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GREEN COFFEE EXTRACT IMPROVES HUMAN HEALTH: A SYSTEMATIC REVIEW

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ABSTRACT

Green Coffee Extract (GCE) is a food product and/or supplements that are derived from raw or unroasted, green coffee beans. It is also present in roasted coffee, but much of the active principle is destroyed during the roasting process. The GCE contained chlorogenic acid as a major ingredient and mediate many of the health benefits. Oral ingestion of GCE may reduce body weight in overweight and obese persons. But mechanisms of chlorogenic acids still unknown, although it thought to be related with the preventing carbohydrate uptake from the intestines after a meal. Chlorogenic acid protects neurons from hydrogen peroxide induced stress through a powerful antioxidant activity, which fights against the free radicals produced in our body as a byproduct of metabolism. It lowers the risk of liver, colon, breast, skin and rectal cancers but the molecular mechanisms and target underlying the chemopreventive effects remain unknown. Ferulic acid, which is a metabolite of GCE containing chlorogenic acid, decreases blood pressure and improves vasoreactivity. GCE may be considered a novel antihypertensive food component. It reduces the risk of gylcemic disorders like Type 2 diabetes mellitus (DM), when people consume it for a long time, by inhibiting glucose-6-phosphatase enzyme, that promotes sugar formation in the liver by glycogenesis. GCE as supplemental or food products, may cause occupational type I allergies have been noted to be associated with green coffee dust, which

may be due to the presence of a 'Cof A 1' allergin and appears to be present in the plants *Coffea canephora*, *Coffea Arabica* and *Coffea liberica*.

KEYWORDS: Green Coffee Extract; Chlorogenic Acid; Antioxidant; Free Radicals; Hypertension; Obesity; Diabetes; Caffeine.

ABBREVIATIONS

GCE: Green Coffee Extract; DM: Diabetes Mellitus; LDL: Low Density Lipoprotein; NO: Nitric Oxide; MEK1: Mitogen activated protein kinase/extracellular signal-regulated protein kinase; TOPK T: Cell-originated protein kinase; ERK: Extracellular Signal Regulated Kinase; AP-1: Activator Protein-1; NF-*k*B: Nuclear Factor Kappa light chain enhancer of activated B cells; TPA: Tetradecanoylphorbol 13-Acetate; EGF: Epidermal Growth Factor; NQO1: NADPH quinine oxidoreductase 1.

INTRODUCTION

Hypertension, obesity and diabetes are the most critical issues for human health.[1-3] These are the lifestyle related disease and modifications in lifestyle are effective for its prevention. Different strategies which help to maintaining normal health by engaging in moderate physical activity and consuming a diet rich in fruits, vegetables and low fat dairy products with a reduced content of saturated and total fat.[3] However, the efficacy of some of these food product and/or supplements like green coffee extract has been shown to be promising. It help to reduce blood pressure in hypertensive rats[4] and humans[5] and improves vasoreactivity[6], obesity [7-9], diabetes mellitus[10-12] liver cancer as well as gallstones[13] and lowers the risk of colon, breast, skin and rectal cancers.[14-17]

However, the stimulating effect of caffeine on the central nervous system has significantly reduced the frequency of consumption due to its side effects on the cardiovascular system[18], central nervous system[19] and endocrine system.[20] On the other hand, scientific studies have revealed that both coffee and caffeine play a preventive role against various degenerative diseases of modern society, moderate daily consumption of coffee helped to reduce the risk of type-2 diabetes[21] and promotes lipolysis in rat adipocytes.[22] Human studies show that caffeine enhances energy expenditure[23] and improves the clinical conditions of diabetic patients.[24,25] Another study revealed that caffeine ingestion promotes glucose consumption with an increase in blood epinephrine[26], while pre-exercise consumption promotes ventilation and enhances lipolysis.[27]

Chlorogenic acid, another main constituent of coffee beans, some amount of chlorogenic acid can also be found in a variety of fruits and vegetables[28], has recently been reported to selectively inhibit hepatic glucose-6-phosphatase[29], which is a rate limiting enzyme involved in gluconeogenesis and also show hypotensive effect.[4,30] Similarly, other research has indicated that the consumption of caffeinated coffee can lead to some reductions in long term weight gain, an effect which is likely to be due to the known thermogenic effects of caffeine intake as well as effects of green coffee extract and other pharmacologically active substances present in coffee.[31] GCE has also been postulated to modify hormone secretion and glucose tolerance in humans. This effect is accomplished by facilitating the absorption of glucose from the distal, rather than the proximal part of the gastrointestinal tract.[32]

Taxonomy

The coffee tree belongs to the Rubiaceae family and the genus *Coffea*. Although more than hundreds of species identified only two species namely Arabica (*Coffee arabica*) and Robusta (*Coffee canephora*) have economic importance.[33] These two species Arabica and Robusta account 75-80% and 20% respectively of the total coffee produced worldwide.[34] Arabica and Robusta coffees are different in many ways, including their ideal growing climates, physical aspects, chemical composition. Arabica coffee is more appreciated due to its fine taste, aroma and strong body. It is green to pale green in color have an oval shape in contrast in robusta that is round and brown in color.[35]

Classification

Kingdom:	Plantae
Subkingdom:	Tracheobionta
Superdivision:	Seprmatophyta
Division:	Magnoliopsida
Subclass:	Asteridae
Order:	Rubiales
Family:	Rubiaceae
Genus:	Coffea

Botanical name

Coffea arabica: Arabica or Arabian Coffee

Coffea canephora: Robusta or Congo Coffee

Coffea liberica: Liberian Coffee

Common names

Green Coffee

Coffee Bean

Raw Coffee

Unprocessed Coffee

Definition of green coffee beans/extract

A coffee bean is a seed of the coffee plant and is the source for coffee. The coffee plant is a small tree which produces red or purple fruit often referred to as a coffee cherries or coffee berries. Each cherry contains two seeds or beans. When harvested, the raw coffee beans are green in color. Even though they are seeds, they are referred to as 'beans' because of their resemblance to true beans. As part of the harvesting and production process, the cherries are dried in the sun for several weeks until their flesh splits, releasing the bean. This bean is known as green coffee bean and an extract of unroasted, green coffee beans is known as green coffee extract.[36,37]

Table No:-1 Some of the major differences among *Coffea arabica* and *Coffea canephora* have been listed as.[38-43]

S.No.	Properties	*Coffea arabica*	*Coffea canephora*
1.	Date of species describe	1753	1895
2.	Chromosome (2n)	44	22
3.	Flowering	After rain	Irregular
4.	Time from flower to ripe cherry	9 Month	10-11 Month
5.	Ripe cherries	Fall	Stay
6.	Yield (kg bean/ht)	1500-3000	2300-4000
7.	Root system	Deep	Shallow
8.	Shape of bean	Flat	Oval
9.	Optimal temperature	24-30^{o}c	15-24^{o}c
10.	Optimum rain fall	1500-2000mm	2000-3000mm

Coffee Plant/Biology

All coffee plants are classified in the large family Rubiaceae. They are evergreen shrubs or small trees that may grow 5 m tall. The leaves are dark green and glossy, usually 10 to15 cm long and 6 cm wide. Petioles of opposite leaves fuse at base to form interpetiolar stipules, characteristic of Rubiaceae. A coffee plant usually starts to produce flowers three to four years after it is planted. The first useful harvest possible around five years after planting from these flowers, that the fruits of the plant commonly known as coffee cherries/berries. They

should be harvested at the time when its color changing from green to red. Cuttings, grafting and budding are the usual methods of vegetative propagation.[44,45]

Chemical composition of green coffee extract

The basic chemical constituents of green coffee depend primarily on genetic aspects, especially on species and physiologic aspects such as degree of maturation. In addition to these intrinsic factors, extrinsic factors such as soil composition, climate, agricultural practices and storage conditions affect seed physiology and chemical composition, but to a lesser extent.[46,47] The chemical composition of hybrid coffee (Timor hybrid and Catimor) seeds tend to exhibit intermediate characteristics of the parent species.[48-50] Some of the wild varieties of caffeine free *C. arabica* have recently been discovered.[51-52]

Green coffee mainly contains nonvolatile and volatile compounds. The nonvolatile fraction of green coffee is composed primarily of caffeine, trigonelline, chlorogenic acids, carbohydrates, proteins and free amino acids, lipids, minerals, organic acids and water. In addition, traces of theophylline, theobromine, paraxanthine, liberine and methylliberine are also present in lower concentrations.[52,53]

Table:-2 Chemical composition of green *Coffea arabica* and *Coffea canephora* seeds[33,46,54-62]

Component		Concentration (gm/100gm)	
		Coffea arabica	*Coffea canephora*
Carbohydrates	Sucrose	6.0-9.0	0.9-4.0
	Reducing sugars	0.1	0.4
	Polysaccharides	34-44	48-55
	Lignin	3.0	3.0
	Pectin	2.0	2.0
Nitrogenous compounds	Protein/peptides	10.0-11.0	11.0-15.0
	Free amino acids	0.5	0.8-1.0
	Caffeine	0.9-1.3	1.5-2.5
	Trigonelline	0.6-2.0	0.6-0.7
Lipids	Coffee oil (triglycerides with unsaponifiables, sterols/tocopherols)	15-17.0	7.0-10.0
	Diterpenes (free and esterified)	0.5-1.2	0.2-0.8
Acids and esters	Chlorogenic acids	4.1-7.9	6.1-11.3
	Aliphatic acids	1.0	1.0
	Quinic acid	0.4	0.4
Minerals	Na, Ca, K, P etc	3.0-4.2	4.-4.5

Caffeine

Mostly caffeine is present as alkaloid in green and roasted coffee beans. It is a methylxanthine with bitter characteristics.[63] The content of caffeine is between 1.0% and 2.5% by weight of dry green coffee beans. The content of caffeine does not change during maturation of green coffee beans.[48] Caffeine is the most widely studied and consumed psychoactive substance in history. It acts as an adenosine receptor antagonist and stimulates the central nervous system. Its effects on health are controversial.[64] Low to moderate amount of caffeine intake is generally associated with increased alertness, learning capacity, exercise performance and better mood. But high amount can produce negative effects like anxiety, tachycardia and insomnia in some sensitive individuals, which occurs within 2-6 hours after coffee intake.[57,62,65]

Caffeine consumption may lower the incidence of suicide and hepatic cirrhosis, but it may be associated with high blood cholesterol, coronary diseases and cancer.[62] Acute caffeine consumption had negative effects on glucose tolerance and insulin sensitivity in lean, obese and type 2 diabetic rats and humans, but other compounds present in coffee can counteract this effect.[66] Acute caffeine intake also increases the urinary excretion of minerals such as calcium.[67] However, after long-term consumption, most of these acute effects tend to disappear because of metabolic adaptations in the body.[68] Caffeine metabolites (1-methylxantine and 1-methylurate) have exhibited antioxidant activity *in vitro* and the *in vivo* iron-reducing capacity of regular coffee is higher than that of decaffeinated coffee.[69] The antibacterial effect of regular coffee against cariogenic microorganisms was also higher than that of decaffeinated coffee.[70]

Trigonelline

In green coffee beans, trigonelline is synthesized from nicotinic acid (pyridinium-3-carboxylic acid) by methylation from methionine, a sulfur-containing amino acid. Trigonelline is present in green coffee beans between 0.6% and 1.0%. At roasting temperature (230°C), 85% of the trigonelline is demethylation to nicotinic acid, a B-complex vitamin also known as niacin.[59] It contributes to the bitterness of the brew and is a precursor for the formation of different classes of volatile compounds during roasting such as pyrroles and pyridines.[63] Trigonelline has inhibited the invasiveness of cancer cells *in vitro*.[71] In addition, this compound has been able to regenerate dendrites and axons in animal models,

suggesting that it may improve memory.[72] More recently it has been considered a novel phytoestrogen.[73]

Diterpenes

The diterpenes found in green coffee include cafestol, kahweol, 16-O methylcafestol, cafestal and kahweal. In coffee oil from green coffee beans, these bioactive compounds and their derivatives, which are mainly salts or esters of saturated fatty acids and unsaturated fatty acids[74] represent approximately 20% of the lipid fraction of coffee.[75,76,61] Coffee diterpenes have exhibited anti carcinogenic and hepatoprotective properties against chemical oxidation *in vitro*.[75-77] On the other hand, high consumption of these compounds has been associated with elevated homocysteine and low density lipoprotein levels in plasma, which may indirectly increase the risk of cardiovascular diseases.[78]

Chlorogenic acids

Chlorogenic acids are a valuable, inexpensive source of antioxidants and belong to a group of compounds known as phenolic acids. Which are derived primarily from esterification of cinnamic acids (e.g. caffeic, ferulic and *p*-coumaric) with quinic acid. At roasting temperature, more than 70% of chlorogenic acids are destroyed.

Chlorogenic acids are subdivided according to the nature and number of cinnamic substituents and the esterification position in the cyclohexane ring of the quinic acid.[79] The main subclasses of chlorogenic acids in green coffee are caffeoylquinic acids, dicaffeoylquinic acids, feruloylquinic acids and less abundantly, *p*-coumaroylquinic acids and caffeoyl-feruloylquinic acids. Among these classes, caffeoylquinic acids account for approximately 80% of the total chlorogenic acids content.[80,81]

Some minor chlorogenic acid compounds have been identified. However, these compounds together are not responsible for even 1% of total chlorogenic acids. These minor chlorogenic acids includes dicaffeoylquinic acids, acyl dicaffeoylquinic acids, dimethoxycinnamoylquinic acids, caffeoyl dimethoxycinnamoylquinic acids, diferuloylquinic acids and feruloyldimethoxycinnamoylquinic acids, sinapoylquinic acids, sinapoyl-caffeoylquinic acids, sinapoyl-feruloylquinic acids and feruloyl-sinapoylquinic acids.[47,82-84]

Epidemiologic and clinical studies have been reported that coffee consumption, is associated with health benefits such lower the risk of type 2 diabetes[79,85-89], parkinson and alzheimer

diseases[90] and liver cancer.[91,92] Beneficial properties of coffee bean are due to antioxidant and other mechanisms involving chlorogenic acid compounds.[29,32,66,93-106] The antioxidant capacity of chlorogenic acid is more potent than of ascorbic acid or mannitol, which is a selective hydroxyl radical scavenger.[107]

The antimutagenic property of chlorogenic acids and their metabolites has been demonstrated by a series of animal and *in vitro* studies.[75,108-112] Recent studies have confirmed that these compound act through several mechanisms including free radical scavenging, metal chelation, inactivation of reactive compounds and metabolic pathway changes.[17,76,113-115]

Pharmacologic properties attributed to caffeoylquinic and dicaffeoylquinic acids include antiviral activity against adenovirus and herpes virus[116], hepatoprotective activity in an experimental model of liver injury[117] and immunostimulatory activity.[118] Synthetic dicaffeoylquinic acid derivatives also inhibit HIV-1 replication in cells[119-122] which raises the possibility of novel coffee based anti-HIV drugs.

Soluble dietary fiber

Galactomannans and type II arabinogalactans are the most important types of soluble fiber in coffee. A high intake of dietary fiber is positively associated with several beneficial physiologic and metabolic effects such as lowering blood cholesterol and modulating the blood glucose and insulin responses.[123]

These compounds have received special attention because they cannot be digested by humans. Therefore, they reach the colon as intact and potentially serve as substrates for beneficial colonic microbiota fermentation.[124] Fermentable polysaccharides are degraded by colonic microbiota to short chain fatty acids (e.g., acetate, propionate and butyrate). This process lowers the colonic pH, impeding the growth of certain pathogenic species and supporting the growth of *Bifidobacterium* species and other beneficial lactic acid bacteria.[124]

Carbohydrates

Carbohydrates are major constituents of coffee and may account for more than 50% of the dry weight of green coffee beans. The carbohydrate fraction of green coffee is dominated by polysaccharides, such as arabinogalactan, galactomannan and cellulose, contributing to the tasteless flavor of green coffee. Polysaccharides (soluble and insoluble) account for approximately 44% of dry matter in *C. arabica* and 47% in *C. canephora*.[125] Small amounts

of simple carbohydrates such as fructose, glucose, mannose, arabinose and rhamnose and oligosaccharides such as raffinose and stachyose have been identified in green coffee.[63,60]

Arabinogalactan makes up to 17% of dry weight of green coffee beans. It is composed of beta 1-3 linked galactan main chains, with frequent members of arabinose (pentose) and galactose (hexose) residues at the side chains comprising immunomodulating properties by stimulating the cellular defense system (Th-1 response) of the body. The molecular weight of the arabiniogalactan in coffee is higher than in most other plants, improving the cellular defense system of the digestive tract compared to arabinogalactan with lower molecular weight.[126]

Mature brown to yellow coffee beans contain fewer residues of galactose and arabinose at the side chain of the polysaccharides, making the green coffee bean more resistant to physical breakdown and less soluble in water.[127] Free monosaccharides are present in mature brown to yellow green coffee beans. The free part of monosaccharides contains sucrose, fructose, galactose and mannitol.[128] Mannitol is a powerful scavenger for hydroxyl radicals, which are generated during the peroxidation of lipids in biological membranes.[129]

Protein, peptides and amino acids

Green coffee beans contain approx 8 to 12% proteins of the dry weight. Protein, peptides and free amino acids are vital for coffee flavor. The melanoidin are responsible for coffee's color and to some extent, its antioxidant activity. The total nitrogenous compounds (excluding caffeine and trigonelline) account for 9%-16% of the green coffee chemical composition. However, coffee is not a good nutritional source of protein because it lacks essential amino acids. The amino acids in green coffee beans are degraded under roasting temperature.

Some of the enzymes like catalase and polyphenol oxidase, which are important for the maturation of green coffee beans. The concentration of gamma aminobutyric acid (a neurotransmitter) has been determined between 143 mg/kg and 703 mg/kg in green coffee beans.[130]

Minerals

Green coffee contains both micro and macro elements. Potassium accounts for approximately 40% of the mineral content of green coffee. Phosphorus is another important mineral in

coffee, accounting for 4% of its composition. The remaining mineral content consists of approximately 30 different elements, including sodium, magnesium, calcium and sulfur.[33,131]

Trace minerals in coffee include zinc, strontium, silicon, manganese, iron, cupper, barium, boron and aluminum. The profile of trace minerals in coffee varies according to soil composition, which suggests that it may be possible to differentiate coffees grown in different types of soil by their mineral profile.[132]

Lipids

Lipids are major components of coffee and present on the surface and in the interior matrix of green coffee beans and protecting the interior matrix against oxidation and insects and such molecules have antioxidative activity due to their chemical structure.[133] The lipid fraction of coffee is composed mainly of triacylglycerols (75%), free fatty acids (1%), sterols (2.2% unesterified and 3.2% esterified with fatty acids) and tocopherols (0.05%). Most fatty acids in coffee are unsaturated. Linoleic acid, oleic acid and linolenic acid are not only important for health, but their integrity is important to keep coffee fresh and avoid the staleness caused by hydrolysis and oxidation of triacylglycerols.[60,134-138]

Volatile compounds

Green coffee beans contain some volatile compounds and these volatile compounds are responsible for the unpleasant odor and taste of green coffee and are capable of causing nausea and vomiting upon inhaling of the odor of ground green coffee beans. Approximately 100 different volatile compounds have been identified in green coffee seeds.[63] The most abundant classes of volatile compounds are alcohols, esters, hydrocarbons and aldehydes. Ketones, pyrazines, furans and sulfur compounds have also been identified.[63,139,140]

Beneficial effects of green coffee extract

Weight Loss

Green coffee bean extract promotes the loss of visceral fat. This fat present in the tissues lining the abdominal cavity and surrounding the internal organs. It is typically associated with the “apple” body shape. Visceral fat can lead to an increased risk of metabolic syndrome and Type-2 diabetes.

The effect on green coffee bean extract and chlorogenic acids is multifaceted. Some of the attributed effects of extract are improved glucose and insulin balance and increased satiety.

Glucose absorption was reduced, thus reducing blood and liver fats (triglycerides). It seems the chlorogenic acids and caffeine work together in reducing abdominal fat by increasing lipolysis or fat cells being opened up for energy release.[37,141] Amount of green coffee extract should be 400-1000 mg per day, providing 180-500 mg chlorogenic acids (Chlorogenic acids potency must be 45-50%) and up to 40 mg caffeine per day is required for the effective weight management.[37,141]

Antihypertensive/ Heart Diseases

Hypertension is a primary risk factor for stroke, heart disease, and renal failure and one of the most critical issues for human health.[1-3] High homocysteine concentrations in blood are a risk indicator for cardiovascular disease. Green coffee bean extracts reduce the levels of visceral fat accumulated around the midsection of the body and also help in the decrease of homocysteine levels in the blood plasma, in this way it reduces the heart diseases. This extract also inhibits lipid and low density lipoprotein (LDL) degradation, thereby promoting optimal cardiovascular health. They keep blood platelets from clumping together and improve blood circulation all over the body, thus, prevent hardening of the arteries. In this way, green coffee bean extract is effective against hypertension[4,5,30,36,142] and improves vasoreactivity.[6]

The antihypertensive action of green coffee bean extract was due to the presence of chlorogenic acid as a major phenolic compound and chlorogenic acid in turn contains ferulic acid[143] as a metabolic component that has been shown to act on nitric oxide (NO) derived from the vascular endothelium.[4,30] The vascular endothelium regulates vasoconstrictive and vasodilative functions by producing and releasing various vasoactive factors, including nitric oxide.[144,145] Endothelial dysfunction is considered an initial stage of arteriosclerosis.[146] Green coffee bean extract may be considered a novel antihypertensive food component.[36,147] Amount of green coffee extract should be up to 1000 mg per day, providing 50-500 mg chlorogenic acids and up to 40 mg caffeine per day for the effective management of healthy cardiovascular system and blood pressure.[36,37,147]

Antioxidant

Oxidative stress plays as key role in the pathogenesis of aging.[148-149] Oxidative stress can be caused by various negative impacts, such as gamma or UV radiation, environmental factors, polluted and poor quality food, stress, some medications or treatments, smoking, alcoholism *etc*. These free radicals, if left unneutralized or prolonged oxidative stress inevitably leads to

damage of our cells and contribute to conditions such as cancer, cardiovascular diseases, or diabetes and premature aging.

Oxidative stress can be reduced by antioxidant therapy, by consumption of certain amounts of natural antioxidants contained in vegetables, fruits, berries, vegetable oils, honey, tea, coffee, cocoa, juices, wine, sprouted grains and other foods.[150-152] Chlorogenic acid present in the green coffee bean is a powerful antioxidant activities which fights the free radicals produced in our body as a byproduct of metabolism.[153-157] The amount of green coffee extract should be up to 1000 mg per day, providing 50-500 mg chlorogenic acids and up to 40 mg caffeine per day is required for effective antioxidant activities.[37]

Anti Cancer Agent

Chlorogenic acid is a polyphenol and neutralizes several classes of carcinogenic compounds like chemical induced carcinogenesis *in vitro* and *in vivo*. It lowers the risk of liver, colon, breast, skin and rectal cancers.[14-17] But the molecular mechanisms and target(s) underlying the chemopreventive effects of coffee and its active ingredient(s) remain unknown.

Chlorogenic acid inhibited CT-26 colon cancer cell induced lung metastasis by blocking phosphorylation of extracellular signal regulated kinase (ERKs). Coffee or caffeic acid strongly suppressed mitogen activated protein kinase/extracellular signal regulated protein kinase (MEK1) and T-cell originated protein kinase (TOPK) activities and bound directly to either MEK1 or TOPK in an ATP non competitive manner. Coffee or caffeic acid, but not caffeine, inhibited ERKs phosphorylation, activator protein-1(AP-1) and NF-*k*B transactivation and subsequently inhibited 12-O-tetradecanoylphorbol 13-acetate (TPA), epidermal growth factor (EGF) and H-Ras-induced neoplastic transformation of JB6 P*1* cells. Coffee consumption was also associated with a significant attenuation of ERKs phosphorylation in colon cancer patients. These results suggest that coffee and caffeic acid target MEK1 and TOPK to suppress colon cancer metastasis and neoplastic cell transformation.[158]

Reduced risk of type II diabetes

The metabolic syndrome is an important risk factor of diabetes mellitus (DM) type II[159] and cardiovascular diseases.[160] Recent prospective cohort studies showed that coffee consumption may lower the risk of DM.[10-12,88] It is reported that inverse associations between coffee consumption and the risk of DM.[31,161] Furthermore, it has been shown that

coffee consumption was inversely associated with several glycaemic markers and diabetes[162-163] and positive associations between coffee consumption and insulin sensitivity have been reported.[11,85,164] Coffee consumption of both caffeinated and decaffeinated coffee was associated with a decrease in C-peptide levels in women, indicating that chronic coffee consumption reduces insulin secretion.[165]

Despite the favourable effects of coffee on DM, the exact mechanism involved with the decreased risk of DM remains unclear.[161] Chlorogenic acid in green coffee bean reduces the risk of gylcemic disorders like diabetes Type 2 diabetes, when people consume it for a long time, by inhibiting glucose-6-phosphatase enzyme, that promotes sugar formation in the liver by glycogenesis. If glycogenolysis is inhibited, the body gets its energy from fat cells, reducing the blood glucose levels. Moreover, chlorogenic acid and magnesium in green coffee reduce insulin resistance, which plays an important role in diabetes.[31,166]

Protection against nerve degeneration /Alzheimer's disease

Caffeine exerts positive effects on cognitive and behavioral processes, especially in sub-optimal conditions, when arousal is low. Apart from caffeine, coffee contains other compounds including the phenolic compounds ferulic acid, caffeic acid and chlorogenic acids, which have purported antioxidant properties. Neurodegenerative disorders including Alzheimer's disease are strongly associated with oxidative stress to neurons. This oxidative damage is caused by reactive oxygen species including hydrogen peroxide.

Green coffee bean extract help to improve our concentration power thereby improving learning abilities and alertness. Moreover, it reduces fatigue and increases endurance. It is also effective in treating migrane. Chlorogenic acid protects neurons from hydrogen peroxide induced stress through up regulating the antioxidant enzyme NADPH: quinine oxidoreductase 1 (NQO1). Other studies have indicated that chlorogenic acid may also work to preserve dopaminergic neurons by suppressing inflammation in the neurons.[167]

Reduced the risk of liver disease

The consumption of coffee may help to prevent several chronic liver diseases, including cirrhosis of the liver and hepatocellular carcinoma (liver cancer) as well as gallstones.[13] Despite the evidence supporting a hepato-protective effect of coffee, the mechanism underlying this effect is yet to be elucidated. Coffee is a complex 'blend' of a vast number of different chemicals, any of which may be responsible for its effects on the liver. The

important constituents of coffee, namely cafestol and kahweol, may play an important role. In animal and cell culture models, these diterpenes have been shown to reduce the toxicity of a variety of carcinogens.[76]

Different mechanisms appear to be involved in these chemoprotective effects as an induction of conjugating enzymes (e.g. glutathione *S*-transferases, glucuronosyl *S*-transferases), an increased expression of proteins involved in cellular antioxidant defense (e.g. γ-glutamyl cysteine synthetase and heme oxygenase-1) and an inhibition of the expression and/or activity of cytochromes P450 involved in carcinogen activation (e.g. CYP2C11, CYP3A2). In animal models, the cafestol and kahweol mediated induction of conjugating and antioxidant enzymes has been observed in hepatic, intestinal and kidney tissues. In the small intestine, these inductions were shown to be mediated by Nrf2-dependent transcriptional activation. In vitro investigations obtained in cell cultures of human origin indicate that the effects and mechanisms observed in animal test systems with cafestol and kahweol are likely to be of relevance for humans.[76]

Summary

Overall, results of this comprehensive review show that coffee is a complex mixture of chemicals that provides significant amounts of chlorogenic acid and caffeine. The GCE has been proven to be effective in reducing weight gain and fat accumulation in overweight and obese patients to enjoy a better quality of life. Caffeine was found to be a suppressor of fat absorption, while chlorogenic acid and its related compounds are found to be involved in the enhancement of fat metabolism in the liver. GCE is safe to be taken as an antioxidant for reducing chronic oxidative stress and may help to prevent several chronic diseases like type 2 DM, Parkinson's disease and liver disease including cirrhosis, hepatocellular carcinoma and decreased risk of hepatic injury. Many nutraceutical companies adding green coffee chlorogenic acid to their formulation to combat the several life style related disease.

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