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THE IMPACT OF COFFEE ON THE INITIATION AND PROGRESSION OF VARIOUS DISEASES

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ABSTRACT

Introduction: Coffee is one of the most widely consumed beverages globally and contains numerous biologically active compounds, including caffeine, chlorogenic acids, diterpenes, and polyphenols. These constituents have been extensively studied for their potential effects on human health.

Objective: This review aims to synthesize current scientific evidence regarding the impact of coffee consumption on the development and progression of various chronic diseases, including metabolic, cardiovascular, gastrointestinal, neurological, and hepatic disorders.

Methods: A narrative literature review was conducted using peer-reviewed publications sourced from databases such as PubMed and Google Scholar. Priority was given to large cohort studies, meta-analyses, and recent mechanistic research that explored the effects of both caffeinated and decaffeinated coffee.

Results: Moderate coffee consumption is associated with a reduced risk of several chronic conditions. Epidemiological data suggest inverse associations with type 2 diabetes mellitus, Parkinson's disease, non-alcoholic fatty liver disease (NAFLD), and certain types of cancer, particularly colorectal and liver cancers. Additionally, coffee may offer neuroprotective effects and contribute to improved liver enzyme profiles. However, results regarding cardiovascular health remain mixed, with some studies indicating potential adverse effects depending on preparation methods and individual sensitivity to caffeine.

Conclusion: Coffee consumption—particularly when filtered and consumed in moderation—may provide protective effects against a range of chronic diseases. Nevertheless, individual factors such as genetics, comorbidities, and preparation methods should be taken into account. Further randomized controlled trials are necessary to establish causality and clarify optimal consumption levels for health benefits.

Keywords: Coffee, caffeine, cardiovascular disease, diabetes, inflammation, cancer, coronary heart disease, neurotransmitter, stroke

INTRODUCTION

Coffee is considered as one of the most popular beverages in the world. Americans and Europeans are estimated to consume a similar amount of coffee, approximately 5.1 kg per person per year. It's worth mentioning that individual responses to coffee can vary, and factors such as genetics, overall diet, and lifestyle also play roles in health outcomes. As with any health-related guidance, it's advisable to consult with healthcare professionals for personalized advice, taking into account individual health conditions and circumstances [1, 2].

Coffee and its consumption is an interesting and extensively researched topic among scientists. The action of its individual ingredients affects many processes in our body. The article focuses on the impact on the incidence of colorectal cancer, type 2 diabetes and cardiovascular diseases. Many studies show that drinking moderate amounts of coffee has a positive effect on health. However, we should take into account the amount of coffee consumed, the type of filtering, as well as factors such as age, general health and smoking.

AIMS

The aim of the review was to collect information and emphasize the importance of coffee consumption in relation to the functioning of the body. It should be remembered that many diseases are influenced by the consumption of caffeine and other stimulants. Therefore, it is important to educate the patient and expand his awareness.

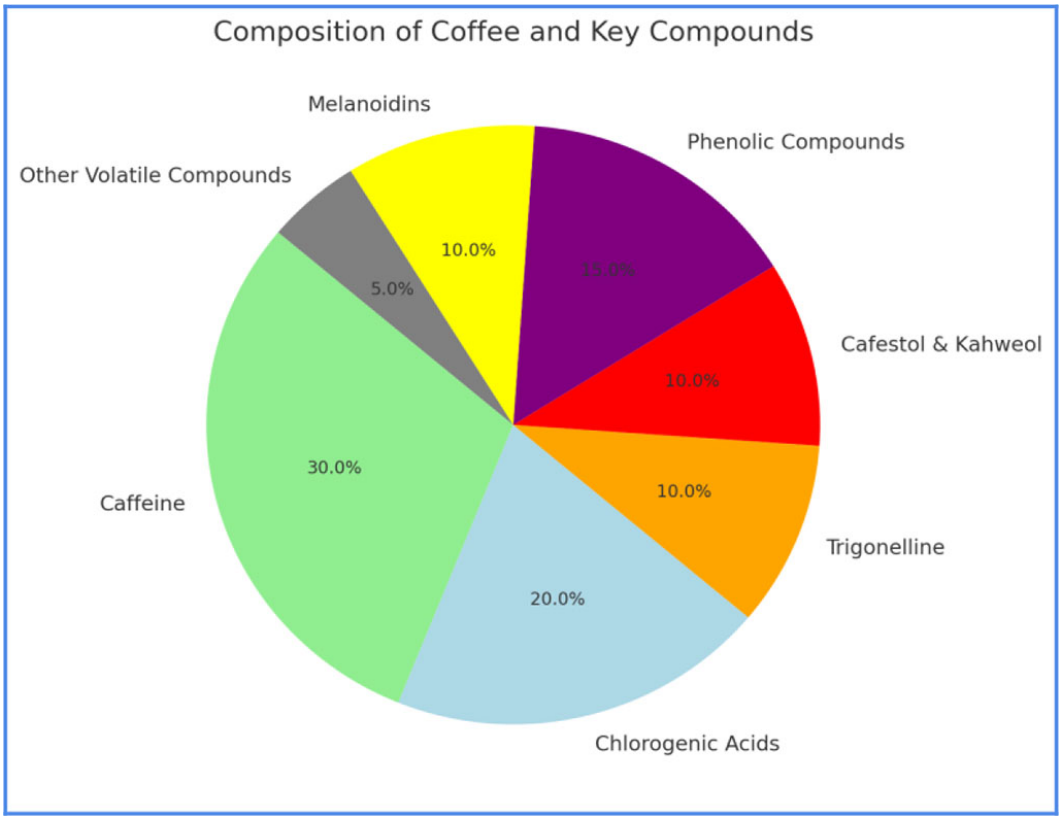
MATERIALS AND METHODS

We have analyzed articles on PubMed and specialized books in detail. The aim of this study is to analyze the impact of coffee consumption on the risk of developing and the progression of selected diseases, including metabolic, neurological, and oncological conditions. The review seeks to present current update on both the positive and potentially negative effects of regular coffee consumption in the context of health.

Specifically, the review will examine the mechanisms of action of bioactive coffee components, such as caffeine, polyphenols, and diterpenes, in relation to their role in the prevention and development of diseases such as type 2 diabetes, cardiovascular diseases, liver cancer, neurodegenerative diseases and liver disorders. We aimed to answer the question of whether and to what extent coffee consumption can be a component of disease prevention, as well as whether there are specific groups of individuals for whom excessive coffee consumption may have negative health consequences.

MECHANISM OF ACTION OF COFFEE INGREDIENTS

Coffee consists mainly of water and coffee beans. The beans are the seeds of the Coffee plant that are roasted and ground to prepare the drink. The taste, aroma and strength of coffee are influenced by various compounds such as caffeine, oils, acids and sugars present in the beans. A wide range of coffee brewing methods cause these ingredients to be extracted in different ways, which affects the final taste of the coffee [3]. Coffee beans contain the basic substance, caffeine, which has the greatest impact on the human body among all the components. During roasting, the beans undergo chemical changes, resulting in the formation of various compounds, such as melanoidins, phenolic acids (chlorogenic, quinic, citric acid), trigonelline, diterpenes (cafestol and kahweol) and volatile compounds responsible for the characteristic aroma and taste of coffee. The exact composition may vary depending on the type of coffee beans, roasting process and brewing method used [3, 4].



Fig,1. Composition of Coffee and its Key Compmounds

The caffeine contained in coffee is absorbed into the bloodstream in the stomach and small intestine within 30-45 minutes, and its half-life is on average 3 hours. Nicotine reduces its half-life by 30-50%. Caffeine easily crosses the blood-brain barrier, where it stimulates the nervous system [3, 4]. The sympathomimetic effect of caffeine consists in inhibiting phosphodiesterase, increasing the activity of catecholamines and cytosolic calcium concentration. The adenosine receptor is the target receptor for caffeine. This is due to the similarity of the structure of the molecules. Adenosine acts as an inhibitory neurotransmitter in the central nervous system. Caffeine is a non-selective adenosine antagonist, which stimulates the brain by having a stimulating effect. In the CNS, the main subtypes of adenosine receptors are A1 and A2a. Stimulation of A2a receptors by caffeine is associated with an increase in cAMP in the cell and leads to dilation of blood vessels [4, 5].

A2a receptors are located, among others, in the nucleus accumbens, and caffeine blocks their action. The basic dose of caffeine consumed by an adult, calculated as 2 cups of coffee, does not cause the release of dopamine in the nucleus accumbens, only in the prefrontal cortex, which is responsible for the increase in activity [5]. In addition, caffeine increases the sense of energy and concentration, reduces the feeling of fatigue, accelerates the reaction rate and improves motor coordination [3]. Caffeine metabolism takes place in the liver, where it is biotransformed via the cytochrome P450 1A2 enzyme into three main metabolites: paraxanthine, theobromine and theophylline. These metabolites also have stimulant effects, although to a much lesser extent than caffeine itself. The effects of caffeine, including its stimulating properties, may last for several hours, depending on individual sensitivity and metabolism [3]. Chlorogenic acid refers to a group of hydroxycinnamic esters combined with quinic acid. During the coffee brewing process, most of it is broken down and absorbed into the bloodstream. Chlorogenic acid has antioxidant, anti-inflammatory and anticarcinogenic properties [4].

Trigonelline is a derivative of niacin, and its average content in coffee is 50 mg/100 ml. It may have antidiabetic properties, which is related to its effect on lipid metabolism. As of today, this component of coffee beans is still being researched for its effects on the body. Cofestol is a coffee diterpene. A large dose of this substance causes an increase in cholesterol levels in the blood. Cofestol is an agonist of farnesoid X receptors, which is responsible for inhibiting the synthesis of bile acids, causing an increase in cholesterol levels [4].

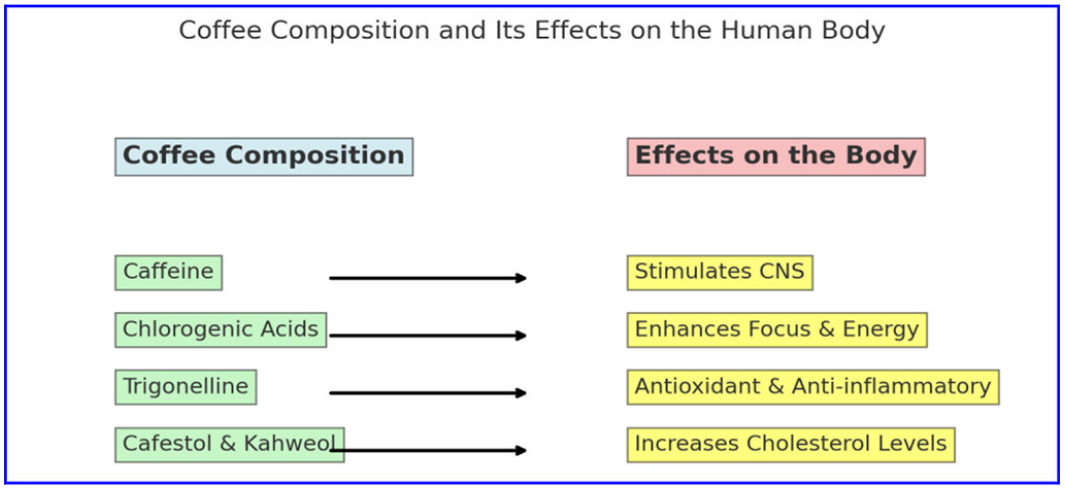


Fig. 2. Coffee Composition and its Effect on the Human Body

In addition to the positive aspects of drinking coffee, it is worth remembering about possible complications. The impact of individual coffee ingredients on the body depends on factors such as tolerance, sensitivity, metabolism and general health. In some people, excessive coffee consumption can cause side effects such as increased heart rate, digestive problems, insomnia and more.

Now we examine the role of the coffee consumption in the prevention and development of diseases such as type 2 diabetes, cardiovascular diseases, neurodegenerative diseases and liver disorders.

THE EFFECT OF COFFEE CONSUMPTION ON COLORECTAL CANCER

The results of some analyses demonstrate that coffee consumption leads to a reduction in the frequency of diagnosing colorectal cancer and susceptibility to this disease.

It is worth mentioning a meta-analysis that examined the results of twelve case-control studies and five cohort studies. This analysis proved that drinking four cups of coffee daily reduces the susceptibility to colorectal cancer by 24% compared to non-coffee drinkers [1]. There were also studies conducted indicating a reduction in the number of illnesses among patients consuming decaffeinated coffee [2].

The Cancer Prevention Study-II Nutrition Cohort involved 107,000 participants, including 47,000 men and 60,000 women. This study did not show an impact of coffee consumption on the occurrence of colon cancer. However, an increase in the risk of cancer in the distal part of the large intestine and rectum was observed. The same study demonstrated a reduced incidence of cancer in all segments of the colon among patients consuming decaffeinated coffee [5].

Recently, two studies were conducted, the results of which indicated no influence of coffee on the susceptibility to colorectal cancer [8, 9]. As seen, numerous studies present conflicting results.

Scientists have proven that patients regularly consuming coffee and suffering from colorectal cancer exhibit lower mortality, slower disease progression, and a reduced progression of changes [6, 7].

Currently, the mechanisms responsible for a potential reduction in the incidence of colorectal cancer in patients consuming coffee are not known. One hypothesis suggests that coffee may decrease the production and secretion of bile acids, which could be involved in the development of this cancer. Many studies have been conducted on this hypothesis, and not all confirm this theory. In one analysis, the concentration of bile acids in the stools of patients who drank a liter of coffee per day for two weeks was examined, and no decrease in bile acid concentration was observed [3].

Another hypothesis is that coffee consumption may increase gastrointestinal motility, resulting in less exposure to bile acids present in feces and a lower risk of cancer development [4].

The association between coffee consumption and a reduced susceptibility to colorectal cancer is still unclear, thus requiring further research. Numerous studies with contradictory results underscore that this topic is still unresolved and continues to be of interest among scientists

THE EFFECT OF COFFEE CONSUMPTION ON TYPE 2 DIABETES

In prospective studies, it has been demonstrated that each cup of coffee consumed per day is associated with a 7% reduction in the risk of type 2 diabetes [14]. Daily consumption of coffee reduces the risk of developing type 2 diabetes by 11% compared to individuals who do not drink coffee regularly [15].

Consuming six cups of coffee daily is linked to a 33% decreased risk of developing type 2 diabetes compared to abstaining from coffee, regardless of gender. Ding et al. demonstrated that consuming decaffeinated coffee provides the same level of protection as coffee containing caffeine [16].

In another study, individuals who habitually drank 5–8 cups of coffee per day were randomly allocated to consume one liter of filtered coffee daily, containing 1100 mg of caffeine, for a 4-week period. They were also assigned a 4-week period during which they abstained from coffee consumption. During the period of coffee consumption, there was an increase in serum insulin levels, while fasting glucose levels remained unchanged compared to the period of no coffee consumption [17].

The biological mechanisms of the positive impact on type 2 diabetes are not yet clear.

A cohort study involving two groups of women identified 34 coffee metabolites, with 12 associated with negative effects and 3 with positive effects. Trigonelline has been associated with a reduced risk of developing type 2 diabetes [18].

Coffee has been proven to lead to increased insulin reactivity and improved insulin sensitivity. It appears that coffee primarily affects postprandial glucose homeostasis [19].

The protective effect of decaffeinated coffee suggests the protective action of other components besides caffeine, such as polyphenols. In mice, chlorogenic acid was observed to inhibit gluconeogenesis by influencing the expression and function of glucose-6-phosphatase.

Additionally, it improved glucose uptake by skeletal muscles through increased expression and translocation of GLUT 4 [20]. Another metabolite, polyphenol - 4-hydroxybutanoic acid, showed no association with diabetes in humans [18]. Further studies on humans are needed to explore the effect of polyphenols on the risk of developing diabetes.

Polyphenols present in coffee stimulate the GLP-1 hormone, which in response to glucose, activates secretion of the insulin from pancreatic beta cells [21].

An elevated level of triglycerides coupled with a decreased level of HDL cholesterol is linked to a higher risk of diabetes. A clinical study demonstrated that consuming 4-8 cups of coffee per day for a duration of 3 months resulted in an elevation of HDL levels. Therefore, it is possible that coffee lowers the risk of type 2 diabetes by raising HDL levels [18].

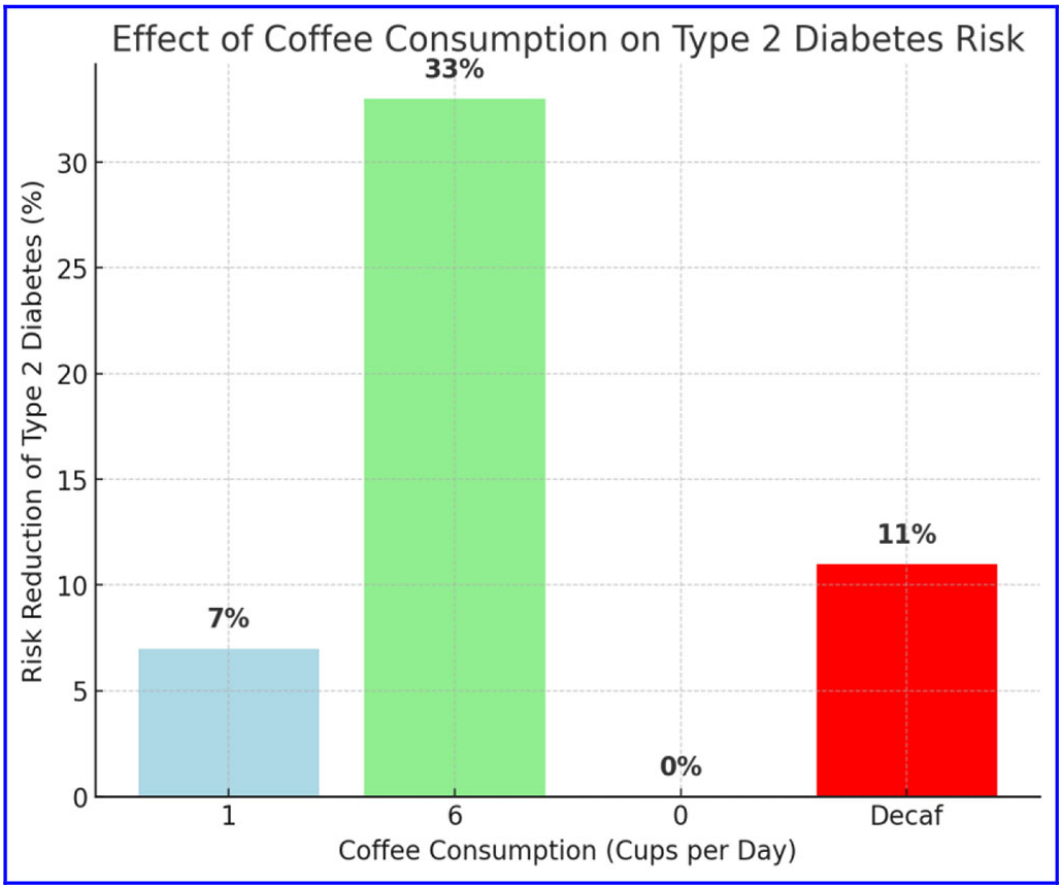


Fig.3. Effect of Coffee Consumption on Type 2 Diabetes Risk

Research indicates a beneficial effect of coffee on type 2 diabetes; nevertheless, further comprehensive,

long-term studies are required to validate its positive effects.

IMPACT OF COFFEE CONSUMPTION ON CARDIOVASCULAR SYSTEM

The connection between coffee consumption and cardiovascular disease is a topic that has garnered significant attention in research over the years. There is a complexity in understanding how coffee may impact cardiovascular health. Here are some general points based on existing research [2]:

Blood Pressure

The impact of coffee on blood pressure has been a subject of debate. Older studies, like Jee et al (1999) and Jenner et al (1988), suggested a positive association between coffee consumption and blood pressure [2]. However, Miranda et al (2021), have reported a potential protective effect, especially in non-smokers [22].

The randomized study by Revuelta-Iniesta and Al-Dujaili (2014) suggested a potential benefit of green coffee in reducing systolic blood pressure [2].

Randomized Controlled Trials (RCTs) have shown that coffee intake around 5 cups per day causes a small increase in blood pressure, when compared to use of decaffeinated coffee or coffee abstinence. While much research has focused on the blood pressure-raising effects of caffeine, there are other substances in coffee, such as polyphenols, soluble fiber, and potassium. These factors can potentially exert beneficial effects on the cardiovascular system [23].

Coronary Heart Disease

Research on coffee consumption and coronary heart disease show inconsistent results. Moderate caffeine intake may be linked to a decreased risk, while heavy consumption could be associated with an increased risk. This variability may be due to factors such as the study population, duration of follow-up, and individual differences [2].

Heart failure

The European Society of Cardiology (2020) study, involving 2,735 participants, indicated that low and moderate coffee consumption was associated with better left ventricular systolic and diastolic function. This relationship was observed in the early adulthood to middle-aged group. Understanding the potential mechanisms is crucial for providing insights into why coffee consumption might be associated with a decreased risk of heart failure. This involves exploring the impact of specific compounds in coffee on cardiovascular health and considering individual differences in responses [2].

Atrial fibrillation

There is a theory that high levels of antioxidants such as cafestol, polyphenol, trigonelline, chlorogenic acid, and quinine in coffee, leads to reduce risk of atrial fibrillation.

Antioxidants are suggested to promote anti-inflammatory processes, which may contribute to the observed protective effects.

According to Bodar et al (2019) adjusting for age, smoking status, alcohol consumption, and physical activity, those who drank 1 to 3 cups per day had a lower risk compared to other intake frequencies.

According to Cheng et al (2014) Meta-Analysis showed that coffee drinking was associated with a lower risk of atrial fibrillation.

Low coffee consumption (<500 mg of caffeine per day) was associated with an 11% reduction, and high coffee consumption (≥500 mg of caffeine per day) was associated with a 16% reduction [2].

IMPACT OF COFFEE PREPARATION ON CHOLESTEROL LEVELS

The manner of coffee preparation, specifically boiled versus filtered, is proposed to have a significant influence on cholesterol levels. This reinforces the idea that the method of preparing coffee may be a factor to consider in understanding its health effects [2].

For example consumption of 2 cups a day Italian-style coffee is associated with increased coronary heart disease (CHD) risk. Notably, this association is mentioned to be unrelated to changes in plasma lipid profile [24].

ATHEROGENIC PROPERTIES OF BOILED OR UNFILTERED COFFEE

Boiled or unfiltered coffee is suggested to be more atherogenic due to its rich diterpene content. Diterpenes may inhibit bile acid synthesis, potentially affecting lipid metabolism and contributing to atherosclerosis [2].

FILTERED COFFEE AND ANTIATHEROGENIC PROPERTIES OF FILTERED COFFEE

Filtered coffee, which lacks certain compounds found in boiled or unfiltered coffee, is suggested to have antiatherogenic properties. It may increase high-density lipoprotein (HDL)-mediated cholesterol efflux from macrophages, potentially benefiting cardiovascular health [2].

It's worth mentioning that individual responses to coffee can vary, and factors such as genetics, overall diet, and lifestyle also play roles in health outcomes.

Moderate coffee consumption is associated with positive outcomes in various aspects of health, including a decrease in all-cause and cardiovascular-related mortality, as well as benefits related to hypertension, cholesterol levels, heart failure, and atrial fibrillation.

However, it also indicates that there's no consistent or conclusive relationship between coffee consumption and the risk of coronary heart disease [2, 23].

THE ROLE OF CAFFEINE IN PARKINSON'S DISEASE

Parkinson's disease (PD) is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons in the substantia nigra, leading to motor symptoms such as bradykinesia, muscle rigidity, and resting tremors. Over the past decades, numerous epidemiological and experimental studies have suggested a potential impact of caffeine, the primary alkaloid found in coffee, on both the risk and progression of Parkinson's disease.

Many epidemiological studies indicate an inverse relationship between caffeine consumption and the risk of developing PD. For example, a meta-analysis conducted by Costa et al. (2010) found that individuals who regularly consumed caffeine had a 25% lower risk of developing Parkinson's disease compared to those who did not consume caffeine [25]. The protective mechanism may be related to the antagonistic effect of caffeine on A2A adenosine receptors, which modulate dopaminergic system function. Blocking these receptors with caffeine may enhance dopaminergic activity, potentially protecting neurons from degeneration [26].

Clinical studies suggest that caffeine may influence motor symptoms in PD patients. A randomized controlled trial conducted by Postuma et al. (2012) showed that administering 200 mg of caffeine twice daily for six weeks resulted in moderate improvement in motor symptoms compared to placebo. This mechanism may be associated with caffeine's modulation of the dopaminergic system, leading to enhanced motor function [27].

Beyond its effects on motor symptoms, caffeine may also impact non-motor symptoms of Parkinson's disease. Studies indicate that caffeine consumption can improve alertness and reduce excessive daytime sleepiness, a common issue among PD patients [28]. Additionally, caffeine may have a beneficial effect on cognitive functions, although the evidence in this area is less conclusive and requires further research.

Caffeine may also influence the effectiveness of pharmacological treatment for Parkinson's disease. Animal model studies suggest that caffeine can enhance the effects of levodopa, the primary medication used in PD therapy, through a synergistic action on dopaminergic receptors [29]. However, in some patients, caffeine may exacerbate levodopa-related side effects, such as dyskinesias, highlighting the need for individualized treatment approaches.

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide, often associated with obesity, type 2 diabetes, and metabolic syndrome. It is characterized by excessive fat accumulation in hepatocytes, which can lead to inflammation, fibrosis, and, consequently, liver cirrhosis and hepatocellular carcinoma (HCC). In recent years, numerous studies have suggested that regular coffee consumption may have a beneficial impact on the course and progression of NAFLD [30].

Epidemiological studies indicate an inverse relationship between coffee consumption and the risk of developing NAFLD. A meta-analysis including five studies with 355 participants found that individuals who consumed coffee had a significantly lower risk of developing NAFLD compared to non-coffee drinkers (relative risk [RR] 0.71; 95% confidence interval [CI], 0.60–0.85). Additionally, regular coffee consumption was associated with a 30% reduction in the risk of liver fibrosis in patients with NAFLD (RR 0.70; 95% CI, 0.60–0.82) [30].

The mechanisms through which coffee may protect against NAFLD are complex and multifaceted. Caffeine, the main component of coffee, may enhance fatty acid oxidation and inhibit lipid accumulation in hepatocytes. Furthermore, polyphenols present in coffee, such as chlorogenic acid, exhibit strong anti-inflammatory and antioxidant properties, which can help reduce oxidative stress and inflammation in the liver.

HEPATOCELLULAR CARCINOMA (HCC)

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors worldwide, with chronic liver diseases such as cirrhosis and infections with HBV and HCV being its main risk factors. Numerous epidemiological studies indicate a protective effect of coffee consumption on the risk of developing HCC [31].

A meta-analysis of 16 studies involving 3,153 cases of HCC found that coffee consumption was associated with a 40% reduction in the risk of HCC compared to no coffee consumption (RR 0.60; 95% CI, 0.50–0.71). Moreover, a dose-response analysis showed that each additional cup of coffee consumed per day was linked to a 20% reduction in HCC risk (RR 0.80; 95% CI, 0.77–0.84) [32, 31].

The mechanisms through which coffee may protect against HCC development include its anti-inflammatory and antioxidant properties as well as the inhibition of cancer cell proliferation. Caffeine and other bioactive compounds in coffee may suppress carcinogenesis processes in the liver, contributing to a lower risk of HCC [31].

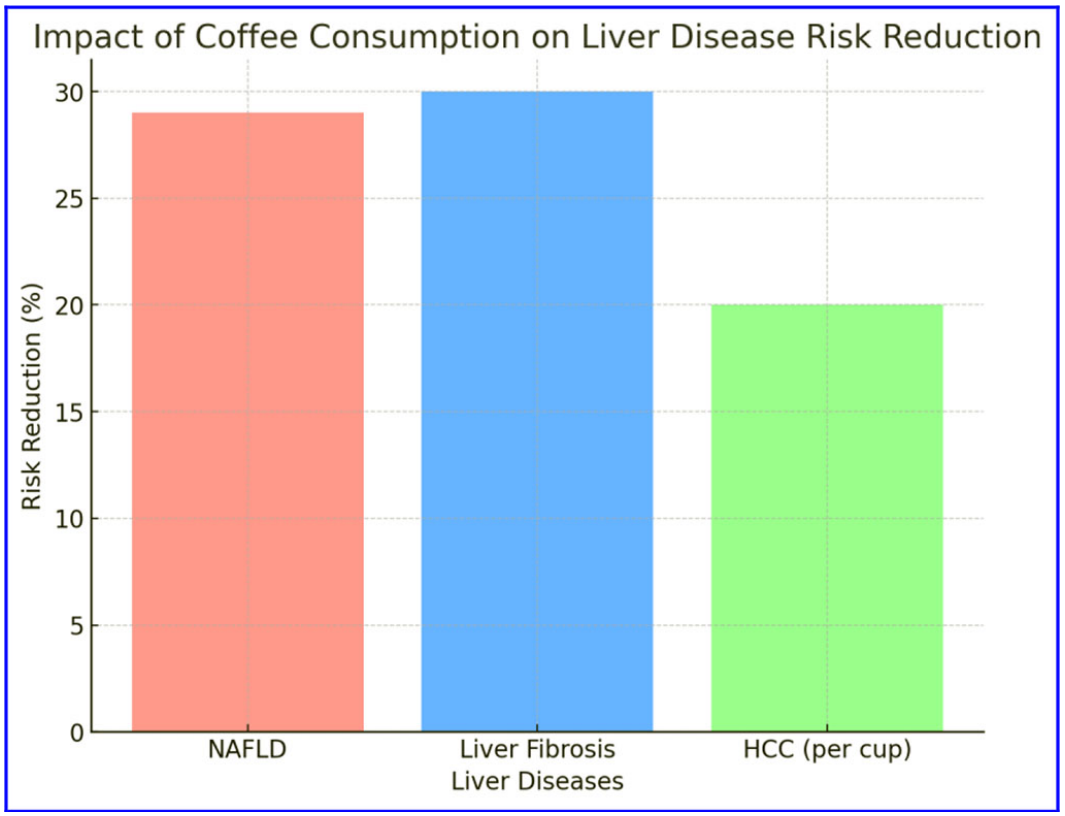


Fig.4. Impact of Coffee Consumption on Liver Disease Risk Reduction

DISCUSSION

The findings presented in this review confirm the multifaceted influence of coffee and its bioactive compounds on various physiological systems and disease processes. As a widely consumed beverage, coffee exerts effects that are both potentially beneficial and, in certain contexts, adverse—depending on the population studied, the amount and type of coffee consumed, and individual susceptibility [1, 3].

One of the most consistently observed benefits of coffee consumption is its inverse association with the risk of type 2 diabetes mellitus. Numerous cohort studies have shown that both caffeinated and decaffeinated coffee reduce diabetes risk [14, 15, 16]. The mechanisms likely involve chlorogenic acid and other polyphenols improving insulin sensitivity and modulating hepatic glucose production [20, 18].

In colorectal cancer, the majority of epidemiological studies suggest a protective effect of moderate coffee consumption [6, 9, 10]. However, some results are inconsistent, and factors like coffee type (filtered vs. unfiltered) and genetic variation may play a role [12,13]. Bioactive compounds in coffee may modulate bile acid metabolism, reduce oxidative stress, and accelerate gut motility [8].

Cardiovascular effects are more nuanced. While moderate intake has been linked with lower risk of atrial fibrillation and hypertension [2, 22], excessive consumption or unfiltered coffee may increase LDL cholesterol due to diterpenes such as cafestol [24]. Individual differences in caffeine metabolism further

complicate the picture [23].

Regarding neurological health, many studies have demonstrated that caffeine's antagonism of adenosine A2A receptors may have neuroprotective effects in Parkinson's disease [26,25,27]. Observational studies support an inverse association between coffee intake and PD risk, but clinical trials show mixed results depending on dose and patient profile [29,28].

In hepatology, coffee consumption is associated with lower risk of non-alcoholic fatty liver disease (NAFLD) and hepatocellular carcinoma (HCC) [30,32]. Proposed mechanisms include reduced inflammation, slowed fibrogenesis, and improved lipid metabolism [19].

Despite promising evidence, limitations include reliance on self-reported intake, variability in brewing methods, and confounding dietary/lifestyle factors [1, 7]. Most studies are observational, limiting causal inferences.

In summary, moderate coffee consumption appears safe and potentially protective for most people. However, clinical recommendations must be individualized, especially for pregnant women, hypertensive individuals, and those sensitive to caffeine. Future studies should focus on randomized controlled trials and personalized approaches to coffee's role in disease prevention and management. [7].

CONCLUSION

Coffee is a complex beverage with multiple bioactive compounds, including caffeine, chlorogenic acid, trigonelline, and diterpenes, each contributing to its physiological effects. Evidence suggests that regular coffee consumption may reduce the risk of colorectal cancer and type 2 diabetes through mechanisms such as modulation of bile acid production, improved insulin sensitivity, and antioxidant activity. Additionally, coffee has shown potential protective effects against non-alcoholic fatty liver disease (NAFLD) and hepatocellular carcinoma (HCC).

However, its impact on cardiovascular health remains inconclusive, with studies reporting both beneficial and adverse outcomes depending on individual differences, genetic predispositions, and brewing methods. While coffee appears to offer several health benefits, further large-scale and long-term studies, particularly randomized controlled trials (RCTs), are necessary to fully understand its role in disease prevention and overall health.

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