World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

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Does coffee really have health benefits?

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World Journal of Advanced Research and Reviews, 2026, 31(01), 1474–1492

Publication history: Received on 13 June 2026; revised on 25 July 2026; accepted on 27 July 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.31.1.1971

Abstract

Coffee is one of the most widely consumed beverages in the world; it is a rich source of antioxidants and caffeine. The benefits of caffeine are widely documented; it is primarily and strongly associated with a reduced risk of type 2 diabetes, as well as protection against cardiovascular, neurodegenerative, and liver diseases, and certain types of cancer. Despite its benefits, controversies persist regarding its potential to cause anxiety, insomnia, irritability, heart palpitations, and tachycardia. Compounds such as cafestol (found in unfiltered coffee) can raise LDL cholesterol. Controversy arises regarding excessive consumption or individual sensitivity, as there are concerns about its addictive potential, which often leads to withdrawal symptoms such as headaches and lethargy. This review provides an overview of both the beneficial and harmful effects of coffee on health across all stages of life.

Keywords: Coffee; Polyphenols; Health; Caffeine; Nutrition; Cafestol; Diabetes Mellitus.

1. Introduction

Coffee is one of the most widely consumed beverages worldwide, deeply Its main active ingredient, caffeine, is a central nervous system stimulant known for its ability to improve concentration and reduce fatigue. However, there has long been speculation about the beneficial effects of coffee—on the one hand, due to caffeine and polyphenols, which help slow cellular aging; on the other hand, because high consumption and caffeine can also have health consequences. For this reason, the relationship between coffee and health is becoming increasingly uncertain today, compounded by various studies linking chronic coffee consumption to the risk of developing various conditions, such as anxiety attacks, nervousness, cardiovascular disorders, infertility and the risk of miscarriage, dyslipidemia, and the risk of developing certain types of cancer, among others (Farraj e tal., 2024; Emadi, & Kamangar, 2025). In this case, it appears that the effect (protective factor or risk factor) of coffee consumption may be dose-dependent; that is, depending on whether it is consumed in moderation or excess, coffee can act as either a protective factor or a risk factor for people's health. The factors driving coffee consumption and its effects manifest differently throughout life. For example, coffee consumption in childhood can disrupt sleep patterns and cause hyperactivity or anxiety because, at this stage, the nervous and immune systems are still developing; whereas in adolescence, it critically interferes with brain development and the sleep cycles necessary for growth—due to the exponential rise in consumption of energy drinks and sugary coffees—and finally, in adulthood, although moderate consumption is associated with cognitive and protective benefits, adults often turn to it to compensate for chronic sleep deprivation and work-related stress (Emadi, & Kamangar, 2025).

However, given the aforementioned controversies and the fact that this relationship is of great significance due to the high consumption of this beverage, it was deemed appropriate to conduct this literature review in order to extract

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scientific information that would shed light on this relationship. For this reason, the objectives of this systematic review are to understand the fine line between functional consumption and harmful abuse, which is essential for assessing the true impact of this beverage on human health.

2. History

The word "coffee" is derived from the Arabic "*qahwah*," which is used to refer to beverages made from plants. Its consumption dates back to around 1000 AD, but it wasn't until the early 14th century that the process of roasting the beans was discovered, and that is when its consumption began to spread throughout the Arab world (Veronica et al., 2021), today, it is one of the most widely consumed beverages worldwide.

Since the dawn of coffee cultivation, two varieties of Arabica coffee have been recognized: *C. arabica*, the Arabica variety or Typical variety, which was cultivated in Dutch botanical gardens. It was later introduced by the French to the Caribbean and from there spread to the countries of Central and South America. The Bourbon variety was cultivated by the French on the Bourbon Islands, also known as Réunion. All varieties of C. arabica cultivated worldwide are derived from these two varieties (Pastelin-Solano et al., 2026).

The coffee tree originated in Abyssinia, now the Republic of Ethiopia. There are two possible origins for the drink's name: the first suggests it derives from the Arabic word *qahwah*, meaning "stimulating," "energizing," or "invigorating"; the other connects it etymologically to the province of *Kaffa* in southwestern Ethiopia (Abyssinia). The Arabs were the first to discover the virtues and economic potential of coffee, as they developed the entire cultivation process and kept it a secret, while also attempting to prevent the export of the product. From East Africa, the bean traveled to Europe and to many Europeans who set out on the American adventure, during which coffee reached the other side of the Atlantic. As a result of the Haitian Revolution, many locals and European immigrants fled to Brazil, bringing coffee with them; over time, this made Brazil the world's leading producer. In Colombia, the first seeds were planted in 1732 by Spanish Jesuit missionaries. The coffee plant arrived in Mexico in 1796 in Córdoba, Veracruz, and later in Michoacán in 1823 and in Tuxtla Gutierrez, Chiapas, in 1847 (Pastelin-Solano et al., 2026).

Although coffee consumption is primarily driven by its cultural and traditional significance (Czarniecka-Skubina, et al. 2021), it has been increasing in recent years due to the positive effects of the various compounds found in coffee (Figure 1) (Kobylińska et al., 2025). It is estimated that this beverage contains around 1,000 compounds divided into different chemical classes, such as phenolics acids (chlorogenic acid), diterpenes (cafestol and kahweol), methylxanthines (caffeine, theophylline, and theobromine), vitamin B_3, trigomelin, and alkaloids (caffeine) (Pastelin-Solano et al., 2026).

Figure 1 Main bioactive compounds of grain of coffee.

3. Benefits During Pregnancy

Pregnancy is one of the most important stages of human life; therefore, dietary choices made during this period will impact the fetus's development, as well as the child's childhood and adulthood. Consequently, caffeine consumption decreases in pregnant women, leading to an increase in its lipophilicity, which allows it to easily cross the blood-placental barrier. However, the fetus and placenta lack the enzymes necessary for caffeine metabolism, which can impair embryonic development, as shown in Figure 2 (Kalo et al., 2024).

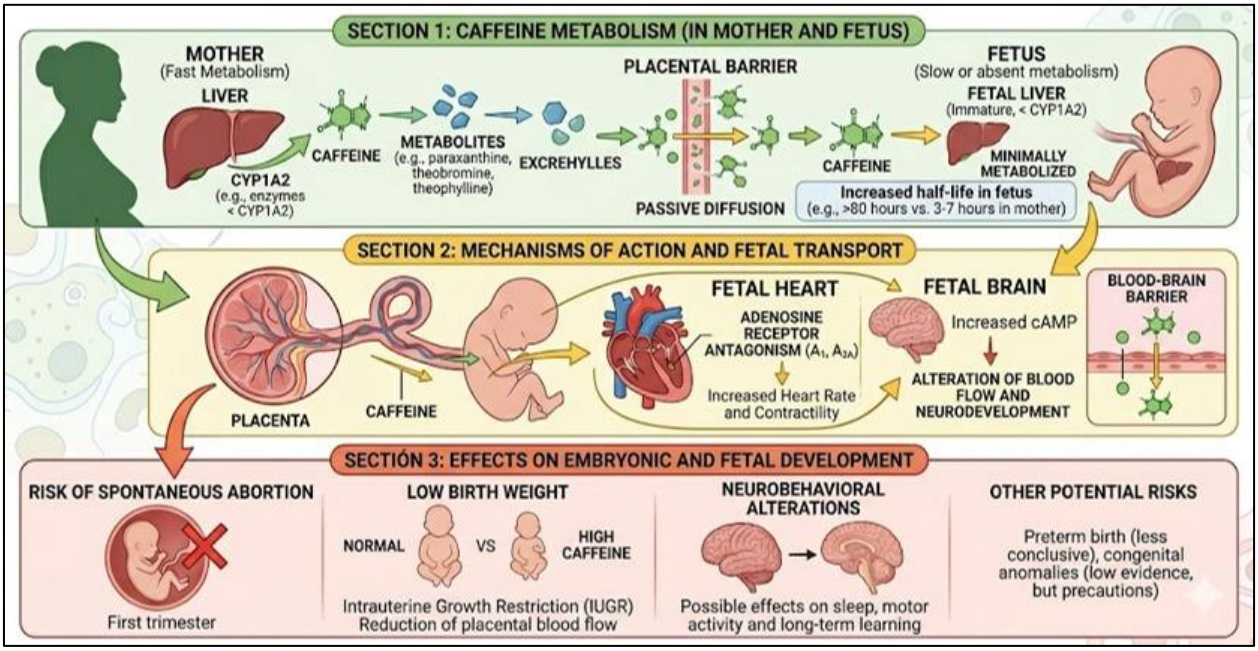

Figure 2 Caffeine metabolism and its effects on embryonic development (Original work created using Gemini).

Several epidemiological studies have shown that caffeine consumption during pregnancy is associated with first-trimester bleeding/spontaneous abortion (Choi, Koo, Park, 2020, Cnattingius, et al., (2000). For this reason, the WHO recommends consuming less than 300 mg/day of caffeine to ensure a safe pregnancy (Qian et al., 2020). New evidence shows that even at these doses, the risk of pregnancy loss and IUGR persists (Chen, 2016).

4. The Effects of Coffee in Childhood

There is growing evidence suggesting beneficial effects associated with coffee consumption during childhood, although research on the effects of this beverage remains limited (Figure 3). Caffeine is a stimulant, and various studies have observed that it has a negative effect on sleep (O'Callaghan, Muurlink, Reid, 2018). Some studies have found benefits of caffeine, where 10.2 ± 17.4 mg/day causes morning fatigue due to its effect on sleep disruption as well as increased arousal (O'Callaghan, Muurlink, Reid, 2018; Drake, Roehrs, Shambroom, Roth, 2018). There are also studies demonstrating the negative effects of this beverage on mood, such as the onset of anxiety and depression symptoms (29,30). However, the cause-and-effect relationship remains unclear.

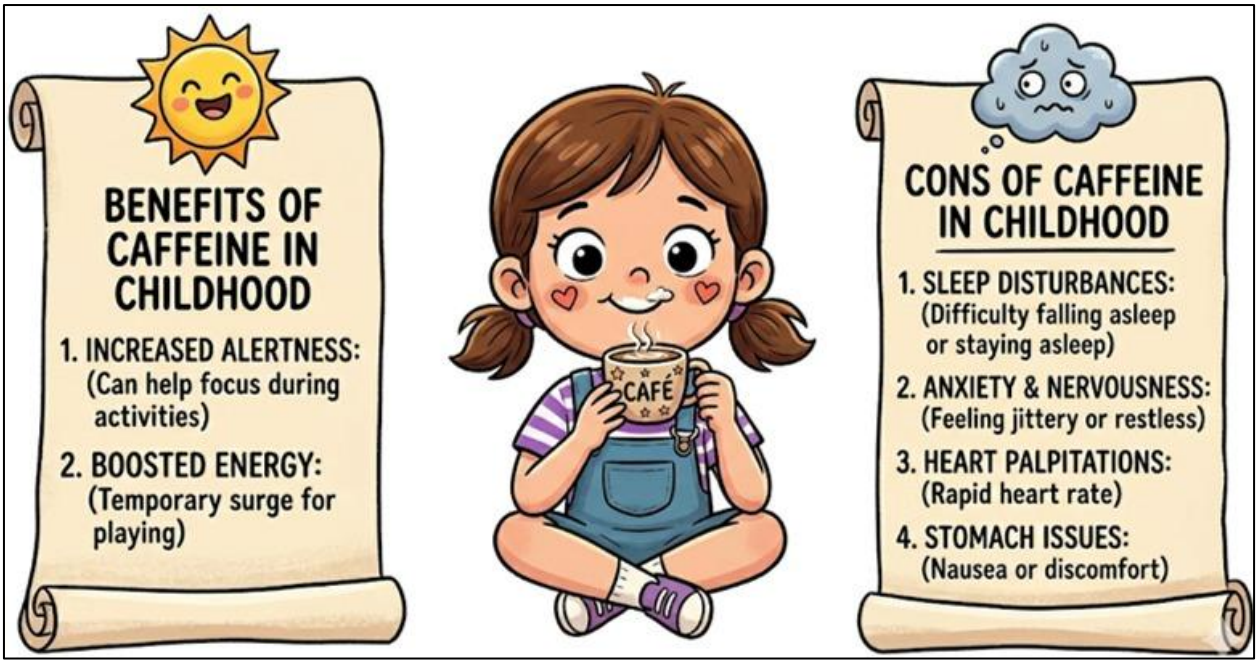

Figure 3 Benefits and cons of caffeine in childhood (Original work created using Gemini).

Some studies report that caffeine intake in children under 12 should not exceed 85 mg/day (Thakre et al., 2015), although some authors suggest that caffeine consumption should be limited or restricted to 2.5 mg/kg/day in children under 12, as the alkaloid could cause health problems (Thakre et al., 2015; Verster & Koenig, 2018). Although caffeine is not recommended for consumption during childhood, various studies indicate that children do consume it, primarily in soft drinks, certain sweets such as chocolate bars, and energy drinks (Verster & Koenig, 2018). As mentioned earlier, children's initial exposure to caffeine can occur during pregnancy via the placenta; therefore, the subsequent effects are not well established due to the difficulty of controlling for variables (Papadopoulou et al., 2018). Consequently, it is considered necessary to conduct an in-depth investigation into the cognitive and physiological effects during different stages of childhood. Furthermore, when children consume caffeine incidentally—that is, when it is not part of any medical treatment—it becomes a controversial issue because it can lead to alterations in growth and development, such as serotonin syndromes, iron absorption deficiencies, and weight loss (Castillo-Ruiz et al., 2025; Torres-Ugalde et al., 2020), and on the one hand, it may have negative effects, and on the other, it could have positive effects such as improved physical and mental performance, as well as neuroprotective effects, which will be described later. Therefore, further evidence is needed in this regard, based on a review of scientific literature, to clarify the effects of caffeine in childhood.

5. Coffee and Mental Health

Some studies link caffeine consumption to the onset of panic and anxiety symptoms (Liu et al., 2024) and to neurodegenerative symptoms in patients with a history of dementia (Antonio et al., 2024). However, it has been noted that coffee reduces the prevalence of depressive symptoms, exerting an analgesic effect that is potentiated by serotonin inhibitors (Szopa et al., 2016). Consequently, one hour after drinking coffee, mood improves, helping to prevent depressive episodes and suicide attempts (Shi et al., 2025; Lucas et al., 2014). It has been demonstrated that, in addition to all the effects described above, caffeine acts positively against the hypnotic effects of ethanol. Furthermore, caffeine can also inhibit the catalepsy caused by haloperidol.

This beverage can increase levels of adrenaline, norepinephrine, and cortisol, causing a blood pressure-raising effect, reducing feelings of tiredness and fatigue, and consequently enhancing the ability to sustain mental effort, in addition to releasing dopamine in the brain (Szopa et al., 2016). Another benefit of caffeine is that it increases cholinergic activity, which enhances intellectual performance related to learning, attention, and short-term concentration, helping to maintain mental acuity and reduce age-related cognitive decline (Shi et al., 2025).

6. Effects of Coffee on Migraines

As is well known, migraine are a highly prevalent chronic condition and ranks as the seventh leading cause of disability worldwide. Some studies suggest that caffeine has been linked both as a trigger for migraine attacks and, conversely, as a treatment (Makhlouf et al., 2026). It is believed that caffeine has a beneficial effect on migraines due to its action on adenosine receptors and the inhibition it exerts on the cyclooxygenase enzyme (Zduńska et al., 2023). In our body, the adenosine receptors A2A and A1 are blocked by caffeine, thereby generating its antinociceptive effect observed in models of neuropathic, nociceptive, and inflammatory pain (Zduńska et al., 2023). Figure 4 illustrates the mechanism by which caffeine induces migraine.

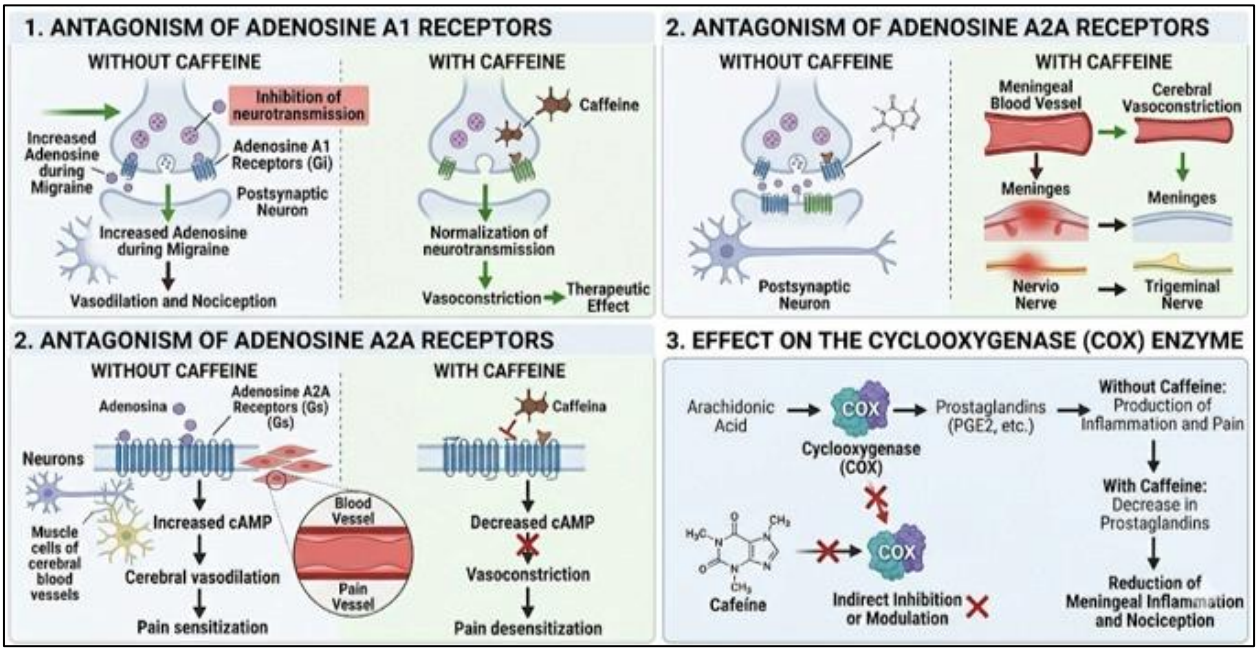

Figure 4 Mechanisms of caffeine in the migraine (Original work created using Gemini).

In addition, adenosine plays an important role, as it has been observed that plasma adenosine levels are elevated during migraine attacks, and exogenous administration of adenosine triggers pain episodes. Furthermore, it has been shown that regular coffee consumption causes changes in the gut microbiota, and the use of probiotics has been found to be effective in treating migraine. For this reason, given the relationship between migraine and the gut-brain axis, it is reasonable to suggest that this is another mechanism through which caffeine affects migraine (Zduńska et al., 2023).

Furthermore, it is believed that caffeine may act as a trigger when consumed frequently; it is also a risk factor for the chronicity of migraine (Rauf et al., 2025; Nowaczewska, Wiciński, & Kaźmierczak, 2020). Caffeine reduces magnesium reabsorption, thereby disrupting neuromuscular conduction and the transmission of nerve impulses. Furthermore, the dehydration caused by its diuretic effect acts as an exacerbating factor in migraine attacks (Rauf et al., 2025; Rodak, Kokot, Kratz, 2021). However, there is insufficient evidence to classify caffeine as a trigger; nevertheless, excessive consumption may predispose individuals to the development of chronic migraine, and abruptly stopping caffeine intake may trigger migraine attacks (Nowaczewska, Wiciński, & Kaźmierczak, 2020)

7. Effects of Coffee on Cardiovascular Disease

Cardiovascular disease (CVD) refers to a group of disorders that affect the heart and blood vessels, and is one of the leading causes of death worldwide (Engstrom, 2016). Some studies have linked caffeine to CVD through several mechanisms: 1) due to its similarity to adenosine, it produces an antagonistic effect on the receptors for this molecule (especially A1 and A2A); 2) it activates the sympathetic nervous system; 3) it activates the adrenal cortex; 4) it has a renal effect by activating the renin-angiotensin-aldosterone system; 5) it inhibits phosphodiesterase (Figure 5) (Chou & Benowitz, 1994).

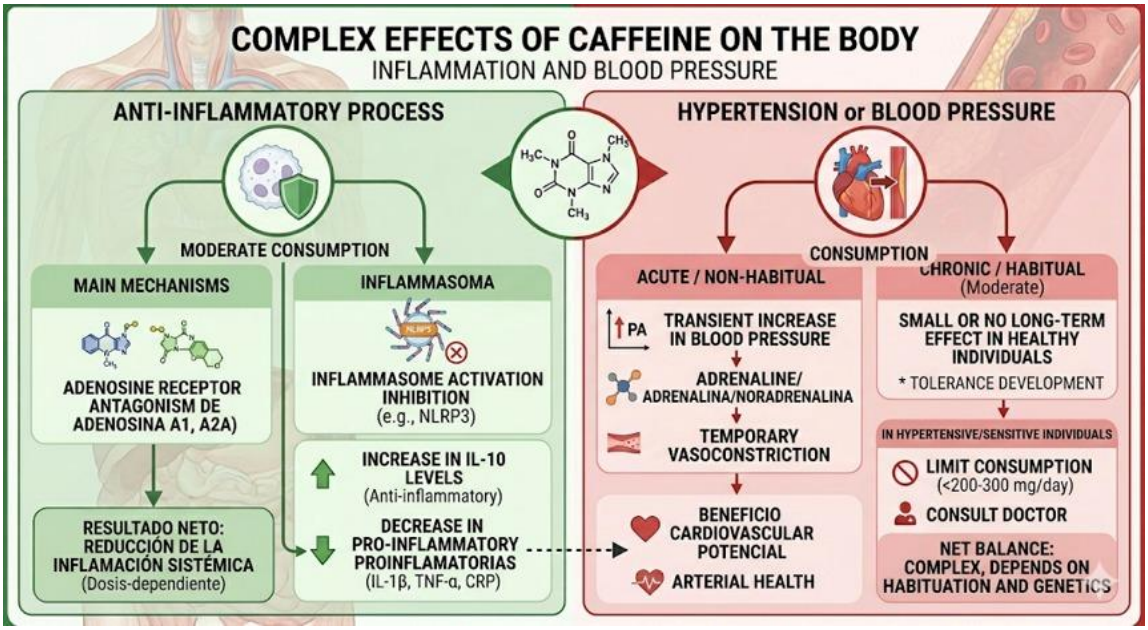

Figure 5 Complex effects of caffeine on the body inflammation and blood pressure.

However, some reported data have found an inverse association between coffee consumption and CVD risk (Noguchi et al., 2015). Some studies have reported that consuming >200 mg of caffeine per day raises blood pressure by 6 mmHg (Farraj et al., 2024). One study found a dose-response relationship between the consumption of 3–7 cups of coffee and the risk of developing CVD, revealing a protective effect (Chou & Benowitz, 1994). Some studies claim that the risk of CVD is reduced by 2% with each additional cup of coffee per day (Hamad, 2024). Although caffeine raises blood pressure readings, possibly due to the production of catecholamines, current evidence does not show an increased risk of CVD; in fact, it may act as a protective factor by reducing these incidents. However, further research is needed to understand the role of caffeine in CVD and to explore potential applications such as therapeutic strategies.

8. The cholesterol-lowering effect of coffee

Coffee consumption leads to an increase in serum levels of total cholesterol and low-density lipoproteins (LDL); this increase is attributed to the diterpene alcohols cafestol and kahweol, as well as the method of coffee preparation (Mo et al., 2025). Cafestol and kahweol influence lipid metabolism, as well as other potential effects on human health. Some studies have shown that coffee consumption and the method of preparation raise cholesterol levels in humans (Halvorsen et al., 1998; Rustan et al., 1997). It appears that the way coffee is prepared is a crucial factor in its cholesterol-raising effects and its impact on health. Thus, the known preparation methods that involve boiling the coffee directly without filtering the resulting liquid appear to have the highest content of diterpene alcohols, while methods that involve passing the coffee through a paper filter appear to be the healthiest, as the diterpene content is very low (Hao et al., 2024; Rustan et al., 1997). The results of studies investigating the impact of consuming coffee prepared with a paper filter show an increase in total cholesterol levels ranging from 0.04 mmol/L (1.5 mg/dL) to 0.5 mmol/L (19 mg/dL) per cup, while coffee brewed without a paper filter shows a cholesterol-raising effect ranging from 6.1 ± 1.4 mg/dL to 14.8 ± 2.0 mg/dL (Zampelas et al., 2004).

As for decaffeinated coffee consumption, the data show a cholesterol-raising effect similar to that of caffeinated coffee, depending on how it is prepared (Rico et al., 2022; Wei et al., 1995). Finally, for instant coffee, the data are inconclusive, as some studies show a slight cholesterol-raising effect. If these data are correlational, serum cholesterol levels may contribute to an increased risk of CVD (Zampelas et al., 2004).

Other studies have detected an increase in triglyceride levels caused by the consumption of 5–6 cups of coffee per day (Post, de Wit, Princen et al., 1997). Therefore, it appears that coffee has a cholesterol-raising effect due to the presence of the diterpene alcohols cafestol and kahweol; furthermore, the concentration of these compounds in the final beverage consumed depends on the specific method of coffee preparation. Similarly, it has been shown that the coffee varieties, *Arabica* and *Robusta*, contain both diterpenes in different concentrations, maintaining the hypercholesterolemic effect; therefore, the appropriate method of consumption to reduce the hypercholesterolemic effect is filtered coffee (Guercia et al., 2024). Cafestol and kahweol, diterpenes present in unfiltered coffee, act on liver receptors (Farnesoid X Receptor

(FXR) and Pregnane X Receptor (PXR)), causing a reduction in the activity of the enzyme cholesterol 7α-hydroxylase (CYP7A1), the rate-limiting enzyme in the conversion of cholesterol to bile acids, leading to its accumulation in the bloodstream (Post, de Wit, Princen et al., 1997).

For this reason, the relationship between coffee consumption and changes in lipid profiles has been a topic of debate in clinical studies, although molecular evidence shows that diterpenes have a cholesterol-raising effect, while the phenolic fraction of the beverage —particularly chlorogenic acid (CGA)— exerts a cholesterol-lowering effect by modulating hepatic transcriptional pathways and the gut microbiota. Studies demonstrating inhibition of the enzyme (Arantes et al., 2016; Zampelas et al., 2004). CGA activates AMP-activated protein kinase (AMPK), leading to the phosphorylation and inactivation of HMG-CoA reductase, and suppresses transcription factors such as SREBP-2, thereby reducing de novo cholesterol synthesis. Additionally, it stimulates the expression of the LDL receptor, promoting the clearance of plasma cholesterol. CGA is metabolized by gastric esterases and by the colonic microbiota, converting into caffeic acid, ferulic acid, and dihydroferulic acid derivatives. Therefore, attributing the benefit to CGA is an inaccuracy; the cholesterol-lowering effect depends on the metabolites generated from CGA (Arantes et al., 2016).

Another critical factor often overlooked in studies is the heat sensitivity of polyphenols. The coffee bean roasting process degrades polyphenols by 70–90%, transforming them into CGA lactones and melanoidins (Fernandez-Rosillo et al., 2025). Therefore, the degree of bean roasting must be accounted for and the cholesterol-lowering benefits analyzed to avoid invalidating the reproducibility of the results.

9. Atrial Fibrillation and Stroke

Ischemic stroke accounts for 80% of all strokes, while the remaining 20% are hemorrhagic strokes (Chugh, 2019). Published studies suggest that regular coffee consumption reduces the risk of stroke. However, the association between coffee consumption and stroke is inconsistent. Some studies suggest that high coffee consumption is associated with a lower risk of stroke, while others suggest the opposite (Smyth et al., 2024; Kim et al., 2012). Regarding atrial fibrillation (AF), it is suggested that regular coffee consumption is associated with a lower probability of developing AF; furthermore, it is believed to have a protective effect due to other compounds present in coffee, such as lipids, carbohydrates, and polyphenols (Bodar et al., 2019; Mostofsky et al., 2016). Additionally, a review found no evidence that coffee increases the risk of developing ventricular arrhythmias, and it is considered that a caffeine intake of 300 mg/day is safe in this regard (Bodar et al., 2019).

10. Caffeine and Diabetes Mellitus

Diabetes mellitus (DM) is a common metabolic disorder that increases the risk of developing diabetic cardiomyopathy and atherosclerotic CVD. The effect of coffee consumption on the risk of developing DM has been studied on multiple occasions (Henn et al., 2025; Lee et al., 2016). Most studies conclude that coffee intake is positively associated with the risk of developing DM, due to the important role of coffee's lipid metabolites in its antidiabetic effect (Su, Hu, Tan, 2026). However, its consumption initially appears beneficial, given that it is associated with weight loss due to two mechanisms: first, it induces greater satiety by reducing appetite, and second, it increases energy expenditure by raising basal metabolism (Henn et al., 2025). In fact, consuming 6 doses of 100 mg of caffeine daily results in a 5% increase in energy expenditure throughout the day (Su, Hu, Tan, 2026).

Although some studies claim to have found no clear evidence of a link between coffee consumption and the risk of developing type 2 diabetes, other studies have found that certain components of coffee—minerals (potassium and magnesium), vitamin B3, and antioxidants (tocopherols and chlorogenic acid)—play a protective role against DM2. Studies support an inverse relationship between coffee consumption and the risk of developing DM 2 because it improves insulin resistance, due to a decrease in circulating catecholamines and the production of non-esterified fatty acids in plasma, and an increase in the expression of type 4 glucose transporters (GLUT4) in skeletal muscle, thereby improving blood glucose level (Guarino et al., 2013). The effects of insulin sensitivity following acute caffeine administration include a decrease in insulin sensitivity and a reduction in glucose uptake by skeletal muscle, mediated by adenosine A1 and A2B receptors (Urzúa et al., 2012). Both GLUT4 and nitric oxide (NO) appear to be the effectors involved in insulin resistance (Guarino et al., 2013; Urzúa et al., 2012). This is where the controversy remains regarding whether or not coffee consumption is advisable for people with DM2. The following figure illustrates the mechanism of caffeine and its effect on diabetes.

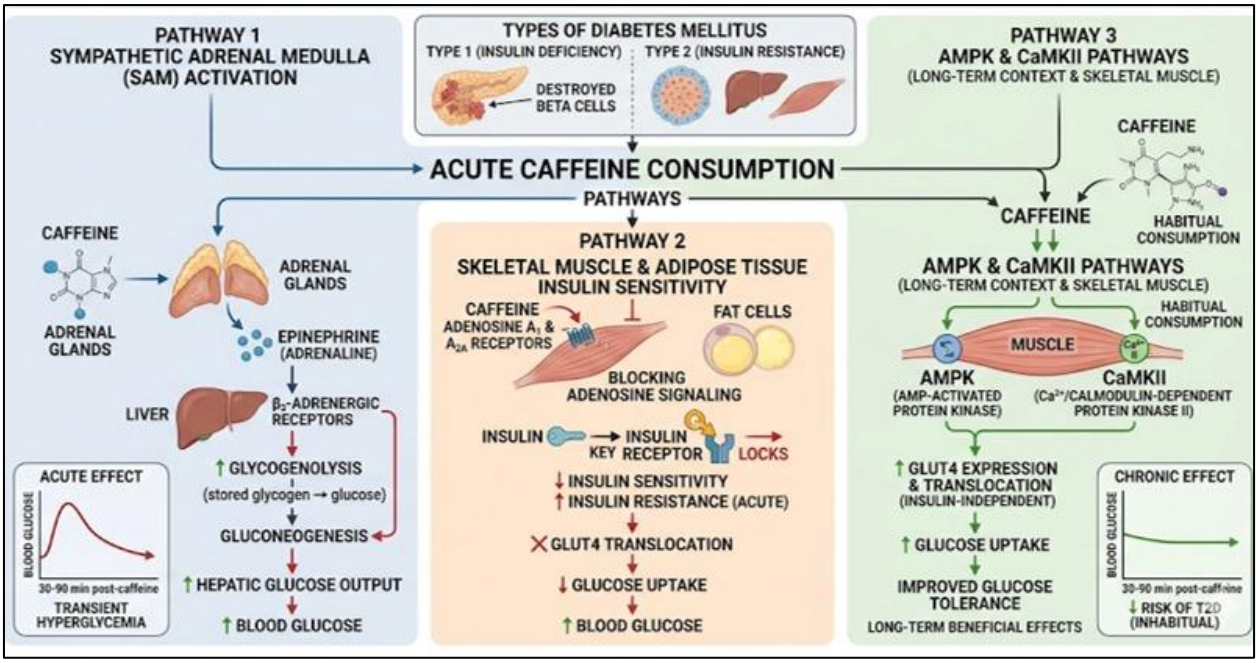

Figure 6 Mechanisms of interaction between diabetes mellitus and caffeine.

Urzúa et al. (2012) found that caffeine inhibited glucose uptake in adipose tissue and facilitated it in skeletal muscle in obese Zucker rats. In non-diabetic humans. Alba-Talero et al. (2024) found that caffeine intake at daily doses similar to those provided by moderate coffee consumption reduced insulin sensitivity, an effect caused by the increase in plasma levels of epinephrine and free fatty acids induced by caffeine. Likewise, this study showed that intravenous administration of caffeine at a dose of approximately 30 µmol/L reduces insulin sensitivity by approximately 15%. Greer et al (2001) found that caffeine reduced blood glucose levels by up to 24% and decreased carbohydrate storage by 35%. Reis, Dórea, da Costa (2018) found a 30% reduction in glucose uptake for a caffeine dose equivalent to 3–4 cups of coffee per day, and a decrease in leg muscle uptake of approximately 55% at rest and 51% during exercise, suggesting that caffeine alters the beneficial effects of exercise on insulin's action on muscle.

In fact, these data contrast with those reported by Roales-Nieto, Moreno, Luciano, & Coronado (2004) analyzed the associations between coffee consumption and cardiovascular disease, diabetes, and cancer, finding evidence of an increased risk of cardiovascular disease associated with coffee consumption, while the data are inconclusive regarding the relationship with diabetes risk. The relationships between coffee consumption and cancer risk appear to be associated with an increased likelihood of developing pancreatic and ovarian cancers; in contrast, coffee consumption has been shown to be a protective factor against colon, rectal, and bladder cancers. In all cases, the available hypotheses regarding the metabolic mechanisms involved in the effect and in the different organs are outlined.

Animal studies indicate that caffeine has both a stimulating effect on insulin secretion and an effect that increases lipolysis (Su, Hu, Tan, 2026). Therefore, coffee consumption is inversely associated with the prevalence of fasting hyperglycemia, an important finding regarding the possibility that coffee consumption may be a protective factor against the risk of DM2 (Su, Hu, Tan, 2026; Lin et al, 2011; van Dam et al. 2004). Nguyen et al. (2024) reported that chlorogenic acid reduces intestinal glucose absorption and cellular oxidative stress. Meng et al. (2013) had also reported that it inhibits the hydrolysis of glucose-6-phosphate, which could reduce glucose release by the liver. Reviewed epidemiological studies confirm (Wong et al., 2025; van Dam et al. 2004; Salazar-Martinez et al., 2004) the relationship between coffee consumption and the risk of DM 2. Some studies (Molonia et al., 2026; Yan et al., 2020; Zuñiga et al., 2028) have confirmed the modulatory effect of chlorogenic acids on cellular glucose uptake and insulin secretion, suggesting they have an antagonistic effect on glucose transport in the intestine, revealing a new function consisting of attenuating intestinal glucose absorption rates and shifting the site of glucose absorption to more distal parts of the intestine. Therefore, drinking coffee—a rich source of chlorogenic acids and magnesium—may offer health benefits. This protective effect may be related to the metabolic effects of chlorogenic acid and magnesium.

On the other hand, la DM 1 is a childhood and adolescent condition characterized by a series of metabolic abnormalities, all of which involve elevated blood glucose levels, due to the autoimmune destruction of pancreatic beta cells, resulting in insufficient or even absent insulin production (Pasi, Ravi, 2022; Saberzadeh-Ardestani et al. 2018). Some studies

indicate that coffee and caffeine are implicated in the intrauterine risk for the development of DM 1, since caffeine has the ability to cross the placental barrier, thereby accumulating in tissues (especially the liver and brain) and causing harmful effects on the fetus (Stutz et al., 2018). In addition to this, other studies suggest a possible link between sugar consumption and the risk of developing DM 1, which is added to coffee (Su, Hu, Tan, 2026).

Based on the above, it appears that there is a link between coffee consumption and diabetes, and that this link is influenced by various factors, such as the type of coffee (regular or decaffeinated), the types of bioactive compounds it contains, the method of preparation (brewed, espresso, filtered or unfiltered), the amount consumed (higher intake, lower risk of disease), and even added sugar, among others. Therefore, while the data obtained are not conclusive, they make it clear that moderate coffee consumption is not contraindicated for people with diabetes nor does it pose an increased risk of developing DM in healthy individuals.

11. Coffee and the Skeletal System

Osteoporosis is a complex, multifactorial disease characterized by a decrease in bone mass along with an alteration in bone microstructure. Although bone mass and bone quality are genetically determined, other factors, such as diet, also influence bone quality. Calcium, along with phosphorus, is one of the major minerals in bone (80–90%) (Pouresmaeili, Kamalidehghan, Kamarehei, 2018). Caffeine interferes with calcium absorption in the digestive tract and also increases its urinary and fecal excretion, which can lead to a negative calcium balance (Massey, & Whiting, 1993). Certain epidemiological data suggest a negative association between caffeine and the risk of osteoporosis, although this remains a subject of debate today (Ratajczak et al., 2021).

Calcium is absorbed through the intestinal tract via two pathways: the transcellular pathway, regulated by calcitriol, and the passive paracellular pathway. Therefore, consuming high amounts of caffeine can negatively modulate the expression of vitamin D receptors in enterocytes, reducing the efficiency of active calcium transport (Areco et al., 2020). Additionally, coffee contains condensed tannins and chlorogenic acids, which have chelating properties in the intestinal lumen, also forming insoluble complexes that limit passive absorption (Winiarska-Mieczan et al., 2023). At the renal level, caffeine acts as a diuretic, leading to increased urinary excretion of sodium and calcium, since both share cotransport systems in the proximal convoluted tubule (Zhang et al., 2015). At the cellular level, coffee affects actin microfilaments and the intermediate filaments of the cytoskeleton. It has been shown that high concentrations of caffeine act directly on tubulin, inhibiting the binding of proteins to form cytoskeletal filaments, which causes failures in chromosome separation and induces apoptosis (Renganathan, Adam, Gelfand, 2026). Actin microfilaments control the elasticity, contraction, and movement of the cell surface. In this regard, caffeine influences the transition from filamentous actin (F-actin) to depolymerized globular actin (G-actin), altering the cells' mechanical resistance so that they do not rupture under physical stress (Tazzeo et al., 2012). Caffeine also inhibits cAMP, indirectly altering the rate at which the filaments contract and uncoil (Tariqul et al., 2019). This cAMP signaling cascade occurs in three steps: a) competitive inhibition of phosphodiesterase; b) activation of protein kinase A (PKA); and c) inactivation of myosin light chain kinase (MLCK).

12. Coffee and Cancer

According to the International Agency for Research on Cancer, coffee is classified as a non-carcinogenic food (DiNicolantonio, & O'Keefe, 2018). Caffeine has been shown to have suppressive effects on metastatic tumor cells, which may contribute to it being considered as a therapeutic alternative for treating cancer; however, the relationship between coffee and cancer depends on the tissue type (Pauwels &, Volterrani, 2021). The possible relationship between coffee consumption and cancer risk has been extensively studied, with numerous publications reporting on both experimental animal studies and various types of epidemiological studies in humans. Additionally, coffee consumption has been associated with a lower risk of liver cancer (Petrick et al., 2015), glioma (Pan et al., 2024), myeloproliferative syndrome (especially polycythemia vera) (Podoltsev et al., 2020), urinary tract (Yu et al., 2019), colorectal (Qu, Cheng, Chen, 2024), melanoma/non-melanoma (Caini et al., 2017), breast (Ganmaa et al., 2008), and pancreatic (Guertin et al., 2015), ovarian (Shafiei et al., 2019), bladder, testicular, and prostate (Yu et al., 2011), esophageal and gastric (Parra-Lara et al., 2020), and pharyngeal (Zhang J, Zhou B, Hao, 2018) cancers. Given that a comprehensive review of this topic would be limited to outlining the current state of knowledge and briefly discussing the main studies for each case, Table 1 presents the findings regarding the relationship between regular coffee consumption and the incidence of various types of cancer.

Table 1 Relationship between coffee consumption and cancer risk.

Cancer Type	Observed Effect	Evidence	Reference
Hepatocellular Carcinoma	Significant reduction	Reduces the risk of cirrhosis and liver cancer by up to 40-50%.	Petrick et al., 2015
Colorectal	Moderate reduction	Decreased risk, especially in the proximal colon. Improves intestinal transit time.	Qu, Cheng, Chen, 2024
Endometrial (Uterus)	Significant reduction	Reduces risk likely due to its effect on estrogen and insulin levels.	Hirose et al., 2007
Pharyngeal and Oral Cavity	Reduction	Studies suggest protection linked to coffee polyphenols.	Zhang J, Zhou B, Hao, 2018
Breast	Neutral / Protective	No increased risk. Some studies suggest a slight risk reduction in postmenopausal women (ER-negative).	Ganmaa et al., 2008
Prostate	Neutral / Slight reduction	Most data indicate no increased risk; some studies show lower risk of aggressive prostate cancer.	Yu et al., 2011
Pancreas	Neutral	Studies have ruled out this association.	Guertin et al., 2015
Bladder and Urinary Tract	Neutral / Inconclusive	No evidence of a clear causal relationship, though some studies suggested a slight risk in smokers.	Yu et al., 2019
Esophagus	Neutral / Caution	Consuming coffee at >65°C/149°F increases risk.	Parra-Lara et al., 2020
Stomach	Neutral	Meta-analyses find no significant association, either positive or negative.	Parra-Lara et al., 2020
Glioma (Brain)	Possible reduction	Decreased risk with caffeine consumption.	Pan et al., 2024
Melanoma / Non-melanoma	Slight reduction	An inverse association with malignant melanoma, due to the photoprotective effects of caffeine.	Caini et al., 2017
Myeloproliferative Syndrome	Little evidence	No conclusive data linking coffee to an increased or decreased risk.	Podoltsev et al., 2020
Ovary	Neutral	Evidence does not show a significant association.	Shafiei et al., 2019
Testicles	Neutral	There is no evidence.	Yu et al., 2011

Several compounds (methylglyoxal, polyphenols, caffeine, and theobromine) have been identified in roasted coffee that may influence cancer development in various ways (Podoltsev et al., 2020; DiNicolantonio, & O'Keefe, 2018). For example, they may act as direct mutagens, as is the case with some of these compounds, or they may affect certain cellular transformation processes and tumor progression. Evidence suggests that caffeine, as well as the diterpenes cafestol and kahweol, may serve as protectors against carcinogenesis in various body tissues. Methylxanthines produce suppressive effects on metastatic tumor cells (Pan et al., 2024; Hirose et al., 2007). At the molecular level, studies have shown that caffeine inhibits vascular endothelial growth factor and IL-8 in human colon cancer cells (Pan et al., 2024). Additionally, caffeine acts on A2A-type adenosine receptors in lymphocytes, which may enhance the immune response against malignant antigens. So far, it appears that coffee plays a protective or at least neutral role against most cancers, while in some cases it is contraindicated, as described in Table 1.

13. Coffee and Neurodegenerative Diseases

Neurodegenerative diseases (NDs) refer to hereditary or acquired conditions characterized by progressive dysfunction of the central nervous system (CNS). According to the National Institute of Neurological Disorders and Stroke, the most

prevalent and severe of these are Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS) (Lamptey et al., 2022). Recent evidence demonstrates the protective effect of coffee consumption on NDS. Caffeine consumption slows the progression of PD symptom development (Simon et al., 2015). This beverage was also found to have a protective effect in HD, ALS, and multiple sclerosis (Adrissi et al., 2024; Simon et al., 2015). It is believed that the neuroprotective effect is due to eicosanil-5-hydroxytryptamine, a component of coffee, thanks to the antagonism it exerts on A2A receptors. This effect leads to a decrease in intracellular calcium and glutamate levels in these cells, which have been associated with excitotoxicity in NDs (Ruggiero et al., 2022; Lamptey et al., 2022).

14. Caffeine abuse and dependence

The following section aims to provide information on the likelihood of a person developing a dependence on caffeine and the effects of caffeine abuse on individuals. In psychological dependence, there is only a desire to consume a substance; in this case, the person uses the substance as a psychological crutch and to feel a certain sense of well-being, and it helps them cope with everyday situations and activities. (REF). Dependence begins to develop after chronic use of the substance and is characterized by an urgent need to consume the substance in order to maintain functioning (Figure 7) (REF).

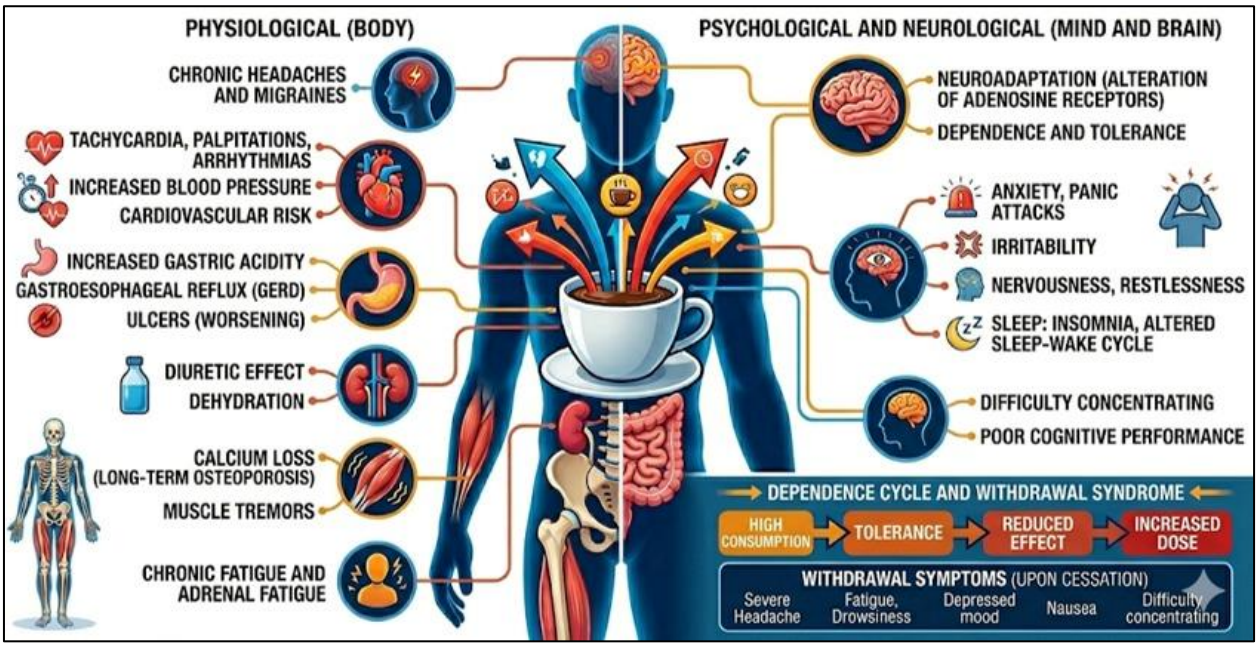

Figure 7 Consequences of caffeine abuse and high-dosage dependence.

Meredith et al. (2013) reports that caffeine abuse is not associated with patterns of compulsive use; however, it is possible to find individuals who continue to consume caffeine despite specific medical advice. It has been found that consuming more than 1 g of caffeine per day can lead to significant psychotic effects, causing physical and cognitive impairment, as well as severe gastrointestinal distress. When caffeine toxicity is moderate, it can cause agitation, tremors, anxiety, and gastrointestinal discomfort (Shi et al., 2025).

Withdrawal symptoms can occur in people who consume large amounts of caffeine, but they can also appear in people who consume the equivalent of one cup of coffee a day or three cans of caffeinated soda. Caffeine withdrawal is undeniable, as physical and psychological symptoms arise when coffee consumption is stopped or the daily dose is reduced. Withdrawal symptoms include headaches, drowsiness, fatigue, impaired attention and concentration, difficulty with coordination, mood swings, drowsiness, fatigue, anxiety, or mild depression, typically appearing within the first 12 to 24 hours, peaking between 24 and 48 hours, and lasting approximately 7 days (Lesar et al., 2025). In some cases, compulsive cravings can lead to occupational or social problems in dependent individuals (Du et al., 2025). Physical symptoms typically appear on the first day of abstinence and can last for several more days; similarly, it has been found that withdrawal is one of the main factors contributing to chronic coffee consumption (Meredith et al. 2013). Consequently, various studies have demonstrated that ceasing caffeine consumption carries a risk of psychological and

endocrine symptoms, leading to weight changes, mental health issues, and certain immune-related diseases (Shi et al., 2025).

15. Conclusion

Coffee is one of the most widely consumed beverages worldwide, with strong evidence demonstrating its positive health effects. There is also sufficient evidence regarding its protective role against various diseases, such as neurodegenerative disorders and cancer. Its benefits are attributed to its caffeine content and a multitude of bioactive compounds that exert beneficial effects. However, its consumption should not be taken lightly, as excessive consumption of this beverage can lead to dependence and even cause psychiatric disorders such as depression. Before consuming it, one should consider the method of preparation to promote various positive effects on the body; therefore, it is very important to pay attention to how each individual reacts, as everyone processes it differently.

Compliance with ethical standards

Acknowledgments

SECIHTI on SNII Stimulus Funding. This manuscript is part of the Delfín Binational Network for Cooperation and Projects between Mexico and Colombia 2025-2026.

Disclosure of conflict of interest

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Statement of ethical approval

This study used retrospective survey data and did not include any animal or human experiments.

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