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## Phytochemical, pharmacological and clinical prospects of green coffee (*Coffea arabica* L.): A boon to the pharmaceutical industry

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### Abstract

Green coffee, the unroasted seeds of *Coffea* species, is a valuable source of carbohydrates, proteins, and fats, along with bioactive compounds such as caffeine, trigonelline, and chlorogenic acid. Among these, chlorogenic acid stands out as a key polyphenol with significant antioxidant properties. The natural antioxidants in green coffee including phenols, chlorogenic acids, and brown pigments contribute to its potential health benefits. Due to its high polyphenolic content, especially chlorogenic acid, green coffee has gained attention for its possible physiological and pharmacological effects. Studies indicate that green coffee and its active components may offer various health advantages, including antiobesity, antitumor, antidiabetic, antihypertensive, anti-inflammatory, and antimicrobial properties. These attributes suggest that it could serve as a non-pharmacological and non-invasive option for managing chronic conditions. The combination of chlorogenic acid and caffeine is believed to influence metabolism, enhance insulin sensitivity, and regulate lipid levels, thereby supporting weight management, blood glucose regulation, and cardiovascular health. Additionally, the antioxidant activity of chlorogenic acid may help reduce oxidative stress, which plays a role in the progression of numerous chronic diseases. Green coffee has also been examined for its potential effects on body weight regulation, cholesterol levels, blood pressure modulation, and cardiovascular disease prevention. While these health benefits appear promising, further research is required to confirm its safety and efficacy. Essential factors such as toxicity, optimal dosage, bioavailability, and possible risks must be thoroughly investigated. Understanding these aspects is crucial to determining the long-term advantages and limitations of green coffee consumption across diverse populations. This review aims to provide an updated overview of the health implications of green coffee, focusing on its bioactive compounds, mechanisms of action, and therapeutic potential while emphasizing the need for continued scientific inquiry.

### 1. Introduction

Plants serve as an essential source of bioactive compounds with therapeutic potential for treating numerous human diseases. Natural products have historically played a crucial role in drug discovery, often serving as templates for the development of novel pharmaceutical agents. Many plant-derived substances act as foundational structures for synthesizing new molecular derivatives (Asmari *et al.*, 2020). The *Coffea* genus, comprising around 125 species, is predominantly found in tropical regions of Africa and parts of Asia. As a member of the Rubiaceae family, coffee plants are recognized for their rich content of volatile oils (Melese *et al.*, 2021). Species

within this family demonstrate a variety of pharmacological properties, including antibacterial, antifungal, antiviral, anesthetic, antioxidant, and anticancer effects. In some cultures, the outer layer of the coffee fruit, locally referred to as “Gisher,” is infused in hot water to create a traditional drink believed to help cleanse the womb of impurities following menstruation or childbirth. This outer layer, which constitutes nearly half of the coffee fruit, is thought to offer several health benefits (Adugna *et al.*, 2021). Coffee is one of the most widely consumed beverages worldwide, boasting a complex chemical composition with approximately 700 compounds contributing to its distinct flavor and aroma (Figure 1) (López *et al.*, 2021). Coffee flourishes in warm, humid environments with temperatures ranging between 18-24°C. The most commercially significant species are *Coffea arabica* and *Coffea canephora* (commonly known as robusta), which together make up 40-60% of global coffee production (Ali *et al.*, 2022). *C. arabica* is cultivated mainly in South America, particularly Brazil, and at high elevations in East Africa, while *C. robusta* thrives in the lower-altitude regions of Central and West Africa, as well as South Asia, with Vietnam being a key producer (International Coffee Organization, 2013).

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**Figure 1: Coffee plant with flowers and berries.**

The coffee fruit contains higher concentrations of bioactive compounds than roasted coffee beans (Silva *et al.*, 2020). Green coffee beans, in particular, are rich in chlorogenic acid (CGA), a polyphenol composed of caffeic and quinic acid esters (Firdissa *et al.*, 2022). Research has demonstrated that CGA exhibits numerous health benefits, including anticancer, anti-inflammatory, lipid-lowering, antihypertensive, and antidiabetic properties (Benti *et al.*, 2021). Other bioactive components such as caffeine, theobromine, theophylline, cafestol, kahweol, trigonelline, tocopherols, and various chlorogenic acid derivatives contribute to coffee's medicinal value (Montagnon *et al.*, 2021). These compounds exhibit anti-inflammatory and antimutagenic effects, playing a role in preventing chronic illnesses and cancer. Furthermore, Wagner *et al.* (2021) identified antiviral, antibacterial, antifungal, antioxidant, and antimycotoxigenic properties within coffee, further underscoring its therapeutic significance (Bobková *et al.*, 2015). Chlorogenic acids have been associated with modulating lipid metabolism and glucose levels, playing a role in metabolic disorders and genetic conditions (Ge *et al.*, 2023). This review also examines the primary chemical constituents, essential oils, and pharmacological attributes of *Coffea arabica*. Several research findings highlight that coffee seeds are rich in bioactive compounds and polyphenols, contributing to their hepatoprotective, antibacterial, antiviral, anti-inflammatory, antioxidant, and lipid-lowering properties (Shen *et al.*, 2023).

## 2. Ethnopharmacology

The ethnopharmacology of coffee encompasses its traditional and medicinal applications across various cultures, largely attributed to its diverse bioactive constituents, including caffeine, chlorogenic acids, trigonelline, diterpenes, and polyphenols (Yohannis *et al.*, 2024). Historically, coffee has been valued for its stimulating properties, primarily due to caffeine, which enhances cognitive function, alertness, and physical endurance. Traditional medicinal practices, particularly in Africa, the Middle East, and South America, have long utilized coffee for alleviating fatigue, headaches, digestive disturbances, and respiratory conditions (Gallardo *et al.*, 2022). The presence of antioxidant and anti-inflammatory compounds in coffee plays a crucial role in protecting against oxidative stress-related ailments, including neurodegenerative disorders such as Alzheimer's and Parkinson's (Asmariet *et al.*, 2020). Additionally, coffee exhibits hepatoprotective effects, reducing the likelihood of liver diseases

such as cirrhosis and hepatocellular carcinoma (Roy *et al.*, 2024). Its polyphenolic compounds contribute to cardiovascular health by regulating blood pressure and cholesterol levels. In ethnomedicine, coffee has been employed for metabolic disorders, as chlorogenic acids influence glucose metabolism, thereby lowering the risk of type 2 diabetes (Ahmed *et al.*, 2024). Furthermore, coffee possesses antimicrobial and gastroprotective properties, aiding in the prevention of bacterial infections and ulcers. Diterpenes such as cafestol and kahweol contribute to its anti-carcinogenic potential by enhancing liver detoxification enzyme activity (Gamage *et al.*, 2021). Traditional healing systems have also recognized coffee's psychotropic effects, using it to alleviate symptoms of depression and mental fatigue. Beyond internal health benefits, coffee extracts have been incorporated into skincare treatments due to their anti-aging, anti-inflammatory, and wound-healing properties. Various indigenous communities have historically used coffee as an appetite suppressant and weight management aid, owing to its thermogenic properties and role in regulating lipid metabolism (Saudet *et al.*, 2021). While its pharmacological benefits are widely acknowledged, excessive consumption may lead to undesirable effects such as insomnia, increased heart rate, and digestive discomfort (Melo Pereira *et al.*, 2020). Ongoing ethnopharmacological research continues to investigate the therapeutic potential of coffee's bioactive components in modern medicine, with a focus on developing plant-based treatments (Acidri *et al.*, 2020). Overall, coffee remains integral to both traditional healing practices and contemporary pharmacology, offering a broad spectrum of health benefits and contributing to disease prevention (Ahmed, 2024).

## 3. Major phytochemical constituents of coffee

Coffee is composed of various bioactive compounds, with caffeine and chlorogenic acids being the most significant. Unfiltered coffee is notably high in cafestol and kahweol, two diterpenes known to impact cholesterol levels (Dong *et al.*, 2020). In many regions, coffee serves as a primary dietary source of caffeine. Besides caffeine, it supplies essential nutrients, including proteins, carbohydrates, lipids, vitamins, minerals, alkaloids, and phenolic compounds (Rao *et al.*, 2020).

### 3.1 Caffeine (Methylxanthine)

Caffeine is a naturally occurring compound present in coffee beans, as well as in over 60 other plant species, including tea leaves, cocoa beans, and cola nuts. Classified as an alkaloid, its chemical designation is 1,3,7-trimethylxanthine (Figure 2). Caffeine functions as a nonselective antagonist of adenosine receptors, influencing numerous physiological processes (Starling-Soares *et al.*, 2023). It is widely acknowledged for its psychoactive stimulant properties and is one of the most frequently consumed substances globally. Its stimulating effects are largely attributed to its ability to block adenosine receptors, particularly A1 and A2A (Karuppagounder *et al.*, 2021). The caffeine content in coffee varies significantly, with levels ranging from 30 mg to 350 mg per 100 ml serving of home-brewed coffee (Lin *et al.*, 2023).

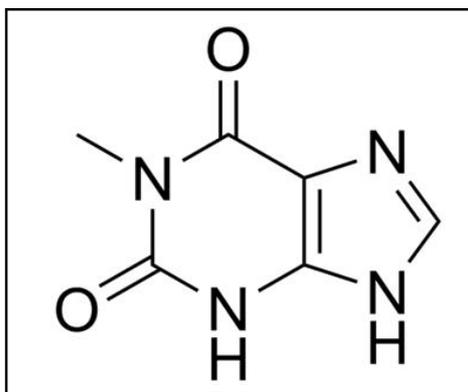


Figure 2: Caffeine (Methylxanthine).

### 3.2 Chlorogenic acids (Polyphenol)

Chlorogenic acid (CGA) is an esterified compound naturally found in coffee (Figure 3). This phenolic ester, synthesized from quinic acid and trans-cinnamic acid. In a standard 200 ml cup of coffee, CGA content typically ranges between 70 and 350 mg, with caffeic acid comprising approximately 35-175 mg of this amount (Muraiet *et al.*, 2023). CGA plays a crucial role in glucose and lipid metabolism, offering potential benefits in managing metabolic disorders such as diabetes, cardiovascular diseases, obesity, fatty liver disease, and cancer (Rojas *et al.*, 2022). Given its therapeutic significance, CGA is being researched as a non-invasive and non-pharmacological option for preventing and controlling chronic diseases (Cwiková *et al.*, 2022).

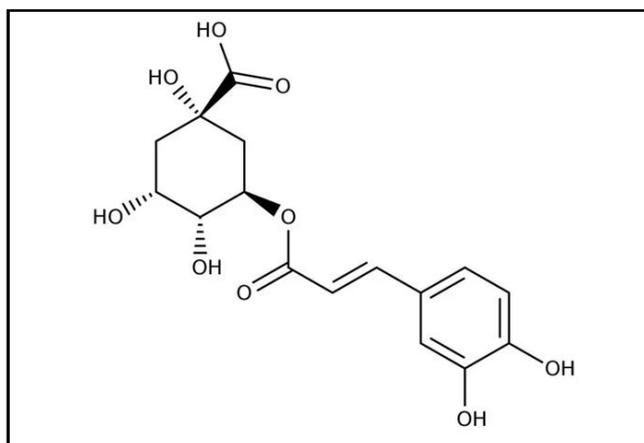


Figure 3: Chlorogenic acids (Polyphenol).

### 3.3 Coffee lipids (Kahweol and Cafestol)

Coffee beans, particularly those of *C. arabica*, contain lipid-based compounds known as kahweol and cafestol, which have similar structural characteristics. The levels of these diterpenes in coffee typically range from 0.1 to 7 mg per milliliter (Shnaigat *et al.*, 2022). As fat-soluble compounds, kahweol and cafestol exhibit strong anticarcinogenic properties and have been shown to counteract the effects of aflatoxin B1 (AFB1) in humans (Figure 4). However, in unfiltered coffee, their consumption has been linked to increased blood cholesterol levels (Surma *et al.*, 2023). These diterpenes also play a role in various biochemical pathways that help reduce the genotoxic effects of specific carcinogens, including 5,12-dimethyl benz[a]anthracene, aflatoxin B1, and 2-amino-1-methyl-6-phenylimidazo [4,5-b] pyridine (PhIP) (Eldesouki *et al.*, 2022).

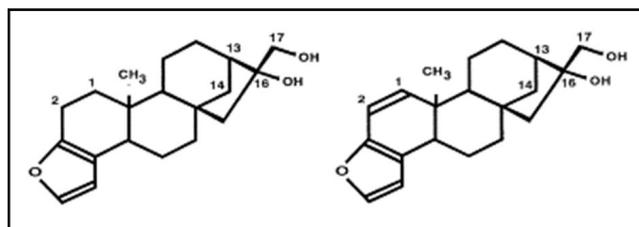


Figure 4: Coffee lipids (Cafestol and Kahweol).

## 4. Phytochemical analysis of coffee

Green coffee contains a diverse range of bioactive compounds, including carbohydrates, phenolic compounds such as caffeine and chlorogenic acid, polysaccharides, proteins, polyphenols, melanoidins, lipids, and essential minerals (Eldesouki *et al.*, 2022). Additionally, it serves as a source of vital minerals like calcium (Ca), potassium (K), magnesium (Mg), copper (Cu), iron (Fe), and manganese (Mn) (Suzuki *et al.*, 2021). The oil extracted through cold pressing of unroasted coffee beans is particularly rich in lipids, including triacylglycerols, cafestol, kahweol, sterols, tocopherols, and diterpenes from the Kaurene family (Speer, 2006). Furthermore, green coffee beans contain significant amounts of chlorogenic acid, caffeine, theophylline, trigonelline, and theobromine, all contributing to their bioactive composition (Acidri *et al.*, 2020). The most abundant chlorogenic acids found in green coffee beans include 3-CQA (3-O-caffeoylquinic acid), 4-CQA (4-O-caffeoylquinic acid), and 5-CQA (5-O-caffeoylquinic acid) (Ky *et al.*, 2021). Okubo and Kurata (2022) highlighted the effectiveness of near-infrared (NIR) spectroscopy in classifying green coffee beans by region of production, yielding results similar to those obtained using SIMCA. Various bioactive compounds have been successfully extracted from green coffee, each offering distinct functional properties (Table 1).

## 5. Pharmacological activities of green coffee beans

### 5.1 Anticancer properties

The International Agency for Research on Cancer (2016) has classified coffee as non-carcinogenic to humans. Numerous studies indicate that coffee consumption is linked to a lower risk of developing certain cancers. Among the bioactive compounds in coffee, kahweol has been recognized for its role in cancer prevention (Tripathi *et al.*, 2023). As an antioxidant, kahweol helps protect DNA from oxidative damage induced by hydrogen peroxide by neutralizing reactive oxygen

species (ROS) and stimulating hemoxygenase-1 to regulate intracellular ROS levels (Liu *et al.*, 2024). Tumor cells frequently exhibit DNA hypermethylation, an essential epigenetic mechanism that can silence critical genes, including tumor suppressors and DNA repair enzymes (de Souza *et al.*, 2020). Research has shown that caffeic acid can inhibit DNA methylation in human cancer cells, thereby suppressing tumor-associated pathways related to cell cycle regulation,

inflammation, and programmed cell death (Safe *et al.*, 2023). Studies suggest that regular coffee consumption is associated with a 3% decrease in cancer-related mortality (Makino *et al.*, 2021) and may offer protective effects against cancers of the kidney (Lee *et al.*, 2017), liver (Larsson and Wolk, 2007), pancreas (Ran, Wang, and Sun, 2016), colorectal region (Schmit *et al.*, 2016), breast (Jiang, Wu, and Jiang, 2013), and prostate (Tverdal, 2015).

**Table 1: Isolated compounds of coffee beans and their activities**

S. No.	Compound name	Phytochemical activities	Reference
1.	Triacylglycerol	Triacylglycerols (TAGs) play a crucial role in energy storage and metabolic processes. They exhibit various phytochemical activities, including antioxidant, anti-inflammatory, and antimicrobial properties. TAGs contribute to cellular signaling, lipid metabolism, and structural integrity. Their bioactive compounds influence health, supporting cardiovascular function and providing essential fatty acids for physiological processes.	Peixoto <i>et al.</i> , 2022
2.	Theobromine	Theobromine, a bioactive alkaloid found in cacao, tea, and coffee, exhibits various phytochemical activities. It possesses antioxidant, anti-inflammatory, and vasodilatory properties, contributing to cardiovascular health. Additionally, theobromine has diuretic effects, supports cognitive function, and may aid in metabolic regulation. Its pharmacological potential makes it valuable for therapeutic applications.	Yousefbeyk <i>et al.</i> , 2022
3.	Caffeine	Caffeine, a natural alkaloid found in coffee, exhibits various phytochemical activities, including antioxidant, neurostimulatory, and anti-inflammatory effects. It influences metabolism, enhances cognitive function, and protects against neurodegenerative disorders. Additionally, caffeine modulates enzymatic activities, improves lipid metabolism, and demonstrates potential in cardiovascular and metabolic health management through its bioactive properties.	Muzaifa <i>et al.</i> , 2022
4.	Diterpene	Diterpenes are bioactive compounds with diverse pharmacological properties, including anti-inflammatory, antimicrobial, anticancer, and antioxidant activities. Found in various plants, they modulate cellular pathways, support immune function, and exhibit neuroprotective effects. Their potential therapeutic applications make them valuable in drug development, particularly for treating inflammatory disorders, infections, and chronic diseases.	Sun <i>et al.</i> , 2022
5.	Ferulic acid	Ferulic acid, a natural phenolic compound, exhibits potent antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. It scavenges free radicals, protects against oxidative stress, and supports cardiovascular health. Additionally, ferulic acid enhances skin protection, modulates immune responses, and may aid in neuroprotection, making it a valuable compound in pharmaceuticals and functional foods.	Daba <i>et al.</i> , 2022
6.	Chlorogenic acid	Chlorogenic acid, a major polyphenol in green coffee, exhibits diverse phytochemical activities, including antioxidant, anti-inflammatory, antidiabetic, and antimicrobial effects. It plays a crucial role in regulating metabolism, reducing oxidative stress, and improving cardiovascular health. Additionally, its potential in weight management and neuroprotection makes it a valuable bioactive compound in therapeutic applications.	Lazaridis <i>et al.</i> , 2024
7.	N-Methyl-2 methyl-pyridinium-iodide	Methyl-2-methylpyridinium iodide exhibits various phytochemical activities, including antioxidant, antimicrobial, and anti-inflammatory properties. Its unique molecular structure contributes to potential therapeutic applications, particularly in combating oxidative stress and microbial infections. Further research is essential to explore its pharmacological significance and potential benefits in medicinal and pharmaceutical formulations.	Ali <i>et al.</i> , 2022
8.	Sterol	Sterols are bioactive compounds with significant health benefits, including cholesterol-lowering, anti-inflammatory, and antioxidant properties. They contribute to membrane stability in plants and animals while also exhibiting potential anticancer and immune-modulating effects. Sterols are widely studied for their role in cardiovascular health and their therapeutic potential in various metabolic disorders.	Nemzer <i>et al.</i> , 2021

9.	Linolenic acid	Linolenic acid, a polyunsaturated omega-3 fatty acid, exhibits significant phytochemical activities, including anti-inflammatory, antioxidant, and cardioprotective properties. It plays a vital role in reducing oxidative stress, supporting immune function, and maintaining cellular integrity. Additionally, it contributes to lipid metabolism regulation, promoting overall health and preventing chronic diseases like cardiovascular disorders.	Sun <i>et al.</i> , 2022
10.	Trigonelline	Trigonelline, a bioactive alkaloid in coffee and fenugreek, exhibits diverse phytochemical activities. It possesses antioxidant, anti-inflammatory, neuroprotective, antidiabetic, and antimicrobial properties. Trigonelline plays a role in glucose metabolism, cognitive function, and cellular protection. Its potential therapeutic benefits make it a promising compound for pharmaceutical and nutraceutical applications.	Gligor <i>et al.</i> , 2023

### 5.2 Antidiabetic activity

The prevalence of type 2 diabetes is increasing worldwide, with estimates predicting that 366 million individuals will be affected by 2030 (Sariá *et al.*, 2016). Green coffee contains caffeine, which acts as a glucose stimulant and mitochondrial activator. Caffeic acid, along with trigonelline, has been found to reduce oxidative stress and support axonal regeneration (Kusumah *et al.*, 2022). Additionally, chlorogenic acid plays a key role in maintaining glucose balance and reducing oxidative stress. Studies have shown that green coffee extract can lower oxidative stress, triglyceride levels, glucose, and oxidized glutathione while exhibiting antidiabetic properties. It has also been found to help prevent and manage type 2 diabetes in rats fed a high-fat diet (Lin *et al.*, 2022). Although, green coffee intake has been linked to a lower risk of diabetes, its specific biological targets and mechanisms remain under investigation. Chlorogenic acid functions as an alpha-glucosidase inhibitor, slowing glucose absorption in the digestive system, which helps reduce post-meal insulin spikes in individuals with type 2 diabetes (Peixoto *et al.*, 2022). Additionally, chlorogenic acid impacts gluconeogenesis and glycogenolysis by inhibiting glucose-6-phosphatase, encouraging the body to utilize fat stores for energy, which aids in regulating blood sugar and body weight (Tantapakul *et al.*, 2022). Furthermore, coffee compounds influence glucose absorption in the intestines by modulating levels of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1), both of which enhance insulin secretion in response to glucose intake (Wulandari *et al.*, 2024).

### 5.3 Antiobesity activity

Obesity, defined by excessive fat accumulation exceeding global health standards (Gómez *et al.*, 2017), is a major public health concern (Clark, 2017). It is associated with multiple chronic diseases, including diabetes, non-alcoholic fatty liver disease (NAFLD), hypertension, coronary artery disease, and certain types of cancer (Steele *et al.*, 2018). Research has linked green coffee extract (GCE) and chlorogenic acid (CGA) to reductions in body weight and body mass index (BMI) (Haidari *et al.*, 2017), regulation of blood pressure (Sirotkin *et al.*, 2021), and improved postprandial glucose metabolism by decreasing intestinal glucose absorption. Green coffee promotes bile production in the liver, which aids metabolism and glucose release into the bloodstream (Patil *et al.*, 2023). Caffeine plays a role in slowing fat absorption by mobilizing fatty acids from fat reserves, while CGA enhances hepatic fatty acid metabolism, thereby lowering triglyceride levels and supporting weight loss (Roshan *et al.*, 2018). Additionally, green coffee bean extract has been found to decrease hepatic triglyceride levels, and CGA further contributes by inhibiting fat absorption (Park *et al.*, 2023). Other bioactive phenolic compounds,

such as neochlorogenic acid and feruloylquinic acid, have been shown to boost hepatic carnitine palmitoyltransferase (CPT) activity (Shimoda *et al.*, 2016). Furthermore, green coffee consumption helps regulate plasma adipokine levels, body fat distribution, and fatty acid oxidation by modulating PPAR expression in the liver (Park *et al.*, 2023).

### 5.4 Antioxidant properties

Caffeine, a primary component of coffee, possesses strong antioxidant properties that help protect against oxidative DNA damage, regulate apoptosis, and influence cell-cycle checkpoints (Banerjee *et al.*, 2014). The diterpenes cafestol and kahweol, also present in coffee, exhibit bioactive effects that reduce genotoxicity caused by carcinogens (Masek *et al.*, 2020). Green coffee contains chlorogenic acid, a phenolic compound known for its antioxidant capabilities, which include neutralizing superoxide anions and hydroxyl radicals. It contributes to overall health by scavenging free radicals and inhibiting oxidative processes (Castro *et al.*, 2018). Chlorogenic acids effectively eliminate reactive oxygen species (ROS), which, while essential for cellular function, can be damaging when present in excessive amounts (Aroufai *et al.*, 2022). Research indicates that coffee consumption helps decrease oxidative DNA damage, boost glutathione levels, and enhance glutathione reductase activity (Ösz *et al.*, 2022).

### 5.5 Antihypertensive activity

Miranda *et al.* (2020) investigated the blood pressure-lowering effects of water-soluble green coffee extract in spontaneously hypertensive rats. Their research demonstrated that 5-CQA contributes to blood pressure reduction, with ferulic acid (50 mg/kg) identified as a key metabolite. The hypotensive response was diminished when atropine sulfate (5 mg/kg) was administered, indicating that ferulic acid likely exerts its effects *via* muscarinic acetylcholine receptors (Haghighatdoost *et al.*, 2023). Similarly, Sugiyanta *et al.* (2023) conducted a clinical study involving 20 healthy male participants, where 10 individuals consumed GCE for four months while the remaining 10 received a placebo. The findings revealed that GCE intake led to a reduction in homocysteine levels.

### 5.6 Antihydroxyl radical activity

Bisht *et al.* (2022) assessed the ability of aqueous green coffee extract to counteract hydroxyl radicals both *in vitro* using the deoxyribose method and *ex vivo* in IMR-32 cells. Their study found that green coffee extract demonstrated greater antiradical activity compared to roasted coffee. They identified 5-CQA as a crucial compound

contributing to both neuroprotection and antiradical effects. Additionally, their research highlighted that roasting coffee leads to the degradation of polyphenolic compounds due to maillard reactions (Xiao *et al.*, 2024).

### 5.7 Anti-inflammatory activity

Pergolizzi *et al.* (2020) examined the anti-inflammatory properties of chlorogenic acid in lipopolysaccharide-stimulated RAW264.7 murine cells. Their study revealed that chlorogenic acid reduces NO, COX-2, and iNOS production without causing cytotoxic effects. Furthermore, it was found to inhibit pro-inflammatory cytokines and other mediators of inflammation.

### 5.8 Antibacterial activity

Ermawati *et al.* (2022) evaluated the antibacterial properties of green coffee extract against *Salmonella enteritidis* and *Staphylococcus aureus* using concentrations of 5%, 10%, 15%, and 20%. The disc diffusion assay showed the strongest inhibitory effect at the 20% concentration. Another investigation assessed the antimicrobial activity of green and roasted coffee bean extracts against human oral pathogens, including *Porphyromonas gingivalis*, *Streptococcus mutans*, and *Lactobacillus casei*. The study found that both green and roasted coffee extracts exhibited antimicrobial properties against these pathogens, suggesting potential benefits for oral health (Abhay *et al.*, 2021).

### 5.9 Role in periodontal disease

Sariet *et al.* (2023) examined the antibacterial effects of pure green coffee extract on periodontogenic bacteria, including *Prevotella intermedia*, *Fusobacterium nucleatum*, and *Aggregati bacteractino mycetecomitans*. The study measured its efficacy using minimum inhibitory concentration (MIC) and minimum bactericidal concentration tests through dilution and culture media methods. The MIC values recorded were 0.2 µg/ml for *P. gingivalis*, *P. intermedia* and *A. actinomycetem comitans*, while *F. nucleatum* exhibited inhibition at 3.125 µg/ml.

### 5.10 Application as a sun protector

Green coffee seeds are rich in linolenic acid, which provides protection against harmful ultraviolet (UV) rays. Due to this protective property, the fatty acids derived from green coffee beans are increasingly considered for use in cosmetic formulations, particularly as ingredients in sunscreens (Rodrigues *et al.*, 2023).

### 5.11 Influence on skin properties

A double-blind, placebo-controlled study by Zofia *et al.* (2020) revealed that ingesting coffee polyphenols resulted in improvements in skin hydration, reduced transepidermal water loss, balanced skin surface pH, and enhanced hydration of the stratum corneum. Additionally, an improvement in skin blood circulation was observed following the consumption of these polyphenols.

### 5.12 Veterinary applications

A placebo-controlled, double-blind study demonstrated that administering 10 ml of coffee seed extract subcutaneously produced a 30% reduction in diarrhea incidence among newborn calves (Biesek *et al.*, 2023). Studies have explored the effects of incorporating green coffee powder (GCP) into poultry diets. For instance, research involving Ross broiler chickens indicated that supplementing their

feed with 2.5 g/kg of GCP led to improvements in body weight and feed conversion ratios. Additionally, this supplementation resulted in a reduction of pathogenic microorganisms in the gut, suggesting enhanced gut health and overall well-being of the birds (Elwy *et al.*, 2020).

### 5.13 Effects on hepatic disorders

Epidemiological studies suggest that coffee consumption may help prevent liver cirrhosis and other chronic liver conditions. Regular intake of coffee has been found to inversely correlate with serum gamma-glutamyl transferase (GGT) and alanine aminotransferase (ALT) levels, indicating potential liver-protective properties (Asbaghi *et al.*, 2020). The complex composition of coffee, which includes cafestol and kahweol, is believed to play a role in detoxifying carcinogens and eliminating harmful lipids and cholesterol from the liver (Lofffield *et al.*, 2021).

### 5.14 Activation of thermogenesis

Putman *et al.* (2023) examined the effects of caffeine on thermogenesis in brown adipose tissue (BAT). The study assessed guanosine-5'-diphosphate (GDP) binding, a key thermogenic marker, and measured oxygen consumption in BAT mitochondria. Following the administration of caffeine (60 mg/kg), BAT temperature significantly increased, while core body temperature remained largely unaffected. Furthermore, caffeine notably enhanced GDP binding, oxygen consumption in BAT mitochondria, and resting metabolic rate (RMR).

### 5.15 Role in wound healing

Lemos *et al.* (2022) explored the effects of an aqueous extract derived from coffee bean press cake (a byproduct of oil extraction from green coffee beans) on wound healing. Their study, conducted on an animal model using topical applications, compared the efficacy of hydrogels containing the extract against those containing chlorogenic acid (CGA), allantoin (a positive control), and carbopol (a negative control). The findings indicated that the green coffee extract demonstrated superior wound healing properties compared to allantoin and roasted coffee extracts, with a noticeable reduction in wound size over time.

### 5.16 Neuroprotective properties

Prandi *et al.* (2022) examined the neuroprotective potential of coffee in a Parkinson's disease model induced by MPTP. The anti-inflammatory and antioxidant compounds in coffee, including eicosanoyl-5-hydroxytryptamide (EHT), were found to reduce protein aggregation, phosphorylation, and neuroinflammation while preserving dopaminergic neurons in transgenic mice. Mice that consumed EHT for four weeks exhibited better neurological outcomes than those that did not (Rizk *et al.*, 2021). Farias-Pereira *et al.* (2021) investigated the effects of coffee consumption in Alzheimer's disease models. Their findings indicated that dietary supplementation with EHT for six to twelve months reduced intercellular amyloid-alpha accumulation and enhanced protein phosphatase 2A (PP2A) activity through demethylation, suggesting a neuroprotective role in Alzheimer's disease.

## 6. Green coffee and its toxicity

As previously discussed, green coffee provides numerous health benefits, largely attributed to its chlorogenic acid (CGA) content (Hutachokn *et al.*, 2021). However, some research suggests that

CGAs may also have negative effects (Oliveira *et al.*, 2020). Rahimi *et al.* (2024) found that administering high doses of CGA to male Wistar rats induced inflammatory responses, including increased leukocyte counts, elevated cytokine levels, and reduced antioxidant reserves. Additionally, a study reported that CGA exhibited prooxidant properties, raising intracellular reactive oxygen species (ROS) levels and triggering apoptosis in myeloid leukemia cell. The research assessed the *in vivo* toxicity of a standardized green coffee extract containing 50% CGA, evaluating its safety through acute and sub-chronic toxicity studies. Excessive consumption of green coffee may lead to adverse effects. While it has a lower caffeine content than regular coffee, moderation is recommended (Bhatt, 2020). Over-consumption may cause restlessness, insomnia, anxiety, irregular heartbeat, nausea, digestive discomfort, nervousness, fatigue, headaches, rapid breathing, agitation, and diarrhea. Pregnant and nursing individuals are advised to avoid green coffee extract (Lorbeer *et al.*, 2022). Additionally, high intake could increase calcium loss through urine, potentially leading to calcium deficiency and increasing the risk of osteoporosis over time (Farchi *et al.*, 2024).

## 7. Conclusion

Coffee is one of the most popular beverages worldwide and is recognized for its high antioxidant content, which helps protect against oxidative stress-related conditions. Green coffee is commonly promoted as a weight-loss aid and is frequently included in weight management supplements. However, its effectiveness and potential risks remain debated due to conflicting research on adverse effects and safety concerns. Some studies have linked coffee consumption to mortality risks. A 22-year study conducted by the Harvard School of Public Health concluded that while coffee may offer health benefits, further research is necessary to confirm these findings. The likelihood of negative effects increases with excessive intake, primarily due to caffeine, which can be reduced by choosing decaffeinated options. Maintaining a balanced diet while consuming green coffee in moderation around three to four cups per day may be beneficial. However, caffeine intake should not surpass the European Food Safety Authority's recommended daily limit of 400 mg for adults.

Green coffee beans contain the highest levels of chlorogenic acids (CGAs), contributing to their pharmacological potential. These include antioxidant properties, improved hepatic glucose utilization, inhibition of fat absorption, enhanced fat metabolism in the liver, suppression of carcinogenic activity, antihypertensive effects, and even HIV-1 integrase inhibition, among others. Due to these benefits, green coffee is considered valuable for nutraceutical applications, reinforcing the importance of exploring natural sources of antioxidants and bioactive compounds.

To fully understand the health benefits and risks of green coffee and caffeine intake, further experimental and clinical research is needed. Studies should aim to identify the specific bioactive compounds responsible for both positive and negative effects, along with their mechanisms of action, dosage considerations, and long-term impacts. Genetic variations related to diet, chronic diseases, and metabolic enzyme polymorphisms may help determine individuals more prone to either beneficial or adverse outcomes. Since coffee remains a globally consumed beverage, additional studies should also examine its long-term effects, particularly in children, adolescents, and pregnant women. Future research should explore its antioxidant, antidiabetic, and anticancer properties using appropriate animal models to deepen understanding of its therapeutic potential.

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## Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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