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Coffee: All You Need to Know

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Abstract

Effect of coffee consumption on human health has always been under debate. This study is an effort to summarize all possible outcomes of coffee consumption on human health including both positive and negative effects. The most common benefits of coffee consumption include the increased agility and mood stability. It has been reported to lower the risk of developing Type 2 Diabetes, CVDs, various types of cancer including hepatic cancer, metastatic prostate cancer, colon cancer, malignant melanoma and endometrial cancer, some neurodegenerative disorders such as. Alzheimer and Parkinson diseases, hepatic fibrosis and cirrhosis as well as general and cause-specific mortality and improves the musculoskeletal activity. Coffee is rich in pharmacologically active components including caffeine and caffeic acid which exhibit excellent antioxidant, anti-inflammatory, anti-microbial and anti-malarial activity. Coffee is also known to influence a person's life span as it has inverse relation with telomeres length. It also prevents from gallstone formation. Most commonly reported negative effects of coffee consumption on human health are heartburn, diuresis and addiction. Pregnant and post-menopausal women are also advised to cut short the use of coffee. Overall, coffee has a great number of health protecting effects on humans resulting in less hospitalization and less mortality.

Keywords: Coffee, Caffeine, chlorogenic acid, diterpenes, beneficial, diabetes mellites, cardiovascular disorders, cancer, anti-oxidant

I. Introduction

Coffee is a commonly found pharmacologically active beverage of modern era. It is extensively used globally due to its energy boasting effect, appealing flavors and aroma. People also use it for social meetings, relaxation, heightening of work performance as well as for keeping oneself active (Wang, Shen et al. 2016). It is reported that daily consumption of coffee around the globe is about 2.25 billion cups of coffee (Morris 2019). Coffee is actually combination of around 800 volatile molecules among which chlorogenic acids and caffeine are of prime importance (Jeszka-Skowron, Zgoła-Grześkowiak et al. 2015). For centuries, the topic of effect of coffee on human health has been under debate. Different cohort studies and meta-analysis have shown controversial findings. In 1991, World Health Organization issued a list of possible cancer-causing substances and coffee was included in the list (Harvard T.H CHAN). In 2016, it was removed from the list as enough evidences and researches were gathered to prove that coffee consumption does not pose any increased risk of contracting cancer in consumer (Nieber 2017). The beneficial effect of coffee on human health are often linked to its active and diverse components such as caffeine, hydroxy hydroquinone (HHQ),

chlorogenic acid and caffeic acid, etc. (Hall, Desbrow et al. 2015). Coffee has been shown to lower the risk of contracting diabetes mellitus, Alzheimer's disease, various cancer lines, nerves damage, Parkinsonism, and liver damage (Nieber 2017). Many studies have reported that it lowers the oxidative stress through stimulation of Nrf2-ARE pathway and by inducing protein and mRNA expression (Martini, Del Bo et al. 2016). The metabolites of Caffeine, a prime component of coffee help in proper cognitive functionality (Abreu, Silva-Oliveira et al. 2011). Cafestol and kahweol of coffee modulates detoxifying enzymes which protects from malignant cells (Cavin, Holzhaeuser et al. 2002). Coffee is found to increase the telomere length, promote the antioxidant and anti-inflammatory activity, lower the risk of cardiac disorders, and enhance the skeletal muscle growth. The harmful effect of coffee is attributed to the fact that high consumption of coffee may raise serum cholesterol, which in turn may affect cardiac health, for example, augmented risk of contracting myocardial and cerebral infarction. It may also cause insomnia and cardiovascular complications (George, Ramalakshmi et al. 2008). Caffeine exert its function through adenosine receptors and a person is suspectable to become addicted to it thus quitting coffee consumption lead to muscle fatigue and other problems linked with addiction (Olekalns and Bardsley 1996). Coffee is found to interfere with oral contraceptives and post-menopausal hormones so it is advised for pregnant and postmenopausal women to avoid high coffee intake (Jahanfar and Jaafar 2015). This review article is an attempt to discuss the potential health benefits of coffee.

II. Coffee and its constituents

Coffee has a rich phytochemistry ranging from macronutrients to micronutrients. It is actually a mixture of nitrogenous compounds, carbohydrates, phenolic compound, lipids, alkaloids, vitamins and minerals. The exact composition of these compounds differs with coffee variety (green or black), processing (decaffeinated or caffeinated) and degree of roasting. Caffeine is the most active and widely known component of the coffee. Coffee is abundant in certain micronutrients i.e. magnesium, sulphate, methyl, aglycone, glucuronide and lactone. It also contains vitamin B3 precursor trigonelline, vitamin E and niacin. Lipid fraction of coffee includes diterpenes; cafestol and kahweol. In addition, coffee is rich in polyphenols like chlorogenic acids. The chief chlorogenic acid of coffee is 5-caffeoylquinic acid, though other chlorogenic acid such as feruloylquinic, dicaffeoylquinic acids and caffeoylquinic acid also exist in considerable amounts (Arnaud 1993). These unique and bioactive compounds are the main causes of positive and beneficial effect on human health linked with coffee consumption.

2.1 Caffeine

Caffeine is actually a purine containing alkaloid with a formula of 1,3,7-trimethylxanthine (Spiller 1998). Natural and major source of caffeine is coffee beans. One cup of homemade coffee contains nearly 30mg to 175mg caffeine (Dömötör, Szemerszky et al. 2015) . It is reported that caffeine is the most extensively used psychoactive drug globally. Caffeine performs its function by the antagonism of the adenosine receptor A_1 and A_2. Adenosine is an endogenic neuromodulator which stimulates the feeling of lethargy and drowsiness. Thus, it is said that caffeine actually stimulates the CNS (Cornelis 2019). Caffeine is an ergogenic drug as its stimulatory effect on central nervous system trigger a chain of physiological reactions resulting in enhanced endurance, performance and increased exercising capacity. Caffeine significantly improves exercise performance by lowering fatigue, enhancing oxygen uptake and improving substrate supply (van Dam, Hu et al. 2020). Furthermore, caffeine

is also reported to exhibit great anti-inflammatory, anti-oxidant and anti-microbial properties. Many meta-analysis and epidemiological researches have proven the reverse correlation between caffeine and development of various nerves damaging disorders, particularly Alzheimer´s disorder and Parkinson's disorder (Grosso, Godos et al. 2017). It has been reported that caffeine intake through coffee leads to lower risk of developing several hepatic disorders including hepatocellular carcinoma, liver cirrhosis and liver fibrosis (Spiller 2019). Moreover, caffeine reduces hepatic fibrosis caused by Non-alcoholic fatty liver disorder and hepatitis C (Shen, Rodriguez et al. 2016). It also exerts several physiological effects such as excessive urination, increased metabolic rate and elevated blood pressure. Caffeine, along with other pharmacologically active components of coffee for example chlorogenic acids and trigonelline, is responsible for hepatoprotective effect attributed with coffee.

2.2 Cafestol and kahweol

Coffee contains two important diterpenes; cafestol and kahweol which stimulates the activity of a cholesterol lowering protein CTEP (cholesterol ester transfer protein) in humans humans (Lee and Jeong 2007). This protein actually transfers cholesteryl esters from bad cholesterol known as HDL to the, LDL and VLDL or good cholesterol. Decreased HDL and increased LDL results in lowering of risk of developing heart diseases. These diterpenes especially cafestol which is abundant in unfiltered coffee has a great anti-inflammatory, antioxidative and antitumorigenic properties (Mellbye, Jeppesen et al. 2015). Kahweol also shows anti-inflammatory effect (Park, Song et al. 2017).

2.3 Chlorogenic Acid

Chlorogenic acids belongs to the family of dietary phenols and are esters of quinic and trans-cinnamic acids. 5-*O*-caffeoylquinic acid, is of prime importance among all chlorogenic acids present in coffee. Coffee supplies large amount of chlorogenic acid and caffeic acid (Jeszka-Skowron M, et. al, 2015). Chlorogenic acid have been reported to show antioxidant property in vitro but Chlorogenic extensively metabolizes into its components by the activity of human colon flora thus its antioxidant activity decreases.
However, chlorogenic acid is said to contribute towards lower risk of several degenerative and non-degenerative diseases linked with coffee consumption leading to increased longevity of person (Farah and de Paula Lima 2019).

2.4 Micronutrients

Coffee is rich in many micronutrients including potassium, magnesium, vitamin B, niacin, and vitamin E. The RDA (recommended dietary allowance) of magnesium for adult men is 420mg/dl. While a cup of coffee contains 7mg magnesium, thus it is said that a cup of coffee could provide 1-5% of RDA of magnesium. Similarly, it provides 1-2% of RDA of potassium. Trigonelline found in coffee is a precursor of vitamin B3. A cup of Roasted Coffee provides 1–3 mg of nicotinic acid (vitamin B3).

III. Benefits of coffee on human health

Coffee is usually consumed as energy boosting drink, However, research has shown that it results in many other health boosting effects also, for example lower contracting risk of Type-2-diabetes (Cornelis 2020), liver carcinoma, cirrhosis and fibrosis (Inoue and Tsugane 2019) and heart failure (Messina, Zannella et al. 2015). Enough evidence is present to link coffee consumption with several beneficial outcomes including all-cause mortality (O'Keefe, DiNicolantonio et al. 2018), lower cancer incidences (Grosso, Micek et al. 2016), lower risk of diseases of the cardiovascular

(Gökcen and Şanlier 2019), neurological, liver, musculoskeletal, metabolic and gastrointestinal systems (Ciaramelli, Palmioli et al. 2019).

3.1 Type 2 diabetes

Many epidemiological researches have reported that a regular and healthy coffee consumption results in lower risk of contracting Type 2 diabetes. The regular coffee drinker are less susceptible of contracting diabetes mellites than the persons who does not drink coffee (Santos and Lima 2016). Reports have shown that coffee lowers the occurrence of impaired glucose tolerance, hyperglycemia and insulin sensitivity (Carlström and Larsson 2018).

In 2002, first evidence was reported to indicate the inverse relation between diabetes and coffee consumption. This healthy outcome of coffee consumption is attributed with fact that coffee suppresses the production of a key mediator of Type 2 diabetes which is high-sensitivity C-reactive protein. A meta-analysis involving 457,922 people reported that coffee consumption has inverse relation with developing type 2 diabetes (Carlström and Larsson 2018). The risk of developing diabetes decreases upto 7% with one cup regular consumption of coffee (Kondo, Goto et al. 2019). A Dutch cohort study indicated that individuals who drink 7 cup of coffee in a day has half a chance of contracting diabetes than those of non-coffee drinker (Gunter, Murphy et al. 2017).

Possible diabetes lowering mechanisms associated with coffee components

Lower activity or damage to Beta cells of pancreas leads to insulin independent diabetes. Coffee is thought to protect the beta-cells from failure and thereby protecting from developing diabetes. Chlorogenic acid of coffee boasts the synthesis of glucagon-like peptide-1 (GLP-1) hormone resulting in inhibition of glucose absorption. This effect is further facilitated by inhibition of other key enzymes responsible for glucose absorption for example alpha amylase and glucose-6-phosphatase (Moua, Hu et al. 2020). The suppression of glucose-6-phosphatase by chlorogenic acid of coffee results in inhibition of glucose production by liver (Yarmolinsky, Mueller et al. 2015).

Glucose level rises in blood by gluconeogenesis and glycogenolysis. The terminal step of both of these pathways is the breakdown of glucose-6-phosphate into glucose with the help of glucose-6-phosphatase and a second translocase protein. In vitro studies in rats has shown that chlorogenic acid competitively inhibits glucose-6-phosphate translocase thereby stopping glucose production (Folwarczna, Janas et al. 2016).

CGA of coffee has also been reported to suppress sodium-dependent glucose transport.

When orally glucose is taken Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) hormones triggers the secretion of insulin from pancreas. Coffee consumption leads to decreased GIP concentration and increased plasma concentrations of GLP-1, signifying that coffee may lower glucose absorption from intestine (Lee, Oh et al. 2016). Moreover, CGA excites glucose transport in skeletal muscle through the stimulation of 5’ adenosine monophosphate-activated protein kinase (AMPK) which contributes to the positive and inverse effects of coffee on diabetes (Folwarczna, Janas et al. 2016).

Cohort studies has shown that magnesium intake lowers the risk of developing type 2 diabetes. And a study involving short-term medical trials have reported that magnesium supplements improves insulin sensitivity (Alperet, Rebello et al. 2020). As coffee also contains magnesium thus it may influence insulin insensitivity linked with lower serum magnesium levels. A cohort study shows considerable inverse correlation between coffee consumption and risk of diabetes observed after alteration for dietary magnesium intake (Hang, Zeleznik et al. 2020).

Recently, an epidemiological study conducted in US involving 7000 adults reported inverse relation of coffee consumption and lower risk of diabetes was high in persons who had previously lost weight (Alperet, Rebello et al. 2020). Even though, this finding needs further supportive evidence and clarification, but it shows that weight loss may contribute towards the beneficial effect of coffee consumption on the development of type 2 diabetes mellites.

3.2 Cardiovascular diseases

The role of coffee consumption on cardiovascular health has been always under debate. Different studies and analysis have shown controversial findings regarding effect of coffee on cardiac health. The effect of coffee on CVDs for example heart failure, stroke and total CVD mortality had been studied extensively but inconsistent results were reported (Palatini, Fania et al. 2016). Especially up to 2012 coffee consumption was linked with augmented risk of cardiovascular disorders. A meta-analysis reported that regular coffee drinker (upto 5 cups daily) as compared to non-coffee drinker had 40-60% increased risk of developing CHD (Miranda, Steluti et al. 2017). Another control case study reported that coffee drinkers were more susceptible to developing CHD or myocardial infarction (MI) (Rodríguez-Artalejo and López-García 2017). However in 2012, Cai reported in his study that moderate coffee consumption can actually guard the heart from fibrillation and stroke (Cai, Ma et al. 2012). A meta-analysis reported 11% decreased risk of undergoing heart failure in coffee drinker than non-drinker.

A major supporting evidence for attribution of coffee consumption with lower CVDs risk was presented in a meta-analysis which combined results of 36 control studies involving both men and women. They concluded that people who drank 3-5 cups of coffee regularly had 15% lower risk of contracting cardiovascular disorders than those who do not drink coffee. However, higher intake of coffee such as. more than 6 cups was not linked to either decreased or increased risk of developing CVDs (Zhou and Hyppönen 2019).

In conclusion, these are not conclusive evidence to link coffee consumption with higher or lower risk of CVDs as shape of association remain uncertain. However, in view of recent studies and analysis it is safe to say that moderate amount of coffee consumption has at least a small effect in guarding heart against fibrillation, stroke, failure and high blood pressure.

3.3 Neurodegenerative disorders

The effect of coffee especially its chief component caffeine has always been positively attributed with providing protection against several neurodegenerative disorders especially Alzheimer, Parkinson and loss of memory during aging. Several supporting evidences and studies has been reported over the years to link regular coffee consumption with decreased risk of developing certain neurodegenerative disorders (Herden and Weissert 2018).

3.3.1 Alzheimer disease

Alzheimer's disease is characterized with dementia and progressive cognitive loss. The clinical manifestation of AD includes formation of lesions in brain and overall neuro-fibrosis of brain. These lesions are caused by accumulation of hyperphosphorylated Tau protein and toxic amyloid beta peptide in neurons and brains (Ulep, Saraon et al. 2018).

A less known component of coffee, eicosanoyl-5-hydroxytryptamide (EHT) along with caffeine act synergistically to guard a phosphoprotein (phosphatase-2A) from in-activation (Wierzejska 2017). In turn this enzyme will cause dephosphorylation of Tau protein. Caffeine along with EHT increase plasma GCSF levels which results in several

therapeutic effects against Alzheimer Disorder. The protective effect of EHT against AD has been successfully demonstrated in a rat model (Kwok, Leung et al. 2016).

A meta-analysis has found that high amount coffee drinker showed 27% risk reduction in developing Alzheimer's disease as compared to non-coffee drinker (Liu, Wu et al. 2016).

3.3.2 Parkinson disease

Parkinson's disease (PD) is clinically manifested by decline in dopamine in midbrain, presence of Lewy bodies which are actually α-synuclein containing proteinaceous inclusions along with several other motor and non-motor problems (Poewe, Seppi et al. 2017).Coffee components attenuates the degeneration of dopaminergic neurons thus lowering risk of contracting PD or delaying its commencement (Chuang, Lill et al. 2016). A meta-analysis combining results of 26 studies from all over the world reported that people who drink coffee had 25% decreased risk of developing PD as compared to those who do not consume coffee. The risk of contracting Parkinson disease lowered upto 24–32% with increased coffee consumption of every 3 cups (Hong, Chan et al. 2020). And intake of more than 4 cups of caffeinated coffee regularly resulted in 80% reduction of risk of PD.

A Finnish cohort study involving 6,710 men and women with tracking period of 22 years reported significant decreased risk of developing PD in persons who intake high amount of coffee regularly (upto 10 cups per day) than non-drinkers (Ascherio, Weisskopf et al. 2004).

3.5 Hepatic cancer and other liver diseases

There has been fortifying evidences presented in support of hepatoprotective effect of coffee in humans during last years. The experimental evidences of protective effects of coffee against hepatitis B & C (Saab, Mallam et al. 2014), non-alcoholic fatty liver disease & alcoholic liver disease (Zelber-Sagi, Salomone et al. 2015), liver fibrosis, hepatic cirrhosis (Petrick, Freedman et al. 2015) and overall liver mortality have been reported and confirmed. Over the years significantly consistent and positive inverse relation between coffee intake and incidence of developing liver disorders has been reported. A regular intake of 2 cups of coffee have been linked with a decreased risk of contracting liver fibrosis and cirrhosis and hepatocellular carcinoma. In addition, over all hepatic mortality incidence also decreases with regular coffee intake (Wijarnpreecha, Thongprayoon et al. 2017, Chen, Chang et al. 2019).

ALT and AST are two liver enzymes and their higher levels are indicative of liver disorder. Coffee drinkers are reported to have lower level of AST and ALT levels, less hepatic fibrosis, less hospitalization and thus less liver mortality. Furthermore, a recent cohort study involving 330 patients with alcoholic and non-alcoholic cirrhosis reported strong reduction in serum enzymes AST and ALT levels upon consuming more 4 than cups of coffee daily (Chen, Chang et al. 2019). The IARC (International Agency on Research on Cancer) assessed various studies and reported that regular consumption of high amount of coffee was attributed with decreased serum levels of biomarkers of liver damage, comprising alanine aminotransferase(ALT) and γ-glutamyl transferase(GLT) in blood (McGlynn, Petrick et al. 2020). Furthermore, patients of nonalcoholic fatty liver disease, and hepatitis C and B virus infection have showed considerable reduction in liver stiffness upon regular coffee intake which may indicate less fibrosis and inflammation in patients (Tamura, Hishida et al. 2019).

People who consume 2 cups of coffee regularly has been reported to have 40% lower risk of primary liver cancer mortality (Dickson, Liese et al. 2015). An analyses which combined data from several cohort and case-control studies, confirmed the inverse corelation between coffee intake and liver cancer (Lukic, Guha et al. 2018).

3.6 Colon function and colorectal cancer

Colon cancer (CRC) is third most common cancer worldwide. Coffee contains several pharmacokinetically active components e.g. polyphenols (chlorogenic acids), diterpenes (cafestol and kahweol) and dietry fibers (melanoidins) have been reported to enhance the colon motility and strengthen the antioxidant profile of colon which can lessen the risk factor of colon cancer (Schmit, Rennert et al. 2016). Even though the exact amount of these compounds differs by type of coffee beans, brewing method, extent of roasting, brewing technique, and amount of coffee consumed however they surely can improve overall colon health. They are found to reduce the bile acid secretion, enhance bowel functions (motility, stool output), modify microbiome and display various antioxidant properties which promotes colon health (Schmit, Rennert et al. 2016).

A meta-analysis assessed 25 case-control studies and 16 cohort studies and reported that people who drink coffee regularly had 15–21% lower risk of contracting CRC as compared to those who do not drink it (Bułdak, Hejmo et al. 2018). Thus, it is safe to say that coffee reduces the incidence of colorectal cancer (Guercio, Sato et al. 2015).

3.7 Gallstone

The beneficial outcome of coffee on lowering gallstone formation has been an interesting and statistically consistent topic. A cohort study involving 46,008 men concluded that regular coffee drinker had lower chance of developing gallstone than non-coffee drinker. Same results were reported for women in another study conducted in 2017 (Wachamo 2017).

The chief source of gallstone formation is cholesterol. Caffeine along with other coffee components inhibits cholesterol from accumulating in crystalline form in the gallbladder. They also initiates the gallbladder contraction thereby increasing flow of bile in bladder and cholesterol may not accumulate in it (Tran, Coleman et al. 2019).

3.8 Mortality

Mortality is the frequency of death in a population. It can be general or cause specific. A study in the New England Journal of Medicine reported that men and women who drink coffee have shown decreased total and cause-specific mortality. A large cohort study tracked 200,000 participants for 30 years and concluded that coffee drinkers had reduced rate of all-cause mortality. According to another study in gastroenterology, people who drank 2 cups of coffee regularly had a 50% reduction in hospitalization and mortality. Another study reported 15% lower risk of early death from all causes, including suicide, CVDs and Parkinson's disease of coffee drinker as compared to non-drinker (Kim, Je et al. 2019). Similarly, 16% reduction in early death was reported for persons who drink 6-7 cups of coffee daily. These positive health benefits of coffee remained almost same for caffeinated and decaffeinated coffee (Li, Liu et al. 2019).

3.9 Cancers

Role of Coffee in progression and suppression of cancers has been a controversial topic since 2016. In 2016, WHO removed coffee from the list of potent cancer causing foods and then onward several epidemiological studies and meta-analysis has been reported in favor of coffee consumption attribution with suppression and lower risk of developing different types of cancers including colon cancer, metastatic prostate cancer, liver cancer, skin cancer including malignant melanoma and endometrial cancer. Similarly, various

animal studies have confirmed protective effect of chlorogenic acid of coffee against cancer growth. Coffee triggers the secretion of bile acids and increases its assimilation within colon thereby decreasing the cancer-causing agent's exposure to colon tissues. Coffee have also been found to lower the incidence of inflammation which is a key risk factor for many cancers. Coffee consumption leads to reduction in estrogen level. Estrogen is a hormone whose increased levels are linked with various types of cancers. Additionally, Caffeine itself may hinder the progression and metastasis of cancerous cells (Wierzejska 2015).

The regular coffee consumption results in enhanced antioxidant activities and decreased inflammation resulting in prevention from various cancers. The American Institute for Cancer Research has confirmed that regular coffee consumption may lower the risk of developing endometrial and liver cancer.

3.10 The effect of coffee on skeletal muscle

Several recent studies have reported that coffee consumption boosts skeletal muscle health. Autophagy is a process which degrades and recycle old worn out cells and cell components which on accumulation may pose serious hazards. Skeletal muscles have the largest rate of autophagy. The enhanced autophagy guards the cell by inhibiting the buildup of impaired proteins and organelles which results in optimization of overall cell functions. Coffee has reportedly been shown to trigger autophagy in-vivo in skeletal muscle thereby increasing health and longevity (Kim and Park 2017). A study on female mice with chronic coffee consumption found that polyphenols of coffee induced autophagy in liver, heart, and skeletal muscles (Kolnes, Ingvaldsen et al. 2010). In conclusion, coffee benefits the skeletal muscle health via prompting autophagy.

Moreover, skeletal muscles are also involved in glucose breakdown and regulation. In diabetic patient, they are responsible for up to 75% of the plasma glucose uptake. However, this uptake by skeletal muscle can be insulin dependent or insulin independent (Jang, Son et al. 2018). Two different studies has concluded independently that coffee consumption results in modification of insulin signaling pathway thereby increasing insulin sensitivity of skeletal muscles (Alotaibi, Abounasef et al. 2019). In an in-vitro study, the role of polyphenols and the several other metabolites of coffee on glucose uptake from skeletal muscle has been studied in a healthy male rat model (Guarino, Ribeiro et al. 2013) and reported that polyphenol caffeic acid activated insulin-independent glucose uptake in skeletal muscle. Coffee intake is also found to enhance the regeneration of muscle injured with cardiotoxin injection (Guo, Niu et al. 2014).

Muscular strength and lean mass declines with age. This condition is called sarcopenia. Coffee intake has been linked with reduced incidence of development of sarcopenia thereby lowers functional limitations and disabilities (Guo, Niu et al. 2014).

Recent studies have proven that coffee consumption results in improved regeneration of injured muscle, enhanced insulin sensitivity, decreased progression of sarcopenia,, enhanced upregulated autophagy and increased glucose uptake in skeletal muscle (Dirks-Naylor 2015). Nevertheless, nearly all of the recent findings demonstrating the beneficial effects of coffee consumption on skeletal muscle have only been employed on animal and in-vitro models. It is spectated that coffee intake may have at least a small beneficial effect on human skeletal muscles.

3.11 Inflammatory bowel disease (IBD)

Inflammatory bowel disease (IBD) is a group of disorders that results in inflammation of digestive system. The commonly known types of IBD are Ulcerative Colitis (UC) and Crohon Disease (CD). A recent study reported that coffee protects the drinker digestive

system against contracting ulcerative colitis. One more study tracked 41,836 postmenopausal women for 15 years and reported that regular coffee intake reduces the severity of inflammatory diseases (Ratajczak, Szymczak-Tomczak et al. 2021). In a mouse model of colitis Chlorogenic acid was found to greatly reduce inflammation. Actually, chlorogenic acid inhibits the NF-κB dependent pathway of inflammation which results in lowering of the macro-scopic destruction and myeloperoxidase activity. Moreover, caffeic acid attenuates IL-1β, IL-6 along with TNF-α which are markers of inflammation thereby resulting in the supression of cyclooxygenase-2 and inducible nitric oxide synthase (iNOS) (Barthel, Wiegand et al. 2015). All these mechanisms exhibited by coffee components make coffee a reliever of IBD.

3.12 The effect of coffee on fluid balance

Caffeine is often thought to cause frequent urination in coffee drinker. However, in 2015 it was reported in a literature review that caffeinated coffee consumption did not lead to diuresis. During recent researches no supporting evidence was found for attributing caffeinated coffee consumption with fluid loss through excessive urination even for high category coffee consumption (more than 6 cups). Zhang et al confirmed that coffee intake was not linked with poor hydration (Zhang, Coca et al. 2015). Additionally, a recent epidemiological study verified that regular consumption of moderate amount of caffeinated coffee is not associated with any fluid loss or dehydration (Seal, Bardis et al. 2017).

3.13 Antioxidant and Anti-inflammatory activities

Most of the coffee consumption beneficial effect on human health are due to antioxidant property exhibited by caffeine present in coffee (Hall, Desbrow et al. 2015). Caffeine is an excellent attenuating agent of hydroxyl radicals generated by the Fenton reaction (AlAmri, Albeltagy et al. 2020). In an in-vitro study on rat liver microsome caffeine has been demonstrated to inhibit lipid peroxidation. Caffeine inhibits the secretion of TBARS (thiobarbituric acid reactive substances) and lipid hydroperoxides. Inhibition of these compound is common pathway of antioxidant mechanism. Especially on metabolism in human body caffeine releases 1-methylxanthine,1-methyluric acid which exhibit efficient in vitro antioxidant activity (Tajik, Tajik et al. 2017).

Inflammation is characterized by various cytokines and chemokines. Caffeine is recognized as a potent agent for lessening of these bio-markers thereby decreasing the inflammation. Caffeine exhibit anti-inflammatory action through adenosine receptor antagonism mechanisms and by inhibiting phosphodiesterase.

3.14 Antimicrobial activity

Although there are a small number of in-vitro studies in support of antimicrobial activity of caffeine present in coffee but they are enough to prove that caffeine possesses some degree of anti-microbial property. An in-vitro study has verified the antimicrobial effect of caffeine against *Streptococcus mutans* and intestinal pathogenic bacteria (Nonthakaew, Matan et al. 2015). Furthermore, a study reported that caffeine can inactivate or inhibit the growth of *Escherichia coli*. These studies have led to recognition of caffeine as antimicrobial agent for treatment of bacterial infection (Jiménez-Zamora, Pastoriza et al. 2015).

15 Effect of coffee on telomeres

Telomeres are repeated nucleotide sequences which are present at both ends of chromosomes. These repeated TTAGGG sequences cap the genetic material and prevents from gene loss. However, these nucleoprotein structures become shorter after undergoing each replication batch as a part of telomeric DNA does not duplicate each time a cell

divides. Their length shortens with age and after complete loss of telomeres genetic material disintegrates leading to cell death.

A research study tracked 20,000 participants and reported that people with short telomeres had 25% higher risk of early death than those who had longer telomeres taking in account other health deterioration factors (Steiner, Ferrucci et al. 2020).

A study in New England Journal of Medicine reported that men and women who drink coffee have longer telomeres. Caffeine consumption's inverse relation with telomere length has been confirmed in a recent study. Study reported that after replication telomeres shortened by 36.7 base pairs for coffee drinker while it shortened by 40.0 base pairs for non-coffee drinker (Liu, Crous-Bou et al. 2016). Thus, it is said that people who drink coffee have longer telomere and by influence they may live longer.

lV. Harmful effects of coffee on health

Regardless of the recent uproar of coffee beneficial effects on human health various negative risks of coffee consumption has also been reported. Some of the common negative aspects of coffee consumption on human health are heartburn, abnormal heart rhythm, increased blood pressure, missed beats, nervousness, anxiety, insomnia, headache, dizziness, muscle tremors, dehydration, urination, restlessness and enhanced bone loss in postmenopausal women (especially when their diets lack sufficient calcium). Diterpenes of coffee are shown to increase serum homocysteine and cholesterol levels thereby damaging heart health in a study although no further evidences were reported in favor of this study. Generally, all the recent studies and assays supports the healthy positive effects of coffee. Nevertheless, it is not wise to ignore the fact that beneficial effect of coffee varied with each study and once in a while many studies showed up claiming potent harmful effect of coffee on heart health, fluid balance and cancer. Coffee is found to make people addictive as well cause heartburn, tachycardia, mood swings and diuresis in drinker. Coffee is reported to interfere with pregnant and post-menopausal women's hormones (Steiner, Ferrucci et al. 2020).

In 2018, state of California ordered all coffee sellers to place a warning label on coffee products because it was found that on roasting coffee beans a carcinogenic substance acrylamide was produce. The National Toxicology Program issued a report on carcinogens in 2014, included acrylamide in the list of probable human carcinogen as reported by experiments on animals. However, till to date there has no evidence been reported in support of adverse effect of acrylamide consumption through food on human health.

However, many cancer experts ruled out the possibility of acrylamide being a potent carcinogen. They claimed that acrylamide metabolism is different in human as compared to in animals. In June 2018, the California Office of Environmental Health Hazard Assessment (OEHHA) issued a new guideline in which coffee was excluded from the list of possible human carcinogens (Martino, Goanta et al. 2016).

V. Conclusion

Coffee lowers the risk of contracting Type-2-Diabetes, CVDs, various types of cancer including hepatic cancer, metastatic prostate cancer, colon cancer, malignant melanoma and endometrial cancer, some neurodegenerative disorders such as; Alzheimer and Parkinson diseases, hepatic fibrosis and cirrhosis. It improves the musculoskeletal activity, exhibits excellent antioxidant, anti-inflammatory, anti-microbial and anti-

malarial activity, prevents from gallstone formation and improves a person's quality and quantity of life as it has inverse relation with telomeres length. Some of the common negative effects of coffee on human health are heartburn, abnormal heart rhythm, increased blood pressure, missed beats, nervousness, anxiety, insomnia, headache, dizziness, muscle tremors, dehydration, urination, restlessness and enhanced bone loss in postmenopausal women. In light of recently published studies, it is safe to say that moderate amount of regular coffee consumption is good protector of health.

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