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Review Article

COFFEE: A HEALTH FUEL-BLOT POPULAR DRINKING

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ABSTRACT

Now, the days begin with cups of coffee worldwide. Caffeine is the main component of coffee, which is vastly consumed as a psychoactive agent, and in varieties of dietary supplements. Day by day coffee and caffeinated-consumption areas are expanding. Only a single cup of coffee contains thousands of biochemical. Otherwise, during roasting, some of which turn to convert other chemicals moieties. Thus, the coffee is an interesting item to the drug scientists. Upon this jackpot, a number of researches have been done on coffee and its chemical components; in which many postulations are still in contentious and some are unclear to the coffee users. Upon going through the stand-point, this study has been snapshot to sketch a complete overview on coffee and its components. Our finding depicts constituents of coffee to have antioxidant, anti-inflammatory, anti-Alzheimer's disease, anti-Parkinson's disease, and cardioprotective activities. But the anti-cancerous effect of coffee components is not clear yet. In conclusion, coffee, and its constituents are in important in phytopharmacological research.

Keywords: Coffee, Coffee components, Health-effects

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INTRODUCTION

Now a day, most people start and finish their day with cups of coffee. Biological source of coffee is the *Coffea arabica* (Family-Rubiaceae). *C. arabica* is indigenous to the forests of the South-Western highlands of Ethiopia and the mountainous regions of Yemen. It is also known as the "coffee shrub of Arabia", "mountain coffee", or "arabica coffee". *C. arabica* is believed to be the first species of coffee to be cultivated. Wild plants grow between 9 and 12 m tall, and have an open branching system; the leaves are opposite, simple elliptic-ovate to oblong, 6–12 cm long and 4–8 cm broad, glossy dark green. The flowers are white, 10–15 mm in diameter and grow in axillary clusters. The seeds (two) are contained in a drupe 10–15 mm in diameter, maturing bright red to purple. Now, it is cultivated in South Sudan, Kenya, in many parts of Africa, Latin America, Southeast Asia, China, islands in the Caribbean, in the Pacific and so on. We are used to coffee for at least 1200 y. It started its journey in the Ethiopia in14th century, then followed to Yemeni Sufi monasteries to the Middle East and northern Africa by the 15th century. The intense trade of the Venetian ships with the Middle East opened the doors of Europe and subsequently to America [1]. Coffee has been cultivated and consumed widely. In fact, it remains a highly popular beverage to these days.

Caffeine, the natural alkaloid which is the major component of coffee, originally isolated from coffee beans in 1820. In the United States about 87% of the general population consumes caffeinated beverages, among which 71% are coffee-infused concoctions [2]. However, *C. canephora* (robusta) is known to contain more caffeine than *C. arabica*. From 1995 to 2007, coffee consumption rose per person from 3.5 to 4.4 in the USA; 3.3 to 4.1 in Europe, and from 7.9 to 12.0 kg/year in Finland [3]. The latest one is the most consumed area, this is due to the beverage is a primary source of dietary polyphenols to them [2].

The debate is due to coffee and coffee components consumption and their unsolved health effects. In this study, we discuss the impact of coffee and its derived components of health emphasized on the pathophysiologic contributions.

Stratagem

For this purpose we have searched for published evidence in the databases up to August 2015; following the keywords "coffee", "caffeine", "chlorogenic acid", "cafestol", "kahweol", "caffeic acid", "coffee constituents" were paired with "activities", "nervous system", "cardiac system", "neuroactivity", "epilepsy" "anxiety", "homocysteine", "renin", "angiotensin", "stroke", "cerebral ischemia", "pregnancy", "inflammation", "adolescent", "cancer", "pharmacokinetics", "Parkinson", "Alzheimer", "childhood", "adults", "dose", "pharmacological action", "toxicological action", "antimicrobial", "beverage", "diet", "diabetes", "liver", "hypertension", "baby", "fetus", "gastrointestinal tract". We have got 10,773 evidences on the searched topics, which were then reduced to 513 after reading the abstracts. Attention was then concentrated on 293 papers then followed by exclusion of 262 due to containing similar information in other reviews and/or meta-analysis or full-length research papers (fig. 1).

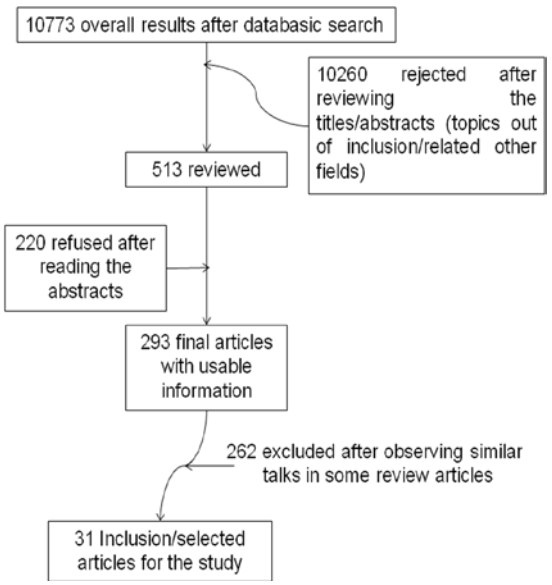

Fig. 1: Sketch of this study

Findings

Caffeine and other coffee components in brief

The complex beverage, coffee contains thousands of compounds including flavor, aroma, bioactive components such as methylxanthines (e. g.-caffeine, theobromine, and theophylline) diterpenes (e. g.-cafestol, kahweol), chlorogenic acids (CGAs) (e. g.-caffeoylquinic acids, feruloyl quinic acids, p-coumaroyl quinic acids), flavonoids (e. g.-catechins, anthocyanins), hydroxycinnamic acids (e. g.-ferulic acid, caffeic acid (CA), p-coumaric acid), tocopherols, and melanoidin.

However, the amount of bioactive components mainly the caffeine depends on species, type, processing, storage as well as roasting process and temperature [4]. In a home-prepared coffee generally, it contains 30 to 175 mg of caffeine (150 ml). Some important chemical moieties found in coffee are shown in fig. 2.

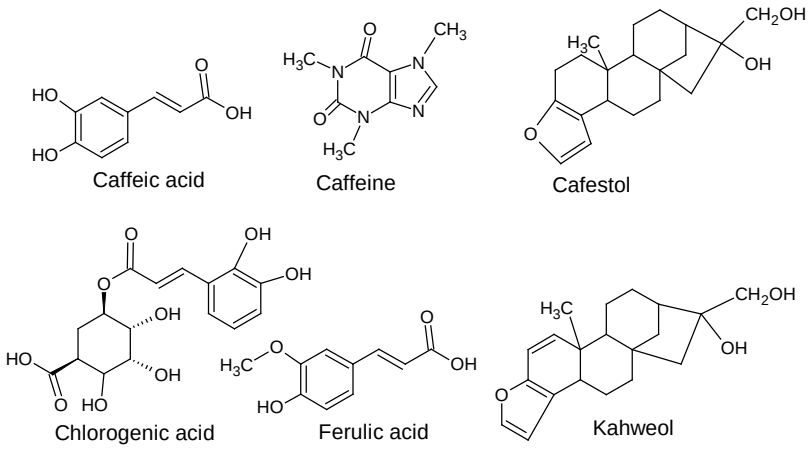

Fig. 2: Important chemical compounds already isolated from coffee

More than 60 plants of which cocoa beans, kola nuts, tea leaves and coffee beans are the most well-known sources of caffeine. Other natural sources of caffeine include yerba maté, guarana berries, guayusa, and the yaupon holly. Not only the coffee but also tea, soft and energy drinks, chocolate products, medications (e. g.-headache treatments, painkillers, over-the-counter stimulants) and few dietary supplements are the main sources of caffeine [4].

The most common polyphenols in coffee are phenolic acids, mainly CA, a type of trans-cinnamic acid, and its derivative, CGA. A single serving of coffee provides between 20 and 675 mg of CGAs depending on the type of roast, and the volume consumed [5]. CGAs constitute a family of esters made up of transcinnamic acids, mainly CA and ferulic acid, and quinic acid. The resulting forms of CGAs include caffeoyl quinic acids, feruloylquinic acids that may be found in several isomeric forms depending on the position of the ester link. Additionally, there can be one or two phenolic acids per quinic acid moiety. 5-O-caffeoylquinic acid is the most common form of CGA, which is often called 'chlorogenic acid.' General pathways of CGA synthesis has been shown in fig. 3.

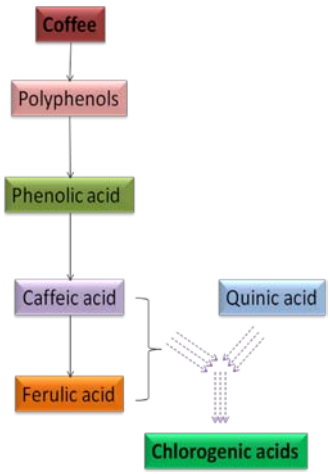

Fig. 3: Chlorogenic acids coining pathway (adapted from 1)

The metabolism of CGAs is still unclear but thought to be in the small intestine and colon [2]. The first step is carried out by the active esterase enzymes, which generate the original phenolic acids in both the small and large bowel. Around two third of CGAs are thought to be absorbed in the colon. The metabolism is carried out by the microbiota, which cleaves the ester bond and provides esterases for further metabolism. Different metabolites of CGAs are found in urine (metabolites and unchanged in 24-h excretion about 27–29%) [1].

Cafestol and kahweol are the two important diterpenes found in coffee oil. They are retained in part by paper or popular sock filters but are preserved when coffee is directly prepared by boiling the ground beans. Caffeine has a half-life of approximately 3–7 h. Its metabolism occurs primarily in the liver, where the cytochrome P_{450} isoform CYP1A2 accounts for almost 95% of the primary metabolism [1].

Health effects of coffee and its major components

On nervous system

Most of the caffeinated supplements including beverages contain caffeine up to 400 mg (table 1), for its stimulant, staminatic and lactic acid build-up reducing effects after exercise [5]. Caffeine is considered one of the popular psychoactive drugs worldwide, biologically which is evident to act through antagonizing the adenosine receptor (AR). Adenosine is an endogenous inhibitory neuromodulator that prompts feelings of drowsiness, and thus, caffeine induces generally stimulatory effects in the CNS [6]. Presynaptically, it reduces synaptic vesicle release while postsynaptically it has been found to stabilize the magnesium on the N-methyl-D-aspartate receptor (NMDA) receptor. The later one is very important for controlling synaptic plasticity and memory function [7]. NMDAR is named after its agonist molecule *N*-methyl-D-aspartate (NMDA) as it binds selectively to it. Activation of NMDA receptors results in the opening of an ion channel that is nonselective to cations with a reversal potential near 0 mV. A property of the NMDA receptor is its voltage-dependent activation, a result of ion channel block by extracellular $Mg^{2+}$and Zn^{2+}ions. This allows the flow of $Na^{+}$and small amounts of Ca^{2+}ions into the cell and K^{+}out of the cell to be voltage-dependent [8]. Calcium flux through NMDARs is thought to be critical in synaptic plasticity, a cellular mechanism for learning and memory. Therefore, the activity of the

NMDA receptor is affected by many psychoactive drugs such as phencyclidine, alcohol (ethanol) and dextromethorphan, anaesthetic such as ketamine and nitrous oxide. And caffeine is a psychoactive agent, whic may act through this receptor.

Table 1: Quantities of caffeine in some daily consumed caffeinated foods and drinks

Products	Serving size (fl. oz)	Caffeine in one serving (mg)
Chocolates	8	1-120
Energy drinks with caffeine added	8.2–23.5	33-400
Carbonated beverages with caffeine added	12	22–69
Alcoholic beverages with caffeine added	1	3-9
Fast foods	A choice of	1-49
Caffeinated waters	16.9-20	42-125
Caffeinated soft drinks	11	30-48
Decaffeinated coffee	4.06	1-5
Espresso	1	50-150
Different tea bag	8-12	2–130
Brewed or percolated, decaffeinated	8	3-12
Instant and regular drip	8	30-330

(Adapted from 3)

Subtypes of ARs are designated as adenosine AR_1, AR_{2A}, AR_{2B}, and AR_3. They also expressed in other tissues such as CNS, vascular endothelium, heart, liver, adipose tissue, and muscle. It is also evident that ARs show specialization for binding to Gi or Gs proteins, and consequently decrease (AR_1 and AR_3) or increase (AR_{2A} and AR_{2B}) the level of intracellular cyclic adenosine monophosphate (cAMP). Thus the later two should be more available to bind with caffeine. Interestingly caffeine is more specific to AR_1 and AR_{2A}. In addition, caffeine at high dose intracellularly in association with ARs may modulate phosphodiesterases and mobilize the intracellular calcium [1].

AR_{2B}, integral membrane protein stimulates adenylate cyclase activity in the presence of adenosine. This protein also interacts with netrin-1, which is involved in axon elongation. Caffeine being an antagonist of it may inhibit this process of the physiological phenomenon. Unlike, other ARs, AR_3 has been shown in studies to inhibit some specific signal pathways of adenosine such as inhibition of growth in human melanoma cells. It is evident to antagonize *MRS1191*, *MRS1523* and *MRE3008F20*, while agonizes Cl-IB-MECA and *MRS3558* [9]. Caffeine should be worked on them oppositely!

Coffee consumption is now thought to be inversely associated with the risk some neurodegenerative diseases such as Parkinson's disease (PD) and [6] and Alzheimer's disease (AD) [10]. In PD it is thought that there may be a link between antioxidants in coffee and the glutamate receptor gene (GRIN2A), whereas the AD may linked to caffeine, CGA or their combination [1]. Recent evidence also shows that polyphenols and diterpenes may act as antioxidant [11] and gamma-amino butyric acid-$_A$ ($GABA_A$)-ergic neuroprotective activity [12].

L-glutamate, the major excitatory neurotransmitter in the central nervous system (CNS) is crucial for some important neurological processes such as cognition, learning, and memory. However, excessive stimulation of which leads to neuronal damage and death; thus the neurotoxicity of L-glutamate may be linked to hypoxic–ischemic brain injury, AD, Huntington's disease (HD), and PD. Now, the compounds acting as an effective inhibitor of L-glutamate will be coins for the suppressor to a number of CNS diseases. In addition, the accumulation of amyloid-beta (Aβ) peptides is considered to be an early stage in the pathogenesis of AD that precedes the formation of intracellular neurofibrillary tangles (NFTs), which is collectively known as the Aβ hypothesis [13]. This Aβ aggregates into oligomers, leading to the production of reactive oxygen species (ROS), the induction of oxidative stress and eventually cell death [14]. The components of coffee such as CGA, caffeine, cafestol, kahweol, and trigonelline, all have antioxidant or anti-inflammatory potential. Otherwise, the metabolism of CGA to caffeine and quinic acid is evident to show greater antioxidant activity [15]. Thus, the said components may prevent oxidative stress mediated neuro-damage.

Among the various cytoprotective enzymes, the protective functions of heme oxygenase-1 (HO-1) have recently been emphasized. HO-1 is a novel enzyme with potent anti-inflammatory, anti-oxidant, and anti-proliferative effects. In addition, evidence indicates that HO-1 provides protection; modulation of HO-1 expression may represent a novel target for therapeutic intervention. In particular, a non-cytotoxic pharmacological inducer of HO-1 may maximize the intrinsic anti-oxidant potential of varieties cells including nerve cells. Taking into account, kahweol was investigated in human neuroblastoma SH-SY5Y cells suggesting having a significant regulation of the antioxidant enzyme HO-1 via the PI3K and p38/Nrf2 signaling pathways [15]. Otherwise, PD also thought to have an inflammation factor [2]. Thus, the anti-inflammatory moieties in coffee may act in this way.

Coffee has also been shown to improve endurance performance in long-duration physical activities. Interestingly in a clinical study, the relative risk of suicide found to decrease by 13% for every cup of coffee consumed daily. However, children can be defined as a risk group because of altered behavior including nervousness or anxiety [6], but there are talks with high caffeine intake and low risk to form of lesion types at autopsy [1] and progression to dementia [16] in adults.

Kahweol (80 μg/paw; male Wistar rats) treatment has peripheral antinociceptive effect and suggests that this effect is mediated by the release of endogenous opioids [17]. In the *in vitro* antioxidant test study three compounds isolated from coffee namely 3-O-caffeoylquinic acid, 4-O-caffeoylquinicacid and 5-O-caffeoylquinic acid exhibited potential antioxidant capacity [18]. In addition, CGA tested in cortical neurons in the primary culture at 10 μM effectively protects neuron against glutamate neurotoxicity, thus suggesting benefits for neurodegenerative diseases such as ischemic stroke [19]. Otherwise, Hall *et al.* [20] suggested that CGA and CA having strong anti-inflammatory and antioxidant may eventually protect nerves from neuroinflammation.

On cardiovascular system (CVS)

It is evident that activation of AR_1 and AR_{2A} receptors has a series of cardiovascular effects on heart rate and BP, separate effects on the myocardium, vascular tone, on the sympathetic nervous system (SNS), and renin–angiotensin system [1]. However, caffeine also shows and an antagonistic effect on $AR_{A3.}$ The AR_1, together with AR_{2A} receptor play a role in regulating myocardial oxygen consumption and coronary blood flow. Stimulation of the AR_1 receptor has a myocardial depressant effect by decreasing the conduction of electrical impulses and suppressing pacemaker cell function, resulting in a decrease in heart rate. However, in altered cardiac function, such as hypoperfusion caused by hypotension, heart attack or cardiac arrest caused by nonperfusing bradycardias, adenosine has a negative effect on physiological functioning by preventing necessary compensatory increases in heart rate and blood pressure (BP) that attempt to maintain cerebral perfusion. Otherwise, a reduction in AR_1 expression appears to prevent hypoxia-induced ventriculomegaly and loss of white matter and therefore raise the possibility that pharmacological blockade of AR_1 may have clinical utility. Caffeine is a nonselective adenosine antagonist that may be used to stimulate respiration in premature infants.

The AR_{2A} receptor is responsible for regulating myocardial blood flow by vasodilating the coronary arteries, which increases blood flow to the myocardium, and may lead to hypotension. Like AR_1 receptors, this normally serves as a protective mechanism, but may be destructive in altered cardiac function. Thus, caffeine may act as both ways on the heart.

In the high BP, there is a concomitant increase of renin and catecholamines and a decrease, followed to an ulterior increase, in heart rate. Although, idiosyncrasy and genetic traits linked to polymorphisms in the adenosine AR_{2A} and in the α(2)-adrenergic receptors may have an effect in it. CGA has been evident to have vascular endothelium protective effect; however the hydroxy hydro quinone, a compound generated by the roasting of coffee beans might interfere it. In fact, arterial stiffness with caffeinated coffee intake was evident earlier. Caffeine intake with who have already the circulatory caffeine may reduce BP [1]. Otherwise, homocysteine has a proportional activity to CVS diseases, which may be connected, to a mutation in the methylenetetrahydrofolate reductase enzyme or by the insufficiency some vitamins such as B_6 and B_{12}. Coffee may increase the homocysteine effect, whichever may be controlled by B_6 [1].

Although, there is no evidence of arterial CVS disease with coffee but there is a risk of ischemic stroke among the non-habitual coffee drinkers. High dose of caffeine is evident to increase the frequency of ventricular arrhythmia; which was thought to be the triggering effect of catecholamines. However, with normal or low dose there is no evidence to produce atrial or ventricular arrhythmia and also the atrial fibrillation. In addition, a moderate dose of coffee may be helpful to manage the risk of heart failure [1].

In inflammation

Inflammatory responses are either acute or chronic. Response type determines their ultimate effects on systemic functions. Acute inflammation is beneficial as it acts as a primary defense against infection and allergens in the healing process; whereas chronic inflammations are harmful due to their extended inflammatory reaction time. However, chronic inflammation may occur after an attack of acute inflammation. Monocytes linger at the site, secrete cytokines and chemokines, and stimulate further macrophage response allowing a continual flow of chemokines and cytokines. Interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 (IL-1) are capable of adhering leukocytes to the endothelium, thus allowing further production of cytokines and the ultimate result is the inflammation. Chronic inflammation acts in a self-perpetuating manner, as this cycle continues unabated. Continued inflammation, in turn, is the genesis of chronic disease, and has a significant effect on the development of atherosclerosis, rheumatoid arthritis, and type 2 diabetes (T2D). Atherosclerosis may connect to chronic inflammation leading to arise endothelial dysfunction. Elevated in circulating adhesion molecule (cAM) and monocyte chemoattractant protein-1 (MCP-1) are evident to coronary artery disease. The coffee components having antioxidant, anti-inflammatory potentials are now being thought to diminish inflammation and inflammatory disasters. A work done on human monocyte cells (HUVECS), showing higher levels of CGA (25–50 µ-mole/l) to be suppressive to IL-1β messenger ribonucleic acid (mRNA), resulting in significantly less cell adhesion and inflammation [2]. Another research was done on rats reported to decrease IL-6, TNF-α, cell death, and inflammation in caffeine-infused animals [21]. In addition, the previously positive result also was demonstrated by Frost-Meyer and Logomarsino [2] on IL-4 and IL-10 inflammatory markers in rats.

Otherwise, cyclooxygenase (COX) enzymes due to their ability to synthesize prostaglandins (PGs) are the known mediators in neuroinflammation. The diterpenes kahweol reduced the amount of cyclooxygenase-2 (COX-2) and MCP-1 in HUVECS, leading researchers to speculate it has anti-inflammatory properties which could be anti-angiogenic. Kahweol also reduces inducible nitric oxide synthase (iNOS) and paw edema in rats treated with carrageenan. The positive value of kahweol and cafestol is also seen in NIHT3T cells exposed to hydrogen peroxide (H_2O_2), where diterpene groups exhibited much less DNA damage [2].

In addition, trigonelline, demethylated to nicotinic acid, supplies 1–3 mg nicotinic acid/240 ml in brewed coffee. Nicotinic acid from N-methylpyridinium showed a promising anti-inflammatory activity, as it reduces MCP-1 and upregulates adiponectin in adipocytes infused with TNF-α. The higher the roasting temperature, the greater the conversion into nicotinic acid [2]. Thus more roasted coffee may be a better source for anti-inflammatory components.

In chlosteolemia

Until date it is evident that cafestol and kahweol, individually or in combination are evident to increase total cholesterol (TC) and low density lipoprotein (LDL). The former increases cholesterol esterase transfer protein (CETP) which, in turn, elevates LDL. Both of them allow significantly less LDL to the cell receptors to be picked up, thus increasing serum load of LDL. Otherwise, the antioxidants present in coffee might perform anti-lipid oxidation/peroxidation role thus the protection lipid (LDL) molecules from oxidative damage. However, in non-habitual drinkers the protective lipid balance might be a beneficiary effect [2]. The ultimate cholesterol balance by coffee has been shown in fig. 4.

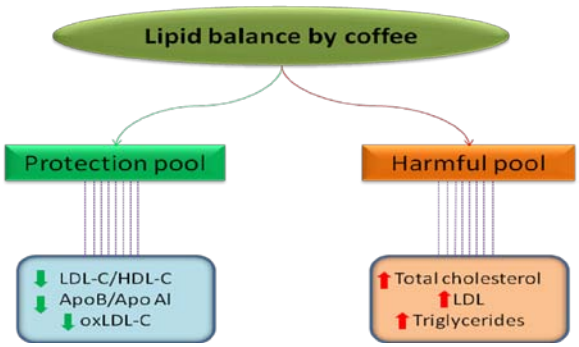

Fig. 4: Net lipid balance results of coffee (adaptation from: 2)

In diabetes

Coffee consumption and a reversal risk of T2D has been evident, although caffeine alone may cause increased glycemic response; whichever may be counteracted by CGAs, other phenolic compounds, magnesium, and trigonelline present in coffee. The activity may be due to their ability to alter absorption and metabolism of glucose, increased the release of incretin and sensitivity towards insulin [4]. Insulin sensitivity may be linked to the impaired glucose disposal in the skeletal muscle [1].

On gastrointestinal tract (GIT)

Caffeine is evident to decrease calcium (Ca^{2+}) absorption in GIT. Thus, the milked coffee and/or increased the dose of calcium and vitamin D are recommended to osteoporotic patients [4]. Mal-absorption of $Ca^{2+}$is due to acidic components of coffee-induced neutralization and rapid urinary excretion of those complexes [1]. Otherwise, chronic exposure to systemic and metabolic acidosis may provide a suitable environment for Ca^{2+}extraction form bones. However, this case is still controversial.

In pregnancy

The placental barrier is readily crossable to a variety of molecules. Caffeine, now being thought that readily cross the human placenta, and equilibrate the concentration with the fetus and mother. Thus, the excessive intake of caffeine may act as abortion-facilitator or even impaired growth to the fetus. Women, who are thus planning to be pregnant and/or already conceived must restrict caffeine<300 mg/day [4]. An additional precaution must be considered by the lactating woman also!

On liver

Hepatoprotective activity other than caused by chemo-organo and microbes such as virus are evident to chain-drinkers of coffee. Although there are talks with coffee consumption and associated reduced levels of

essential liver biomarkers. However, regular coffee consumption is a reversal to the cirrhosis and fibrotic hepatic status resulting from frequent tissue remodeling [1]. Frequent or chronic inflammation following some types of hepatitis is the most frequent cause.

In cancer

Proinflammatory activity of caffeine is thought to be linked to its anticancer property, although there is no clear-cut postulation that how coffee acts as an anticancer agent. Consequently, caffeine does not operate as a phosphodiesterase inhibitor, a pharmacologic effect of the alkaloid when acting at higher concentrations. This lack of stimulation may reduce the intracellular availability of cAMP, an anti-inflammatory agent in T lymphocytes [1]. Caffeine might then act as a pro-inflammatory agent. It is also evident that antioxidative diterpenes at high concentration readily cross the cell walls and plasma membranes; which is mainly associated with their cyto-/genotoxic rather than mutagenic potentials. This activity also termed as their prooxidant or protective effect [22]. Kahweol and cafestol may act in this way.

Insulin sensitivity may be linked to the degradation products of CGA. Otherwise, chronic hyperinsulinemia and insulin resistance are thought to be linked to high risk for some cancers. In addition, CA was found as an anticancer agent in cultured MCF-and MAD-MB-231 human cancer cells, which was suggested for the inhibition potential of DNA methylation [23]. As hypermethylation of DNA is evident to slice essential genes responsible antimutagenic activities, thus inhibition of this process is an anti-tumor activity.

World's second leading cancer associated deaths is the breast cancer. It is most frequent to the women in industrialized other than developing countries [24]. There is evidence linked to coffee drink and the decreased chance of breast cancer [23]. Another most common cancer is the colorectal cancer, which is more universal to the Western region of the world (approximately 10-fold higher than the developing countries) [24]. It has been suggested that cafestol and kahweol may prevent colorectal cancer through their carcinogenic effect along with their ability to induce excretion of bile acids and neutral sterols into the colon, increasing large bowel mobility in the rectosigmoid region; while caffeine also has been shown to inhibit colon cancer cell growth. Colorectal cancer incidence reduction by coffee is 4 and 12 %. Otherwise, the tragedy in ovarian cancer is almost similar to that of the breast cancer, which is the 7th available cause to death of women in cancer. However, there is no mention for ovarian cancer risk in association with coffee consumption [23].

Pancreatic cancer, the other leading cause of cancer-related deaths worldwide [23], has been found to have no link in coffee consumption, to date. Otherwise, the liver cancer (5th most common causes of death) [25] common to the developing countries is due to the oxidative stress may be protected by coffee consumption. Iron is a promoter for hepatocellular carcinoma (HCC), whichever evident to lower status with polyphenols intake, thus the anti-HCC activity. Otherwise, cirrhosis is a major risk factor for the development of HCC. Coffee being inhibits the elevation of liver transaminases thus the hepatoprotective effect mediated through anti-cirrhosis activity [23].

Unfortunately, the rate of kidney cancer incidence has been increasing steadily, which is thought to be the quantity and type of beverages consumed since it is the filtration and one of the major excretion systems in the body. Caffeine is having diuretic and cafestol, kahweol and CGA as antioxidant effects may reduce oxidative damage to genetic as well essential macromolecules in cells. Although an improved insulin sensitivity is linked to reduce kidney cancer incidence [23], but it may inversely relate to obesity [26].

Caffeine's impact on children and adolescents

Caffeine seems to be metabolized more rapidly in children (2–12 y) and adolescents (13–17 y) than the adults. However, the adults are the much caffeine consumer than the formers. Thus, the point 'caffeine metabolism is well enough to habitual or unhabituals!' Interestingly, restless subjects in the former groups are less sensitive to caffeine than the later. Thus arising a question 'is there any corollary between genetic inheritance on CNS stimulation and in caffeine-induced one?' Otherwise, caffeine youngsters, non-consumers as well as irregular ones are evident to less sleep or even sleeplessness other than insomnia, thus the possibility of broken health and craziness. It is to be speculated that the consumers such as children [4], who are under growth stage should be avoided caffeinated foods and drinks, due to it is still unknown is there any adverse effect of caffeine on the developing brain.

Being psychoactive agent, caffeine pretense the drowsiness associated with psycho depressants such as alcohol, this is actually a counter-balance activity; therefore, an especial caution should be recommended to the groups having cardiac complications. However, a daily intake of 110–345 mg caffeine for most adults it seems potentially beneficial effects on health, while for children and adolescents it is limited to 45–85 mg and 100–175 mg, respectively [4].

Miscellaneous

Headaches, nausea, anxiety, hypertension, and restlessness, are the most common problems associated with excessive caffeine intake. However, the amount of caffeine required to produce adverse effects varies from person to person depending on weight, sex, age, and differences in susceptibility. Most consumers experience, and enjoy, increased alertness, improved mood and focus, and the capacity to remain awake. For others, caffeine can have disagreeable symptoms; some people metabolize caffeine more slowly than others due to variability in the enzymatic activity of the metabolizing enzyme CYP1A2. Caffeine also has addictive properties, with a persistent desire to consume caffeine-containing foods or drinks and withdrawal symptoms (headache, lethargy, and irritability) when caffeine ingestion is abruptly discontinued. Caffeine also enhances memory consolidation [4]. Otherwise, people with dyslipidemia may consider brewed or filtered coffee to avoid cafestol and kahweol as these are the main cholesterol raising compounds in coffee. An overview on the pharmacokinetics of caffeine has been sketched out in fig. 5.

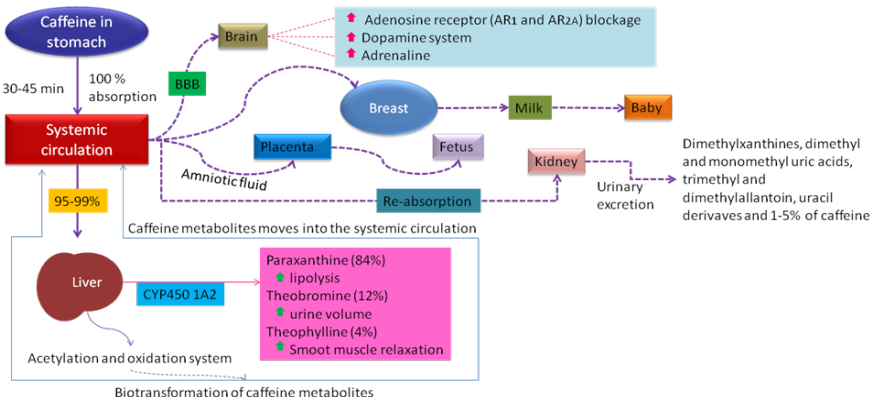

Fig. 5: An overview of caffeine pharmacokinetics in human (adaptation from: 4)

Caffeine after ingestion, readily absorbed into the systemic circulation (within 30–45 min), approximately 90% is cleared from the stomach within 20 min and peak plasma concentrations are reached within 1–1.5 h. Variations of half-life (t1/2) falls within 3-7 h as neonates>females>contraceptive users>pregnant women. However, caffeine is promptly reabsorbed by the renal tubules and only 1–5% is excreted unchanged in urine within 48 h. Caffeine is metabolized mainly by the CYP450 1A2 isozyme of the hepatic microsomal system, undergoes demethylation, resulting in paraxanthine, theobromine, and theophylline. Finally, caffeine metabolites are biotransformed by microsomal enzymes to dimethylxanthines, dimethyl and monomethyl uric acids, trimethyl and dimethylallantoin, and uracil derivatives, which are filtered by the kidneys and exit the body in the urine.

A Recent study with coffee extract showed strong antimicrobial activity (MIC: 1-15 mg/ml) against *Staphylococcus aureus* and *Staphylococcus epidermidis* and cytotoxic activity in breast adenocarcinoma MCF7 cells [27]. Otherwise, a polyphenol from coffee consumption improves postprandial hyperglycemia associated with impaired vascular endothelial function in healthy male adults [28].

Consumption of caffeine during conceives seems to augment the risk of pregnancy loss [29]. Coffee consumption may link to detrimental effect in maternal complications and childhood leukemia [30]. However, coffee may be linked to Nuclear Factor-kappa-β in prostate cancer cells, which in turns suggests for its anti-prostate cancer activity [31].

CONCLUSION

Lifestyle is a major fact and are therefore important determinants of healthy and longevity of life, which mainly depends on numerous factors including socio-economic status. But it is evident that the food behavior and exercise may act as a preventive measure against various ailments. In fact, the chemical components coming from various sources play a pivotal role in a healthy lifestyle. Among the most other drinks, coffee and caffeinated products are considerable, because it covers numerous supplements bowled to children to adults. Although a good number of research have been done on coffee, it is, however, to be questionable the impact of coffee in the fetus, developing brain, and organ systems. Few mechanisms have been postulated such as antioxidant, anti-inflammatory, PD, AD and cardioprotective activities, but the real facts still to be found out. In addition, the anticancerous effect of coffee and its components are not clear yet. Fortunately, the researches with coffee and coffee products are continuous. Therefore we must keep hope for the fulfillment of the marked points.

ABBREVIATION

AD: Alzheimer's disease, ALN: alanine aminotransferase, ARs: adenosine receptors, AST: aspartate aminotransferases, Aβ: amyloid-beta, BP: blood pressure, CA: caffeic acid, cAM: circulating adhesion molecule, cAMP: cyclic adenosine monophosphate, CETP: cholesterol esterase transfer protein, CGAs: chlorogenic acids, CNS: central nervous system, COX: cyclooxygenase, Cox-2: cyclooxygenase-2, CVS: cardiovascular system, CYP: cytochrome P450, GABAA: gamma-amino butyric acid-A, GGT: gamma-glutamyltransferase, GIT: gastrointestinal tract, GRIN2A: glutamate receptor gene, HCC: hepatocellular carcinoma, HD: Huntington's disease, HDL: high-density lipoprotein-cholesterol, HO-1: heme oxygenase-1, HUVECS: human monocyte cells, IL-1: Interleukin-1, IL-1β: Interleukin-1β, IL-6: Interleukin-6, IL-8: Interleukin-8, iNOS: nitric oxide synthase, LDL: low density lipoprotein cholesterol, MCP-1: monocyte chemoattractant protein-1, mRNA: messenger ribonucleic acid, NFTs: neurofibrillary tangles, NMDA: N-methyl-D-aspartate, NMDARs: N-methyl-D-aspartate receptors, PD: Parkinson's disease, PGs: prostaglandins, ROS: reactive oxygen species, SNS: sympathetic nervous system, T2D: type 2 diabetes, TC: total cholesterol, TNF-α: tumor necrosis factor-alpha.

CONFLICT OF INTERESTS

There is no interest in conflict

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