chlorogenic acids; kahweol; cafestol; cardiovascular diseases; anti-obesity properties.

1. INTRODUCTION

Coffee is a primarily consumed beverage all over the world and it is consumed mainly due to its body stimulating effect and desirable bitter taste [1,2]. Traditionally, the consumption of coffee has been correlated to negative health outcomes, however, studies have revealed that it might exert some health benefits also [3]. It has been reported that coffee imparts numerous potential health benefits due to the contents such as caffeine, cafestol, kahweol, chlorogenic acid and also some micronutrients like potassium, magnesium, niacin and vitamin E present in it [4, 5].

Green coffee is enriched in a polyphenol named as chlorogenic acid (CGA) which imparts many health benefits such as antibacterial, antifungal, antiviral, antioxidant, chemo-preventive and other biological activities [6,7]. Moreover, coffee is also an enriched source of caffeine [8] and caffeine leads to psycho-stimulant effects, thereby lessening the risk of developing neurodegenerative diseases like Parkinson's and Alzheimer's diseases [9].

Caffeine also stimulates lipolysis, thereby, increasing sympathetic activity and also increases resting energy expenditure [10]. Due to the presence of bioactive compounds, coffee generally behaves as anti-obesity, antioxidant, anti-diabetic, anti-inflammatory, hepato-protective, anti-genotoxic, cytotoxic and immune-modulator agent; and also acts as inhibitor for invasion, angiogenesis, metastasis, cell cycle progression and cell proliferation [11-14].

So far, several studies have depicted that coffee has led positive effects against many chronic diseases such as cancer, obesity, cardiovascular diseases and neurodegenerative diseases [15-19]. Despite of these numerous health benefits, the presence of cholesterol-increasing agents in coffee has made its excessive consumption as a threat for cardiovascular diseases [8]. However, moderate coffee consumption, around 3 to 4 cups in a day is good for human health [20]. The present review presents explicit information about coffee and its constituents and their properties on prevention and treatment of various diseases. Here, recommendation on the consumption of coffee has also been discussed.

2. COFFEE AND ITS CONSTITUENTS

Coffee has become a substantial part of our daily diet and makes up a significant place among beverages [21]. Coffee has been renowned for its stimulating effects and peculiar delicious taste after roasting [22]. Coffee fruit belongs to the family *Rubiacea*, genus *Coffea* and more than ninety species belong to this family. However, only two species namely *Coffea arabica* and *Coffea canephora* are commonly cultivated in the world and hold significant economic value [23].

Coffee contains carbohydrates, vitamins, lipids, isoflavonoids, nitrogenous compounds and micronutrients [24]. The bio-active constituents found in coffee are hydroxy-cinnamic acids (p-coumaric, caffeic and ferulic acids), diterpene alcohols (kahweol and cafestol), methylxanthines (theophylline, caffeine and theobromine), chlorogenic acids (p-coumaroylquinic, feruloylquinic and caffeoylquinic acids), flavonoids (anthocyanins and catechins), tocopherols and melanoidins [3].

Caffeine (1,3,7-trimethylxanthine) is one of the bioactive compounds found in coffee. It is a methylated purine base formed as a degradative product of purines [25]. It is completely absorbed by small intestine and stomach in around 45 minutes after its consumption. It reaches to its highest concentrations in the blood stream between fifteen minutes to two hours. After absorption, it is distributed throughout the human body and liver metabolizes it. A reaction catalyzed through cytochrome P450 oxidase enzyme system separates methyl 1 and 7 groups of caffeine and ultimately three methyl-xanthines are formed. These methyl-xanthines are paraxanthine (84%), theobromine (12%) and theophylline (4%) [26].

Since, caffeine and adenosine have similar structure, so caffeine acts as an adenosine receptor antagonist and therefore has impact on the peripheral and central nervous systems [27]. Caffeine not only stimulates the central nervous system but also elevates blood pressure, wakefulness and metabolic rate; and reduces DNA degradation and hydroxyl radicals [21]. Coffee causes stimulation of cardiac muscle and relaxation of smooth muscle especially bronchial muscle and acts on the kidney to produce

diuresis [28]. Caffeine increases the capacity for muscular work by producing a slight increase in the basal metabolic rate.

Along with caffeine, diterpene molecules such as kahweol and cafestol also reduce the risk of colorectal cancer [29]. Furthermore, cafestol increases the activity of glutathione-S-transferase, thereby increases degradation of toxic compounds, protects against aflatoxin induced genotoxicity and thus exerts hepato-protective effect [30].

However, these two diterpenes namely kahweol and cafestol also exert adverse health effect such as increasing LDL and total cholesterol [31]. Among diterpenes, cafestol reduces the activity and expression of cholesterol-7-α-hydroxylase enzyme. This enzyme acts as a rate-limiting enzyme during bile acid synthesis and thus exerts cholesterol increasing effect [32]. Fortunately, the levels of kahweol and cafestol in coffee are significantly reduced after filtration [33].

Diterpene molecules not only exert negative effects such as increasing blood lipid levels, but also exert positive effects such as antioxidant activity and protection from cancer [34]. Another diterpene molecule, kahweol exhibits anti-inflammatory effects. This action of kahweol is attributed to its ability to inhibit inducible nitric oxide synthase and macrophage cyclooxygenase-2 expression and its modulator effect on NF kappa-β expression [35].

Another bioactive constituent of coffee, CGA is frequently linked with anti-inflammatory, anti-bacterial, anti-hypertensive and antioxidant activities. Moreover, CGA exerts inhibitory effect on fat accumulation and modulator effect on glucose metabolism [36]. CGA stimulates glucose uptake in both insulin sensitive and non-insulin sensitive adipocytes and it also plays a role in glucose metabolism. CGA decreases serum and hepatic triglycerides, LDL cholesterol and LDL oxidation levels. Thus, activates lipid metabolism in liver and inhibits lipid absorption in small intestine [37].

2.1 Coffee and Diseases Relationships

Coffee prevents many chronic diseases including cancer, type 2 diabetes mellitus, cardiovascular, renal, neurological and liver diseases, and endocrine disorders [22].

3. EFFECT OF COFFEE ON IMMUNE SYSTEM

Coffee is an enriched source of polyphenols. It is reported that polyphenols led an impact on immune function and chronic inflammation [38]. The polysaccharide constituents in coffee such as cellulose, galactomannans and arabinogalactan proteins (AGP) account for nearly 50% of dry weight of coffee bean. AGPs exhibit prebiotic, cholesterol-lowering, emulsifying and immune-modulatory properties [39].

The Type-2 arabinogalactan fraction increases proliferation of splenocytes and peritoneal macrophages, also activates production of IFN-γ, TH-1 type cytokines and IL-1. It inhibits dermatitis and has been proved effective against allergic reactions [40].

Gostner et al [41] reported that coffee extract suppresses mitogen induced tryptophan degradation and neopterin formation in human peripheral blood mononuclear cells. Therefore, it has been suggested that coffee extract has anti-inflammation and immunosuppression properties. Lopez-Garcia et al. [42] reported that higher coffee consumption led to lower endothelial dysfunction or plasma concentration of many markers of inflammation. Loftfield et al. [38] suggested that lower levels of circulating inflammation markers among persons who drink coffee had somewhat associated relationship of coffee drinking with cancer and other chronic diseases.

4. EFFECT OF COFFEE ON CANCER

International Agency for Research on Cancer [IARC] in 2016 has characterized coffee as non-carcinogenic to humans [43]. The consumption of coffee has been linked with decrease in endometrial various cancer risk [44]. Studies suggested that kahweol present in coffee had great anti-cancer property and is responsible for cancer chemo-prevention [45]. Kahweol also possesses anti-oxidant property. It protects DNA against hydrogen peroxide-induced oxidative stress by removing reactive oxygen species (ROS) and stimulates heme oxygenase-1 to control intracellular ROS levels [35]. Besides kahweol, CGA also have antioxidant and anti-inflammation properties [46]. Furthermore, caffeic acid has the ability to suppress DNA methylation in cancer cells. It inactivates in a number of ways

contributing in tumorigenic process such as apoptosis, stress and inflammatory response and cell cycles regulation [47].

Chae et al. [48] reported that consumption of coffee exerted anticancer effect by causing reduction in some transcription factors. Cancer is developed by increased activation of the transcription factor specificity protein 1 (Sp1). It has been revealed that this transcription factor gets significantly reduced in kahweol treated cells.

Carcinogenesis is suppressed by activating NF-E2-related factor 2 (Nrf2), another transcription factor [49] and activation of Nrf2 in human increases with coffee consumption [50].

The chemo-preventive effect of coffee depends on the mechanisms involved in regulation of genes expression involved in the detoxification, metastasis, angiogenesis, apoptosis, inflammation and DNA repair processes [51].

Coffee exhibits anti-carcinogenic effect by exerting inhibitory/suppressive effects at every step of carcinogenesis action process. Interestingly, coffee prevents development of cancer by removing pro-carcinogens, inhibiting oxidative damages and stimulating cellular defense systems in the initial phase of carcinogenesis. Coffee exerts anti-carcinogenic effect by promoting apoptosis, eliminating damaged cells and performs anti-inflammatory actions during progression of carcinogenesis. Coffee also inhibits cell adhesion, metastasis and invasion during metastasis phase of carcinogenesis [52].

5. EFFECTS OF COFFEE ON COLORECTAL CANCER

Colorectal cancer is third widespread cancer in the world [53]. Till date, surgeries and adjuvant treatments have been considered as the most effective treatments. However, the mortality of colorectal cancer remains high and therefore the application of chemo-preventive agents recently has drawn attention as promising strategies for human cancers [45]. Coffee is hypothesized to be protective in colorectal cancer because it contains many anti-carcinogenic compounds [19]. Many studies have supported this hypothesis [19,47,54]. Coffee can protect against colorectal cancer by increasing the motility of large intestine in recto sigmoid region. Cafestol and kahweol contents present in coffee exhibit antioxidant property by promoting release of natural sterols and bile acids into colon. Caffeine present in the coffee inhibits colon cancer cell growth [47,55].

Colorectal Cancer Report [56] revealed that iron increased the risk of colorectal cancer owing to its catalytic activity on the generation of reactive oxygen species (ROS). The presence of polyphenols in coffee inhibits absorption of iron and contribute anti-carcinogenic attribute to coffee [57].

Furthermore, Kang et al. [58] hypothesized that coffee protected against colorectal cancer at the molecular level. It has been revealed that caffeic acid targeted colon cancer metastasis and kinases such as MEK1 or TOPK to suppress the transformation.

6. EFFECT OF COFFEE ON PANCREAS AND LIVER CANCER

Pancreas cancer is the eighth most wide spread cancer responsible for death in the world [59]. Pancreas Cancer Report, 2012 suggested that coffee exhibited no significant effect on pancreas cancer risk [60]. The studies revealed that either there was no significant relationship between coffee consumption and pancreas cancer or there was a feeble correlation amongst its consumption and elevated risk of pancreas cancer [61-64]. However, other studies depicted an inverse relationship between coffee consumption and risk of pancreas cancer [59, 65].

Liver cancer, also known as hepatocellular carcinoma is one of the most lethal cancers worldwide [66]. Wierzejska [67] reported that consumption of coffee might lead a protective effect against liver cancer. According to a report published by the World Cancer Research Fund International in 2015, high consumption of coffee is a potential safeguard against liver cancer [68]. The coffee combats hepatocellular carcinoma by inhibiting the activity of phase 1 activating enzyme and early mutagenic events through stimulating phase 2 detoxifying enzymes. Coffee possesses anti-inflammatory, anti-oxidant and anti-fibrotic properties [69]. A meta-analysis study also found that consumption of coffee might reduce the risk of liver cancer [70]. It has been suggested that there is an inverse relationship between the risk of hepatocellular carcinoma and coffee consumption and this relationship is possibly mediated by

inflammation, metabolic, liver damage and iron metabolism biomarkers [71].

In addition, studies have revealed that consumption of coffee might have impact on the liver enzymes. In a study, it has been observed that daily consumption of 3 to 4 cups of unfiltered coffee increased alanine aminotransferase (ALT) levels and filtered coffee consumption decreased alkaline phosphatase and bilirubin levels in healthy individuals [72]. Low levels of markers of liver damage including gamma-glutamyl transferase enzyme and alanine transaminase enzyme have been correlated with coffee consumption. Thus, coffee consumption is linked to a reduced risk of cirrhosis, a risk factor for the development of liver cancer [73]. Klatsky et al. [74] found a correlation between coffee consumption and lower prevalence of elevated ALT and aspartate aminotransferase (AST) enzyme levels. These results supported the hypothesis that coffee is protective against liver disease including cirrhosis.

7. EFFECT OF COFFEE ON BREAST CANCER

It is considered that around 10 to 15% of breast cancer cases are due to the factors associated with lifestyle including dietary habits [75]. Studies have suggested that consumption of coffee reduced the risk of breast cancer [76,77]. Contrarily, other studies suggested that there was no correlation between breast cancer risk and coffee consumption [78-80]. The Breast Cancer Report, 2010 also mentioned that there is no correlation between breast cancer and coffee [81]. On the other hand, there are reports indicating inverse relationship between breast cancer and coffee consumption. These reports suggested that consumption of high-caffeine-containing beverages such as coffee is inversely related to bioavailability of testosterone hormone and is affirmatively associated with sex hormone binding globulin. These hormonal changes lessen the risk of breast cancer [47]. There are reports indicating that regular consumption of coffee significantly elevated the ratio of 2-hydroxyestrone (2OHE) to 16-α-hydroxyestrone (16-α-OHE). An inverse relationship has been suggested between this ratio and risk of breast cancer [82]. Besides, there is a statistically substantial decrease in the risk of breast cancer among women consuming 6 or more cups/day of coffee. Caffeine contents in coffee protect against risk of breast cancer in females with BRCA1/2 gene mutation [83]. The protective effect of coffee has been reported against breast cancer among females with BCAR1 mutation [84].

8. EFFECT OF COFFEE ON PROSTATE CANCER

The prostate cancer is more frequently found in male humans of developed countries [85]. The studies have depicted the association between higher coffee consumption and lower prostate cancer [86-89]. This inverse relationship has been associated with potentially chemo-preventive contents such as cafestol, kahweol, chlorogenic acid and caffeic acid present in coffee [90]. The constituents, cafestol and kahweol exert anti-carcinogenic properties by stimulating phase 2 enzyme [91]. Kamiyama et al. [92] reported that CGA exhibited antioxidant activity. Lee and Zhu [93] reported inhibition of DNA methylation by caffeic acid. Li et al. [76] observed that consumption of coffee positively controlled the serum levels of total testosterone and sex hormones and thus may affect the risk of prostate cancer.

9. EFFECT OF COFFEE ON ENDOMETRIAL CANCER

Zhou et al [94] revealed that if any woman drinks coffee, she is on a decreased risk of endometrial cancer at the rate of 5% risk reduction by each cup of coffee per day. Caffeine and methylxanthine in coffee may increase the amount of sex-hormone-binding globulin, thus reducing the concentrations of sex-steroids and leading to down regulation of endometrial hyper proliferation. Chlorogenic acid produces catechins, caffeic, ferulic and coumaric acids that are partly lost during roasting. Melanoidins that are mainly produced during roasting and diterpenes have anticarcinogenic effects.

10. EFFECT OF COFFEE ON SKIN CANCER (MELANOMA)

Various bioactive compounds such as 5-O-caffeoylquinic acid, cafestol and kahweol found in coffee, have been demonstrated to target different pathways of UV-mediated melanoma carcinogenesis. The inverse association of coffee and melanoma may be mediated through various mechanisms including detoxification of carcinogens, inhibition of carcinogenesis, induction of cancer cell apoptosis as well as suppression of oxidative stress and DNA

damages. The role of over-expression of cyclooxygenase-2 (COX-2) in response to UV radiation in the development of malignant melanoma has been reviewed. Caffeic acid has been shown to suppress and down-regulate UVB-induced COX-2 expression [95].

Coffee intake has been associated with reduced risk of oral, pharynx, liver, colon, prostate, endometrial cancer and melanoma; and increased lung cancer risk [96].

Caffeine and other nutrients contained in coffee and tea exhibit protection against non-melanoma skin cancer (NMSC) and basal cell carcinoma (BCC) development [97].

However, Zeegers et al. [98] showed increased urinary tract cancer risk by approximately 20%. Their study was based on a meta-analysis of 37 epidemiological studies.

11. EFFECT OF COFFEE ON NEUROLOGICAL DISEASES

Parkinson's is one of the common neurodegenerative diseases worldwide. It has been reported that caffeine present in coffee exerted a protective impact on Parkinson's disease. However, the exact action of coffee on Parkinson's disease is unclear. It is believed that this mechanism is mediated by caffeine effect on adenosine A2 receptor [99].

Caffeine behaves as an adenosine receptor antagonist by inhibiting adenosine A2 receptors and stimulates the central nervous system [100]. Martyn and Gale [101] reported that caffeine exhibited neuroprotective effect because of its ability to inhibit adenosine A2 receptors concentrated in dopamine enriched areas of the brain. Caffeine also exhibits neuro-protective effects by reducing MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) induced neurotoxicity in animal models of Parkinson's disease [102]. It is reported that consumption of 2 to 3 cups of coffee per day could protect against Parkinson's and Alzheimer's diseases [103].

12. EFFECT OF COFFEE ON TYPE 2 DIABETES MELLITUS

High coffee consumption is linked with low risk of type-2 diabetes mellitus and better glucose tolerance [104]. Alperet et al. [105] reported that more than twenty prospective cohort studies conducted in USA, Asia and Europe, indicated an inverse relationship between type-2 diabetes and coffee consumption. However, there is not much information available about the mechanism responsible for this inverse relationship [106]. It is reported that caffeine, chlorogenic acids and magnesium compounds in coffee could affect glucose metabolism [107]. Theophylline, a metabolic product of caffeine in liver, exerted anti-diabetic activity by controlling glucose metabolism [108]. Chlorogenic acids exerted anti-diabetic activity by reducing glucose output from liver, exhibiting its anti-oxidative properties, and reducing glucose absorption in the intestine through inhibiting the enzyme glucose-6-phosphate translocase [18]. Chlorogenic acids have also been shown to inhibit gut incretin hormones and protect pancreatic β cells against oxidative stress through antioxidant property [109].

Trigonelline exerted anti-diabetic activity by modulating involved enzymes such as glucose-6-phosphatase, glucokinase, carnitine palmitoyl transferase and fatty acid synthetase of glucose and lipid metabolism [110]. Magnesium contents of coffee influence diabetes by improving insulin secretion and sensitivity [111]. Coffee has a protective effect on the risk of adult-onset diabetes and this effect is mainly mediated by postprandial glucose homeostasis [112]. It is now evident from studies that regularly 3-4 cup/day coffee consumption is linked with lower risk of type 2 diabetes mellitus [24,110]. Ding et al. [113] demonstrated a robust inverse association between coffee consumption and risk of diabetes. Compared with no coffee consumption, consumption of 6 cups/day of coffee was associated with a 33% lower risk of type 2 diabetes. Caffeinated coffee and decaffeinated coffee consumption were both associated with a lower risk of type 2 diabetes.

13. EFFECT OF COFFEE ON CARDIOVASCULAR DISEASES

Coffee has both positive and negative effects associated with cardiovascular diseases [114]. Numerous mechanisms have been proposed to explain the harmful as well as protective effects of certain compounds present in coffee on cardiovascular disease development. Coffee exerts negative impact in cardiovascular diseases in the form of increasing blood pressure, serum lipid levels and serum homocysteine levels [115]. Olthof et al. [116] reported that CGA present in coffee, increased

the total homocysteine levels in plasma. Homocysteine caused unfavorable effects on the smooth muscle cells and cardiovascular endothelium, resulting in induction of cardiovascular problems [117].

Furthermore, caffeine in the coffee increases acute blood pressure by stimulating sympathetic nervous system and increasing release of norepinephrine with activation of renin-angiotensin system and led direct effect on the adrenal medulla [118,119]. Farag et al. [120] also reported that caffeine increased blood pressure in healthy normal young men and women. Diterpenoid alkaloids such as kahweol and cafestol are considered as coffee fats. These are responsible for increasing blood lipids [121]. However, filtration of coffee reduces these compounds [122]. In a meta-analysis study, consumption of unfiltered coffee has been found to increase serum levels of LDL and total cholesterol [123]. Kahweol and cafestol elevated the levels of serum cholesterol by reducing the activity of LDL receptor. This caused accumulation of LDL cholesterol outside the cells and supported development of atherosclerosis [124]. However, diterpenes have positive physiological effects such as hepatoprotective and antioxidant effects [125]. Meta-analysis study also revealed that coffee consumption exhibited a beneficial association with blood pressure compared with no coffee consumption as control [126]. Coffee consumption (3-5 cups a day) is associated with a lower risk of incident cardiovascular disease, coronary heart disease and stroke [127]. Consumption of coffee also reduces mortality from all causes of cardiovascular disease [128]. However, decaffeinated coffee does not appear to alter lipid levels [129].

14. EFFECT OF COFFEE ON OBESITY

The intake of coffee polyphenols decreases dietary-induced obesity. Polyphenols contents in coffee increased energy expenditure through suppressing transcription factor sterol regulatory element binding protein-1c (SREBP-1c), which in turn controlled the expression of lipogenic enzymes such as stearoyl CoA desaturase 1 and acetyl CoA carboxylase in liver and adipose tissue [130].

Nagao et al. [131] suggested that regular consumption of chlorogenic acid reduces body fat, especially the abdominal fat and visceral fat. Caffeine present in coffee suppresses fat absorption. CGA causes decrease in hepatic triglyceride levels [132]. Cho et al. [133] reported that both CGA and caffeic acid exhibited anti-obesity effects by decreasing cholesterol and fatty acids biosynthesis. These components altered the plasma adipokine levels thereby increasing PPAR-alpha expression leading to fatty acids oxidation in liver.

Gavrielli et al. [17] found that moderate coffee consumption effectively reduced energy intake all day and after meals. In addition, coffee consumption also has potential beneficial effects on some metabolic risk factors such as hypertension, abdominal obesity and hyperglycemia [134]. Therefore, coffee consumption has been associated with a lower risk of metabolic syndrome [135].

It has also been shown that green coffee extract had anti-obesity activity with reducing body fat accumulation by regulating adipogenesis, and genes and proteins associated with lipid metabolism in white adipose tissue and liver and thus led to loss of body weight [108,136,137].

14.1 Coffee Consumption and Weight Loss

Moderate coffee consumption can be associated with weight loss. The caffeine in coffee stimulates the nervous system. It also causes our body to produce a small amount of adrenaline. Both these factors send inducing signals to the body to break down stored fats and insert them into the blood. Coffee also increases our metabolism by 3 to 11%, depending on consumption level, which enables our body fat to process in our blood as energy [138].

14.2 Coffee and Mortality

A dose response meta- analysis study revealed that coffee consumption reduced all-cause mortality on consumption of 3 to 4 cups coffee a day compared to no consumption [139].

14.3 Coffee and Liver

Coffee intake versus no coffee consumption has been associated with lower risk for a range of liver ailments. A 29% lower risk of non-alcoholic fatty liver disease [140] and a 27% lower risk for liver fibrosis has been shown on coffee consumption [141].

14.4 Coffee and Depression

Coffee compounds such as trigonelline, N-methylpyridinium, chlorogenic acid, catechol, pyrogallol, and 5-hydroxytryptamides have been demonstrated to increase calcium signaling and dopamine release. Increased dopamine release may counteract the depressed status, as depression is associated with alteration of the dopamine system. Moreover, as depression has also been correlated with a low-grade inflammation, certain phenolic compounds contained in coffee, such as chlorogenic and caffeic acids, may exert beneficial effects through their antioxidant and anti-inflammatory activity [142].

14.5 Coffee and Musculoskeletal System

The meta-analysis study performed by Lee et al. suggested that daily consumption of coffee is associated with an increased risk of fractures in women and a contrasting decreased risk in men [143].

Coffee consumption has been found to be associated with increased risk of rheumatoid arthritis. As caffeine contents in coffee exert catabolic effects on articular and growth plate cartilage, it causes osteoarthritis (OA) and longitudinal bone growth inhibition (LBGI), which leads to growth retardation with its prenatal or direct exposure. Caffeine intake also negatively affects the physiology of both articular and growth plate cartilage, increasing consumers predisposition to suffer OA and LBGI [144,145].

14.6 Coffee and Renal Diseases

A meta-analysis of cohort and case-control studies has been conducted to pool the relative risk (RR) estimates of the association between coffee and urolithiasis. It has been observed that coffee consumption is associated with a decreased risk of urolithiasis [146]. Moreover, Coffee consumption has been found to be associated with reduced risk of urinary incontinence [147]. Wijarnpreecha et al [148] demonstrated no significant association between coffee consumption and chronic kidney disease (CKD) in males.

14.7 Coffee and Gastrointestinal System

Coffee consumption reduces the risk of gallstone disease. Coffee inhibits gallstone formation by stimulating cholecystokinin release, eventually enhancing gall-bladder contractility and decreasing cholesterol crystallization in bile [149].

14.8 Coffee and Pregnancy

High caffeine intake during pregnancy is associated with a significant increase in the risk of low birth weight (LBW) and this risk appears to increase linearly as caffeine intake increases [150]. A dose response analysis study revealed that increase in the risk of pregnancy loss increased by 19% for every increase in caffeine intake of 150 mg/day and by 8% for every increase in coffee intake of two cups per day [151]. It has been reported that there is detrimental association between maternal coffee consumption and childhood leukemia risk [152]. However, in meta-analysis cohort study performed, no important association between maternal caffeine consumption during pregnancy and the risk of preterm birth has been found [153].

15. COFFEE CONSUMPTION RECOMMENDATIONS

According to European Food Safety Authority (EFSA) recommendations, consumption of caffeine is safe up to 400 mg/day in healthy adults. In line with an active lifestyle and a healthy diet, moderate coffee consumption (3 to 5 cups/day) has been associated with a wide range of desired physiological effects. For healthy adults (other than pregnant and lactating women), this amount of consumption is safe. However, according to EFSA recommendations, pregnant and lactating women can consume caffeine only up to the extent not exceeding 200 mg/day, that is, the consumption of coffee is likely to be less than two cups per day [154].

16. CONCLUSION

Coffee is one of the major sources of bioactive compounds in modern diet, and its demand continues to rise. Coffee is widely consumed throughout the world. Its health benefits depend on caffeine, chlorogenic acids, caffeic acid, kahweol and cafestol. Regular coffee consumption of 3 to 5 cups/day (moderate consumption) can reduce the risk of type-2 diabetes mellitus, Alzheimer, Parkinson and cardiovascular diseases and exerts numerous protective effects. It is reported that coffee oils,

cafestol and kahweol increased LDL and total cholesterol levels. However, with the filtration of coffee, the contents of kahweol and cafestol considerably got reduced and filtered coffee consumption may limit the elevation in serum cholesterol levels. Similarly, kahweol is also responsible for advantageous effects such as anti-oxidant and anti-inflammatory properties. Therefore, consumption of 2 cups (200 mg caffeine) per day for pregnant and lactating women and 3 to 5 cups (400 mg caffeine) per day for adults will be beneficial. Further research on the mechanism of action of coffee constituents and clinical trials are required for a better understanding of the effects of coffee on human health. In addition, composition of coffee can be engineered through alteration of the roasting process; the possibility of utilizing this information to improve health-related properties of the beverage.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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