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Health benefits and effects of coffee consumption: Implications for chronic disease prevention

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Abstract: Coffee is one of the most preferred beverages, second only to water, and is mentioned as potentially advantageous in the 2015 Dietary Guidelines for Americans. Coffee components are responsible for its positive benefits on glucose tolerance and diabetes. They also play anti-inflammatory, antioxidative, anticarcinogenic, antimicrobial, antihypertensive, immunostimulant, and antithrombotic roles in the human body. New methodologies in epidemiological findings and experimental investigations suggest that coffee consumption may benefit in the prevention of various chronic diseases, including type 2 diabetes mellitus. Most prospective cohort studies have revealed no link between coffee consumption and an increased risk of cardiovascular disease. Additionally, there is ample convincing evidence that both decaffeinated and caffeinated coffee have similar health benefits, indicating that, in addition to caffeine, various other compounds contribute to the health effects. For adults taking 3-4 cups of coffee daily (moderate amount) or 300-400mg/day caffeine, some documentation of health benefits and somewhat a little proof of risks concerning wellness is also available. In conclusion, moderate coffee intake (3–4 cups/day) offers health benefits with minimal risks.

Keywords: coffee, caffeine, cardiovascular disease, type 2 diabetes, insulin resistance

1. Introduction

Coffee is one of the most favored and practical beverages worldwide (Abalo, 2021). Coffee is the most preferred caffeine source for adults, whilst tea is the preferred choice for adolescents (Nieber, 2017). There are three different kinds of coffee beans that include Robusta, Liberica, and Arabica (Antwerpes et al., 2020). Robusta is native to Vietnam and has 2.5% more caffeine and a strong taste compared to other types of coffee. A low-yielding type of coffee known as Liberica is native to West Africa as well as Malaysia. Arabica is native to Southwestern Ethiopia and contains a low amount of caffeine and has a smoother taste; even 80% of coffee in the world is prepared from these types of beans. Coffee is used for its energizing and stimulating properties, which are influenced by a complicated blend of biological components. Coffee contains a variety of biological substances, including caffeine, chlorogenic acids, sucrose, and trigonelline, which aid in the identification of distinct coffee species (Barghouthy et al., 2021). Polyphenols that include chlorogenic acid, antioxidants, ferulic acid, melanoidins, and microelements such as magnesium and vitamin B3 are also the major components of coffee. These ingredients help to improve the gut microbiome, modulate metabolism, and reduction of oxidative stress as well (Abalo, 2021).

Due to its high antioxidant activity, coffee is one of the main natural sources of antioxidants. (Bazal et al., 2021). It's a common misconception that an adequate amount of coffee consumption isn't safe for patients with CVDs. (Beaudoin & Graham, 2015) Consumption of an adequate amount of coffee is considered favorable for different health problems and presents outstanding anti-inflammatory (A. Belayneh & F. Molla, 2020), antioxidant, anti-carcinogenic, and other potential benefits. Habitual intake of coffee-containing beverages plays an important

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role as a modifiable risk factor in CVDs (Nieber, 2017), and the risk of type-2 diabetes, heart diseases, and some types of cancer can also be reduced. Blood pressure, heart rate, and arterial fibrillation can be increased by the daily consumption of high amounts of caffeine present in coffee (Brown et al., 2016). Coffee that has been boiled and unfiltered appears to raise plasma cholesterol and triglyceride levels, but appears to be good for metabolic syndrome (Casiglia et al., 2018). The overall risk of cardiovascular diseases, coronary artery disease (Chieng and Kistler, 2022), Stroke, Heart Failure, and ischemic heart disease (IHD) seems to be lower in individuals who consume an adequate amount of coffee. Coffee also shows various antioxidant activities and has potential for decreasing lifestyle-related diseases. This article's main goal is to study and discuss recent findings on the benefits and drawbacks of coffee drinking, as well as its links to Type 2 diabetes and cardiovascular disease in human beings. (Chieng and Kistler, 2022)

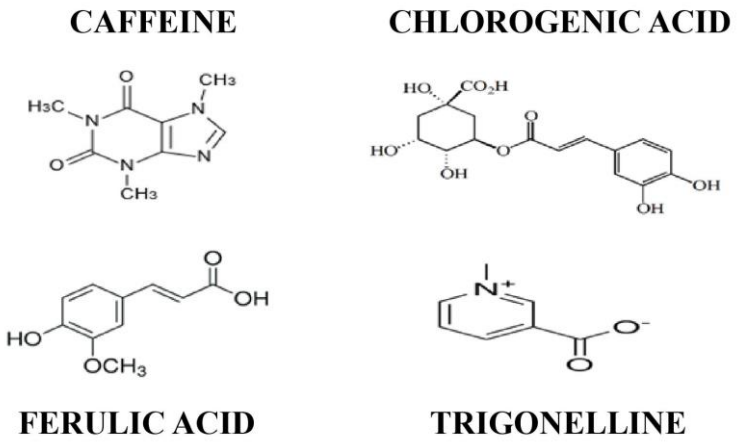

Figure 1: Chemical structures of Caffeine, Chlorogenic acid, Ferulic acid, and Trigonelline

2. Review search methodology

2.1. Search strategy

To assemble the studies for this review, the electronic databases PubMed, Google scholar, ncbi, Web of Science, JAMA Internal Medicine, European Journal of Nutrition, The American Journal of Medicine, The American journal of clinical nutrition, International journal of cardiology, The European Journal of Preventive Cardiology and Research gate were searched for publications up until and including September 2021, as the interest was in observational or interventional studies accessing the outcomes of coffee use on cardiovascular illness and type 2 diabetes. Studies that had been published in languages other than English were disregarded. Headings, subheadings, text terms, and word variations were used in the search technique. Furthermore, the citation list of the collected articles was examined to discover potentially relevant new publications.

2.2. Study selection and data extraction

The titles and summaries of publications extracted and selected for inclusion in the review were evaluated. The full texts of the selected papers were obtained and read to figure out the potential for being included. Following that, data were methodically extracted from the included papers.

3. Caffeine

Caffeine is methylxanthine (1,3,7-trimethylxanthine). Following the consumption of coffee, caffeine is quickly absorbed (within 45 minutes). The gastrointestinal tract absorbs it, and it is metabolized by the liver's Cytochrome P-450 enzyme. Caffeine metabolites (paraxanthine, theobromine, and theophylline) are further metabolized to uric acid and excreted in the urine. The blood-brain barrier is easily crossed by caffeine and its derivative paraxanthine. In adults, the life span of caffeine ranges from 2.5 to 4.5 hours, which is almost entirely accessible. Caffeine has an 80-hour half-life in newborns due to their limited ability to metabolize caffeine. Caffeine metabolism is stimulated by smoking, which reduces the half-life by up to 50%. During pregnancy (especially in the 3rd trimester) half-life of caffeine decreases by up to 15 hours. Healthy adults can typically consume 400mg of caffeine daily.

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Table 1. Serving sizes of different caffeine-containing beverages and their caffeine content

Beverage (Serving Size)	Caffeine content (mg)
Cappuccino (150ml)	65mg
Decaffeinated coffee (150ml)	3mg
Instant coffee (150ml)	65mg
Starbucks Café Latte (473ml)	150mg
Espresso (25ml)	106mg

4. How does coffee work in the body?

In the brain, caffeine adheres to and inhibits adenosine receptors. When caffeine binds to and blocks adenosine receptors, its natural ligand, adenosine, can't bind and activate them. Adenosine is produced from ATP during metabolism, when phosphate groups are cleaved off and energy is released, so adenosine accumulates during activity and wakefulness. Caffeine makes us feel awake and less weary since adenosine receptor activation in the brain decreases alertness and produces sleepiness. There are 2 types of adenosine receptors in the brain (caffeine can bind to both types). Stimulatory A2A receptors are found primarily on cholinergic neurons (involved in the onset of sleep), and inhibitory A1 receptors are found primarily on GABAergic neurons (involved in the modulation of sleep). People who drink a lot of coffee regularly have more adenosine receptors on their neurons, so they need more coffee to stay awake. However, the good thing is that adenosine can still perform its vital functions and promote sleep. (Soliman et al., 2018)

5. Health benefits of habitual coffee consumption

Habitual coffee consumption has numerous health benefits for malignancies, cardiovascular, metabolic, and psychiatric illnesses. (Thomas & Hodges, 2020) Patients with hepatitis C and the immune system's major virus, the immunodeficiency virus, benefit from coffee's neurocognitive effects as well. (Antwerpes et al., 2020) According to a recent study, using coffee can benefit those who have Multiple Sclerosis (MS). (Herden & Weissert, 2020) Regular intake of caffeine can dramatically lower the potential threat and development of Parkinson's disease (PD). It also lowers the risk of dementia, stroke, sleep disorders, and anxiety. Regular coffee consumption is linked to five single-nucleotide polymorphisms (SNPs) and lessens the potential risk of acquiring type 2 diabetes and prediabetes. Some studies have shown that individuals with the GG genotype of TRIB1 (a gene linked to cholesterol metabolism) exhibited a considerably decreased vulnerability to coronary heart disease. (Abalo, 2021) Coffee also inhibits intestinal absorption of fatty acids, increases the body's metabolic rate, making it effective for weight loss. Coffee, on the other hand, boosts the production of triglycerides and low-density lipoprotein. These studies made a solid case for the reduction of metabolic, endocrine, and cardiovascular disease risk attributed to frequent, moderate coffee use. (Chieng & Kistler, 2021)

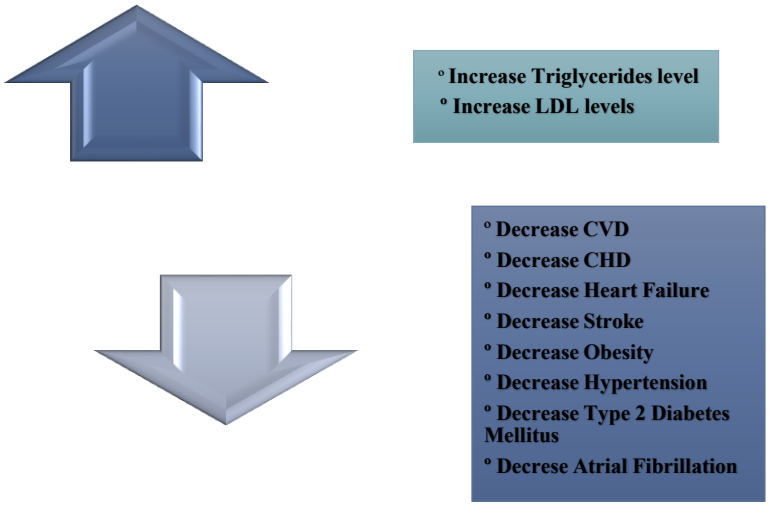

Figure 2: Regular, small amount of coffee drinking is linked to lower rates of coronary heart disease, atrial fibrillation, type 2 diabetes mellitus, stroke, hypertension, obesity, and heart failure. Consuming coffee raises one's lipid profile.

6. Coffee and pharmacokinetic properties of drugs

Numerous factors can affect the pharmacokinetic properties of medications through a variety of methods, such as influencing absorption, distribution, excretion, and enzyme metabolism. Drinks and beverages are some of the major factors that influence pharmacokinetics. One of the well-known drinks that pharmacologically interacts with several medicinal medications is coffee. Due to its main ingredients, such as caffeine and chlorogenic acid, coffee has multiple wellness benefits, but it also has clinically significant pharmacokinetic interactions with many crucial over-the-counter and prescribed medicines. The oral medication administration route has plenty of advantages; however, the pharmacokinetic attributes of many therapeutic pharmaceuticals given with the aid of this method are compromised due to the intake of foodstuffs and beverages such as coffee and other caffeine-containing items. Coffee use may have an impact on the dissolving profile, gastrointestinal (GI) pH, GI unloading time, and inhibition of glucose-6-phosphatase, all of which may have an influence on medication administration. When it reacts with acidic drugs, it forms complexes with various chemicals. The polarized carbonyl groups in coffee and the hydrogen atoms in the medicines form a hydrogen bond, which mediates this interaction. Additionally, coffee increases the number of soluble complexes formed between medicines and organic acid anions. By blocking ADH, coffee increases the generation of diluted urine (Belayneh and Molla, 2020).

Frequent urination is among the most harmful side effects of increasing your coffee intake. Raising the glomerular blood pressure within the kidney's capillaries increases urination. As blood filtration rises because of this mechanism, urine production rises (Belayneh and Molla, 2020).

Coffee can also reduce the gastrointestinal absorption of various substances, both natural and synthetic. The absorption of iron, for instance, is lowered when coffee or other caffeinated beverages are eaten with meals high in iron. Consequently, it is suggested to drink coffee one to two hours before a meal. The well-known stomach acid secretion stimulant caffeine. It lowers the pH of the stomach via elevating the secretion of stomach acid, i.e. hydrochloric acid, due to its bitter taste, which activates numerous type 2 bitter taste receptors (TAS2Rs). The amount of gastric acid produced in the stomach affects how much of the medicine is absorbed. Two cups of coffee can boost the absorption of 650 mg of aspirin, an NSAID, which is 120 mg of caffeine equivalent. By boosting gastric acid secretion, aspirin's bioavailability and high-end levels in the blood are both enhanced by coffee, but its elimination from the body is left unaffected (Belayneh and Molla, 2020).

A study from Spain demonstrated an increase in plasma concentrations of numerous drugs, including mexiletine, a Class IB antiarrhythmic, caused by co-administration with caffeine. This interaction may be due to the competitive inhibitory effects of caffeine, particularly methylxanthines, on cytochrome P450 isoenzymes (particularly CYP1A2) responsible for the metabolism of these medications (Belayneh and Molla, 2020).

7. Coffee and cardiovascular diseases

Caffeine, a xanthine alkaloid, is one of the key components of coffee. It has a similar structure to adenosine. Therefore, it acts as an opposing deterrent of adenosine receptors, including A1, A2a, and A2b, and increases the plasma levels of adenosine. In coronary arteries, adenosine works as a vasodilator, and various adenosine roles are dependent on the placement of the type of adenosine receptor. Through the inhibition of cAMP phosphodiesterase, caffeine tends to boost intracellular cyclic adenosine monophosphate (cAMP) levels. It also has cardio-acceleratory activity and therefore causes vagally-mediated bradycardia via activation of the baroreflex. Coffee also contains chlorogenic acid, which is a powerful antioxidant. By triggering the AMP-activated protein kinase (AMPK) communication pathway and inhibiting NAD(P)H oxidase activity, it also affects the circulatory system.

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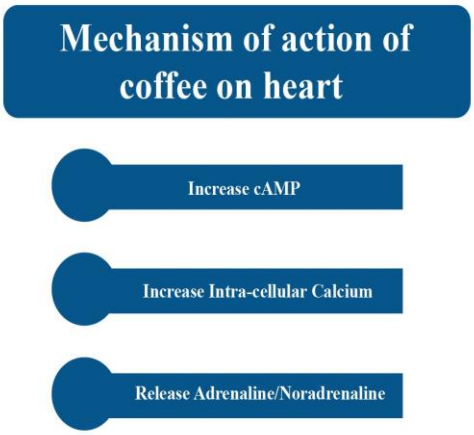

Figure 3: Mechanism of action of Coffee on the heart. Coffee activates the sympathetic system through various processes

7.1 Coffee and risk of arrhythmias

Coffee consumption is considered safe by recent evidence. According to the studies, coffee provides protection from atrial arrhythmias, specifically atrial fibrillation (AF). Coffee gives protection against arrhythmias by its antioxidant effects and cardiomyocyte adenosine receptor antagonism. Additionally, information is provided regarding the interaction among coffee, tea, and ventricular arrhythmia (VA), ventricular tachycardia (VT), and sudden cardiac death (SCD), although these studies are confined to tiny samples, and nearly all of them do not demonstrate an elevated risk. Coffee doesn't trigger ventricular ectopy (Chieng and Kistler, 2022).

In a prospective study, 1475 randomly chosen men and women's responses to caffeine were studied. According to research, higher levels of caffeine consumption, more than 320 mg per day, decrease the incidence of atrial fibrillation (AF) compared to lower levels. On univariate analysis, individuals who metabolize caffeine slowly due to CYP1A2 gene polymorphisms reported larger reductions in AF (Casiglia et al., 2018). In a different investigation, 33,638 women in total who were primarily healthy aged 45 without cardiovascular disease and (AF) arterial fibrillation were studied at baseline in a randomized controlled experiment and given 22, 135, 285, 402, and 656 mg/d of coffee. The results showed that elevated caffeine consumption had no relationship with an elevated risk of AF. (Conen et al., 2010). According to another study, 1-7 cups of coffee per week or 320mg per day caffeine helps to reduce the risk of atrial fibrillation. (Bazal et al., 2021). Different studies concluded that 400mg caffeine consumption daily or 5cups of coffee daily doesn't cause cardiac arrhythmias. (Voskoboinik et al., 2019). Drinking coffee can lessen arrhythmia risk by 3% (Kim et al., 2021).

7.2 Coffee and risk of heart failure

Coffee use has been shown to cause a reduction in the likelihood of heart failure (HF). A systematic review disclosed a J-shaped pattern regarding the use of coffee and heart failure, with those who took four cups per day having a lower incidence of the condition. Numerous recent studies have found that the increasing intake of coffee dramatically decreases the potential threat of HF. Overall, it was found that people who take 2 cups/day have the lowest incidence of HF. But higher caffeine intake is also associated with reduced HF. Nevertheless, coffee is beneficial for individuals with already existing heart failure. Mean exercise time and peak minute ventilation were significantly increased in individuals having intravenous caffeine at 4mg/kg body weight (approximately 2 cups of coffee (Chieng and Kistler, 2021).

In a prospective observational study of 34,551 participants who were 48 to 83 years of age and did not have a history of HF examine the effect of coffee on HF was examined. Food-frequency questionnaires were utilized to gauge dietary intake. The doses 2, 3, 4, and ≥5 cups per day were observed. In the end, it came to light that there is no correlation between the occurrence of HF episodes and coffee drinking (Levitan et al., 2011). The bond between coffee intake and the danger of heart failure was found in prospective population-based cohort research that included 59,490 people, aged 25 to 74, and without HF at baseline. Many previous studies have

stated that coffee is bad for the heart, but according to recent studies and research, coffee reduces the occurrence of heart failure. There is no correlation between increasing coffee use and reducing the danger of heart disease. According to a study, those who gulp two cups of coffee daily are less than thirty percent at risk than those who don't (Poole et al., 2017). Another study stated that 3-4cups of coffee consumption daily is linked with a 10% decreased risk of heart failure (Stevens et al., 2021). The consumption of coffee is related to decreased risk of serious cardiovascular events, such as hospitalization associated with acute heart failure. Moreover, caffeine consumption has been established to elevate the functional capacity of patients who already have heart failure. A comparison study was conducted in 37,315 males who did not have a history of myocardial infarction, diabetes, or heart failure to determine coffee consumption by using food frequency questionnaires. The study group was determined by dividing them into those who consume 0, 12, 3-4, or 5 cups of coffee daily. This observation was supported by the fact that the incidence of heart failure hospitalization or death rose with more coffee consumption indicated in the study (Iten et al., 2024).

7.3 Coffee and risk of coronary heart disease

A moderate amount of coffee intake minimizes the likelihood of coronary heart disease. Many epidemiological studies have checked the connection between coffee and coronary heart disease. According to findings, high intake of coffee raises the likelihood of coronary heart disease (CHD) and myocardial infarction (MI) (Shateri and Djafarian, 2016). According to 8 case-control studies risk of CHD is greater among those who consume 5 or more cups of coffee daily. From further case control studies, it was concluded that taking about 3-4 cups of coffee daily didn't elevate the CHD possibility. People who drink 600 ml or additional amounts of coffee each day have a 3x greater likelihood of contracting coronary heart disease than those who only consume 300 ml. Decaffeinated and moderate use of coffee seems to have nothing to do with a higher probability of CHD (Rodríguez-Artalejo & López-García, 2018). According to a recent meta-analysis of 36 study findings, intermediate coffee drinkers (3-5 cups per day) were at a 10-15% lower chance of acquiring coronary heart disease compared to individuals who don't drink coffee (Rodríguez-Artalejo & López-García, 2018)

7.4 Coffee and risk of stroke

According to various studies, patients with stroke can take moderate amounts of coffee (3 cups a day) (Liebeskind et al., 2016). Even regular coffee use isn't associated with the chances of stroke (Nakagawa-Senda et al., 2018). Risk is only lower for ischemic stroke, but not for hemorrhagic stroke. According to a study, there was a 19-20% lower chance of stroke in people who took only 1 or 2 cups of coffee each day compared to those who deliberately avoided coffee (Daneschvar et al., 2021). The risk of stroke can be increased by taking 5 or more cups of coffee each day.

The association between the danger of stroke and coffee intake has been reported in various observational epidemiological studies. A total of 91462 coffee consumers participated in the studies. High, frequent, and no consumption had no association with the chances of stroke (Qian et al., 2020). Another prospective cohort study was conducted, including 9946 subjects (3870 men and 6076 women) between the ages of 19 and 93 years from 12 different communities. During a follow-up of about 18.4 years, a total of 2024 deaths occurred, including cancer, stroke, and coronary artery disease (CHD). No discernible link associated with coffee intake and all-cause mortality was observed; persons who drank 1-2 cups of coffee daily had noticeably fewer deaths from stroke. This association turned out in men only (Sakamaki et al., 2021). In another study, 1935 patients were examined for the possible determinant of MI onset due to the intake of caffeinated coffee and found no relationship between post-MI mortality and coffee consumption.

7.5 Coffee and risk of myocardial infarction

According to the recent evidence, it was suggested that in patients who had suffered myocardial infarction (MI), the risk of all-cause mortality can be reduced by about 40-50% by consuming ≥3 cups of caffeinated, filtered coffee daily. The chances of cardiovascular disease and ischemic heart disease (IHD) mortality can be reduced in those who have already suffered a myocardial infarction (MI) by having either caffeinated or decaffeinated coffee. In a meta-analysis of prospective studies, a total of 3271 patients who already had acute myocardial infarction (AMI) were examined to determine the association of coffee consumption with the mortality rate of AMI. All 3 groups (heavy, moderate, and non-coffee drinkers) showed a remarkable reduction in risk ratio. Following AMI, the rate of mortality decreases with the regular/habitual consumption of coffee (Brown et al., 2016).

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7.6 Coffee and risk of ischemic heart disease

One longitudinal prospective study showed that coffee ingested either with or without caffeine was linked to decreased ischemic heart disease (IHD) risk. There was also around a 40% lower risk of cardiovascular disease (CVD) mortality for patients with IHD who consumed more than two cups of caffeinated coffee daily (van Dongen et al., 2017).

Table 2. Different studies related to coffee intake and ischemic heart disease

Year	Author	Study model	No of participants	Dose	Significant outcomes
2021	Kim	Prospective cohort study	30,000 participants	One additional daily cup of coffee	There is no association between an increased likelihood of cardiac arrhythmia and habitual coffee use or gene-mediated variations in caffeine conversion.
2021	Sakamaki	Cohort study	9946 participants (both men and women)	1-2 cups/day	There was no noticeable relationship found between the intake of coffee and fatality. The death rate due to stroke was remarkably lower among coffee consumers, specifically men.
2020	Said	Mendelian randomization study	407072 participants	120-180 mg/day caffeine	Despite protective associations in observational analyses, intake of caffeine might not protect against coronary artery disease.

2018	Casiglia	Prospective study	1475 unselected men and women	320 mg/day	The rate of arterial fibrillation was decreased as compared to lower levels of consumption.
2017	Lee	Prospective cohort study	146830 subjects	≥3cups/day	Higher intake can have protective benefits (38% lower risk) in middle-aged healthy women.
2017	Van	Prospective study	4365 patients with a background of myocardial infarction (MI).	375ml/day or ~3cups	The likelihood of death from CVD and IHD can be minimized by 20–30% with filtered coffee.
2016	Brown	Meta-analysis of prospective studies	3271 patients after an acute myocardial infarction (AMI).	Light coffee drinkers (1-2cups/day), Heavy coffee drinkers (>2cups/day), non-coffee drinkers.	Consistent use of coffee lessens one's chance of death after an AMI.
2015	Larsson	Prospective cohort study	4311 men and 2730 women	2 cups per day	Risk of arterial fibrillation (AF) isn't linked with coffee consumption.
2011	Wang	Prospective population-based cohort study	59,490 men and women free of HF	0, 1-2, 3-4, 5-6, 7-9, and ≥10 cups	The possibility of HF doesn't increase due to both women's and men's coffee use.
2011	Levitan	Prospective observational study	551 participants with no history of HF.	2, 3, 4, and ≥5 cups per day	There was an absence of a relationship regarding drinking coffee and the frequency of HF episodes.
2010	Conen	Randomized Controlled trial	33,638 healthy women	22, 135, 285, 402, and 656 mg/d	AF is not more likely to occur if caffeine is

					consumed in high amounts.
2009	Ahmed	Comparative study	37,315 men with no history of HF	0, 1-2, 3-4, 5 cups per day	HF hospitalization or mortality rates were increased due to the coffee intake.

8. Coffee and risk of hypertension

Caffeine intake can induce a significant rise in blood pressure (BP) as an outcome of result of drinking coffee. In contrast to nonhabitual drinkers, regular drinkers, however, build tolerance without any discernible rise in blood pressure. Therefore, it is obvious that caffeine plays a role in the BP-influencing role of coffee. Overall, clinical studies and data suggest that the chances of hypertension can be further reduced by habitual and moderate amounts of coffee intake. Aortic stiffness and, reduction in both systolic and diastolic BP can be achieved by coffee (Chieng and Kistler, 2021).

In a systematic review, the chances of hypertension seemed to be reduced with daily intake of 7 cups of coffee. While a very little reduction was seen with daily consumption of 1 cup (Grosso et al., 2017). Another systematic review revealed that coffee use is related to a dose-response inverse in hypertension (Xie et al., 2018). In another study, a total of 52 adults (26 males and 26 females) with normal blood pressure were studied, who were given caffeine to examine stress reactivity. The results showed that systolic BP and the response of cortisol to stress in both sexes were increased (Bennett et al., 2013). In a Randomized Controlled Cross-over trial, examine the coffee's impact on 15 healthy individuals. The study revealed that administration of 3.3 mg per kg body weight caffeine sodium benzoate for 2 days increased systolic and diastolic Blood Pressure and decreased heartbeat with no indication of increased cardiac output or contractility (Bazal et al., 2021). In the multicentre prospective cohort, the Brazilian Longitudinal Study also showed the effect of coffee on 15,105 individuals who were given ≤1, 1-3, and >3 cups of coffee a day. It had been found that tobacco use contributed to the link between the incidence of hypertension and coffee intake. Only non-smokers were found to benefit from adequate use of coffee (1-3 cups/day) when it comes to reducing the possibility of hypertension (Stevens et al., 2021).

Table 3. Different studies related to coffee intake and Hypertension

Year	**Author**	**Study model**	**No of subjects**	**Dose**	**Significant outcomes**
2021	Stevens	Prospective cohort study	15,105 individuals free from hypertension (smokers and non-smokers)	≤1, 1-3, and >3 cups	Only those individuals who never smoke presented the advantageous impact of adequate coffee use (1-3 cups/day) on the potential risk of hypertension

2021	Bazal	Randomized Controlled Cross-over trial	15 healthy individuals	3.3 milligrams of caffeine sodium benzoate per kg body weight for 2 days	Systolic and diastolic blood pressure rose with caffeine use, and systemic vascular resistance gradually went up as well. .
2013	Bennett	Randomized Controlled Trial	Almost 52 healthy men and women, along with a family history of hypertension	3.3Mg/kg of anhydrous Caffeine Single dose	Both genders showed a distinct extra rise in systolic blood pressure as well as a cortisol response to the stress.

9. Coffee and type 2 diabetes mellitus

All recent systematic reviews concluded that there exists a probable association between coffee consumption and reduced chances of type 2 diabetes. Daily 3-4 cups of coffee appear to be linked with almost 25% reduced likelihood of acquiring type 2 diabetes. Coffee drinking was found to have an inverse relationship with type 2 diabetes, both in men and women. According to the findings, both caffeinated and decaffeinated coffee are connected to a reduced likelihood of type 2 diabetes, with caffeinated coffee exhibiting a slightly higher risk reduction (Carlström and Larsson, 2018). Meta-analysis suggested an almost 30% reduction in the risk of developing type 2 diabetes. Contrasting both the smallest and most prevalent categories of coffee consumption, which had a median of 5 cups each day, suggested 30% reduced chances of type 2 diabetes (Mirmiran et al., 2018). The underlying mechanisms contributing to these health benefits are likely multifactorial, but it is believed that there are mainly six mechanisms that are involved. The first one is effects on thermogenesis, so effects on mitochondria and energy expenditure. Secondly, its antioxidative effects. The third is the modulation of the immune system and antioxidative effects, and the modulation of the microbiota by modulating the bacteria in the gastrointestinal channel. And the last one would be modulation of adenosine receptor signaling by caffeine. Increased coffee consumption can lower the incidence, or prevalence, of recently identified type 2 diabetes (Yarmolinsky et al., 2015). Changes in coffee consumption are linked to changes in diabetes risk over time. Instead of boosting acute metabolic regulation, long-term effects of habitual coffee use emerge to preserve healthy liver and beta cell function (Kolb et al., 2021).

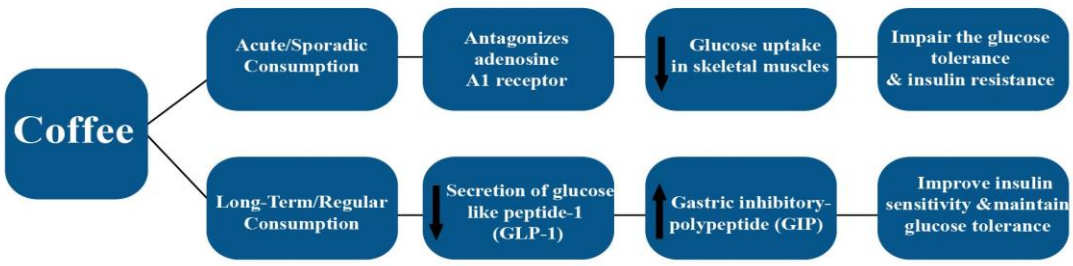

Figure 4. Effects of acute and long-term coffee consumption on (T2DM) type 2 diabetes mellitus

Coffee has complicated impacts on glucose homeostasis. Caffeine reduces insulin sensitivity, which contributes to the release of adrenaline (Carlström & Larsson, 2018). Adenosine A1 receptor antagonistic activity triggered by acute coffee consumption might decrease glucose absorption in skeletal muscle. Taking coffee limits intestinal glucose absorption by increasing the production of glucagon-like peptide-1 and suppressing the secretion of gastric inhibitory polypeptide. Coffee polyphenols offer immense anti-inflammatory and antioxidant impacts on insulin sensitivity and the breakdown of glucose (Naveed et al., 2018).

In patients with type 2 diabetes, daily 4 or more cups of caffeinated coffee didn't raise the risk of cardiovascular disease (CVD) or mortality (Carlström & Larsson, 2018). Even though the elderly patients (>60) with pre-existing type 2 diabetes also presented improvement in fasting blood glucose with the intake of more than 3 cups of coffee daily (Ghavami et al., 2021). A systematic review reported that acute caffeine ingestion has generally been reported to adversely affect glucose tolerance, but more prolonged interventions (2-16 weeks), caffeinated coffee frequently has positive effects on glycemic metabolism, lowering glucose response curves and increasing insulin secretion (Reis et al., 2019).

Table 4. Different studies related to coffee intake and Diabetes Mellitus

Year	Author	Study model	No. Of participants	Dose	Significant outcomes
2020	Said	Mendelian randomization approach	407072 participants	300-360mg/day	There is no relationship between the use of caffeine and the prevalence of type 2 diabetes mellitus (T2DM).
2012	Ohnaka	Randomized Controlled trial	45 overweight individuals	5 cups of caffeinated or decaffeinated coffee daily, or 5 cups each day of instant coffee or none.	Both caffeinated and decaffeinated coffee may hinder the decline of glucose tolerance..
2009		Prospective cohort study	3,497 diabetic men	Maximum of four or fewer cups of coffee containing caffeine per day	There is no causal association between regular use of coffee and a higher mortality rate in diabetic males.

2007	Thomas	Randomized Controlled trial	12 healthy individuals and overweight individuals	Fortified coffee Instant coffee	Fortified coffee intake causes a 6.9% reduction in glucose absorption as compared to instant coffee.
2005	Bidel	Finnish study	4000 people with T2D	About 3 or more cups of coffee per day	Indicated reduced probability of (CVD) Cardiovascular disease mortality in people with T2D consuming 3 or more cups daily.
2002	Van	Epidemiological study	17000 men and women	7 or more cups/day	T2D risk is reduced by 50% compared to people who take at least 2 or fewer cups of coffee each day.

10. Conclusion

Consuming coffee in modest amounts (3-4 cups daily) is usually harmless and can result in fewer cases of cardiovascular diseases, stroke, heart failure, and type 2 diabetes. Caffeine and chlorogenic acid are seen as being primarily responsible in terms of these benefits. Unfiltered coffee is unhealthy since diterpene cafestol increases the LDL cholesterol, but filtered coffee has no effect on the increase of LDL cholesterol in the body. Despite caffeine having the potential of raising blood pressure, the other ingredients in coffee, such as magnesium and vitamin B3, counteract this reaction. The risk of stroke can be reduced, and weight gain can be prevented by switching to unsweetened coffee instead of sweetened beverages. Finally, coffee may also be a healthy habit in a balanced amount without loads of cream or sugary dressing. In future studies, one should study the long-term effects of various brewing techniques and the impacts of coffee bioactive compounds in the prevention of diseases.

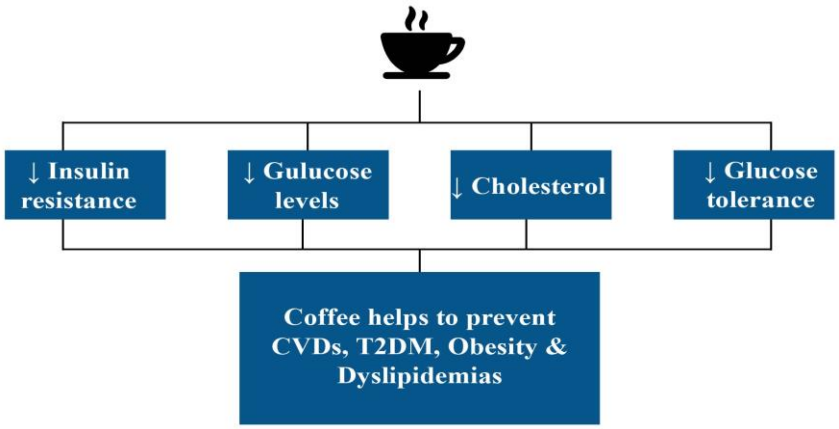

Figure 5: Health benefits of coffee.

Authors' contribution

Nasir Hussain and Hooria Ahmed conceptualized and wrote the manuscript, and other authors drafted and revised the manuscript.

Ethics approval and consent to participate

Not applicable.

Competing Interest

The authors declared no conflict of interest.

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