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Exploring the Health Benefits of Coffee Bioactive Components and Their Mechanisms

Wenyu Chen

Haidian Foreign Language School, Beijing, China
b10731011@office365.npust.edu.tw

Abstract: Coffee is a beverage that contains a variety of bioactive compounds such as caffeine, chlorogenic acid, and diterpenes that have potential benefits to human health. Due to the severe neurodegenerative diseases (NDDs) and cancer, exploring new aspects of these disease's treatment like coffee's health benefits is necessary. Recent studies have shown that coffee consumption is associated with reduced risks of stroke, type 2 diabetes, and certain cancers. However, the mechanisms and interactions of these bioactive compounds are not unclear. So this study reviews the extraction methods of caffeine, chlorogenic acid, and diterpenes and their health effects. Also, this paper analyzes the antioxidant, anticancer, and neuroprotective properties of coffee with specific examples like the risk of stroke, diabetes, and several NDDs. As a result, the paper provides valuable information on the health benefits of coffee and offers support for dietary recommendations, hoping future studies could focus on exploring the long-term health impacts of coffee consumption in different populations with more specific categories.

Keywords: Coffee, Component, Health.

1. Introduction

Coffee is a widely consumed beverage around the world. Coffee's function effect on human health has long been a popular topic. Currently, because of consumers' cognition improvement in coffee's potential benefits, the global coffee market gradually expanded. As more and more researchers exploration of coffee's chemical components, coffee's potential benefits are becoming more apparent. Coffee contains a variety of bioactive ingredients, such as caffeine, chlorogenic acid, and diterpenoids. These components are considered to have a positive impact on human health by producing antioxidant effect, anti-inflammatory effects. They could even function with other mechanisms to benefit human health. This is because the complex interaction between these bioactive compounds can further enhance coffee's health-promoting properties.

With the dramatic increase in the global aging population, the incidence of neurodegenerative diseases (NDDs), such as Alzheimer's and Parkinson's disease (AD and PD), and cancer is continuously rising, which brings a heavy burden on societies and economies [1, 2]. Hence, discovering the potential health benefits of coffee's components possesses essential public health significance.

Besides, clarifying the interaction between coffee intake and the risk of epidemic diseases can also provide scientific dietary advice for the public and new ideas for the prevention and treatment of related diseases. For example, from an antioxidant perspective, a meta-analysis conducted up to 2011

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showed a weekly negative association between coffee and stroke risk. Moderate coffee consumption that is 1-6 cups per day occurs to have a significant negative association with stroke. Consuming 3-4 cups of coffee per day can reduce the risk of stroke by about 17% [3]. In addition, the result from a review [4] which analyzed nine cohort studies supports the hypothesis that consuming coffee chronically could reduce the risk of type 2 diabetes (T2DM). Also, the most interesting thing from a meta-analysis which evaluated 18 studies' information has shown that the risk of diabetes will decrease by about 7% per extra cup of coffee [5]. From an anti-inflammatory aspect, research has shown that coffee intake is associated with the reduction of hepatocellular carcinoma (HCC). There are a variety of bioactive ingredients (like caffeine, chlorogenic acid, etc.) that can reduce the risk of HCC by reducing oxidative stress, inhibiting adipogenesis, and other mechanisms [6]. For neurodegenerative diseases (NDDs), a study revealed that caffeine consumption could offset the genetic risk of PD in people at high risk of carrying mutation in the LRRK2 gene [7]. Besides, another study on mice concluded that coffee could be used for prevention and treatment of AD, because it contains ingredients that can work with caffeine to increase the plasma G-CSF levels, benefiting mice with AD [8].

In this paper, the focus will be on the potential role of coffee in antioxidant properties, anti-cancer effects, and defense against NDDs to analyze the bioactive components of coffee and their mechanisms on human health.

2. Analysis of component

2.1. Caffeine

The chemical name of caffeine (CAF) is 1,3,7-trimethylxanthine. It is a type of natural alkaloid. Caffeine is mainly contained in coffee beans, tea leaves, and cocoa beans. Besides, it is also found in other 60 or so types of plants [9]. The molecular form of caffeine is $C_8H_{10}N_4O_2$, and its molecular weight is 194.19g/mol. There are many different types of methods to extract caffeine from plants. In addition to traditional methods like solvent extraction, recently, there are some new methods can be used for extraction, such as ultrasonic assisted extraction, and ionic liquid extraction [10]. Solvent extraction of caffeine need to ground the coffee beans first. And then add water and sodium carbonate into it to heat and boil, to dissolve the caffeine and neutralize the tannic acid. Next, the residue will be filtered and get an aqueous solution. The aqueous solution then will be extracted with methylene chloride several times, followed by the separation and drying of the organic phase. After the solvent is evaporated, purified the crude caffeine by ethanol recrystallization can finally get a pure caffeine crystals [11]. The extraction rate of caffeine that uses methylene chloride as a solvent can reach 94-96% [10].

Caffeine will not harm human health if people consume it at levels of 200 mg or 400 mg daily. Consuming coffee/caffeine long-term can prevent cognitive decline and decrease the possibility of stroke, Parkinson's disease (PD), and Alzheimer's disease (AD). However, caffeine may disturb sleep by prolonging sleep latency, decreasing total sleep time, and decreasing the deep sleep phase while increasing the light sleep phase.

2.2. Chlorogenic acid

Chlorogenic acid is a phenolic acid compound that is widely found in many plants. It has many biological activities, like antioxidant, and antibacterial, and decreases blood pressure and lipids [12]. The molecular form of chlorogenic acid is $C_{16}H_{18}O_9$. There are many types of methods to extract chlorogenic acid from coffee beans such as microwave-assisted extraction (MAE), ultrasonic-assisted extraction (UAE), ethanol extraction, etc [13,14].

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One considerable alternative of traditional solvent extraction for isolation of phenolic compounds is microwave assisted extraction (MAE). Under the greatest conditions which are 5 minutes, 50°C temperature, and 800W power, with water solvent, the extraction rate of chlorogenic acid can reach 31-62% [13]. The reason why chlorogenic acid can antioxidant is that it can cleans free radicals from the body and reduces oxidative stress damage [15]. In addition to that, chlorogenic acid can regulate glycolipid metabolism by inhibiting α-glucosidase activity. The absorption of glucose in the gut will slow down, and this process can control postprandial blood sugar levels (blood sugar levels after meals). It can also regulate the concentration of incretin, by increasing the production of glucagon-like peptide-1 (GLP-1), so the toxicity of hyperglycemia to islet beta cells can be mitigated [16].

2.3. Diterpene

Diterpenes are a class of natural products composed of four isoprene units. They belong to terpenes. They exist widely in plants and have many biological activities like antibacterial, antiviral, anticancer, and so on [17]. The chemical structure of diterpenses mainly consist of four isoprene units. The core structure of it usually consists of many ring structures such as single-ring, double-ring, or multi-ring [17].

In coffee, diterpenoids mainly include Cafestol and Kahweol, which belong to furan diterpenoids in chemical structure. They are also bioactive components in coffee. Besides microwave-assisted Extraction (MAE) and Supercritical Fluid Extraction (SFE), Soxhlet extraction is another traditional method to extract diterpenoids (cafestol and kahweol) from coffee [18]. When using Soxhlet extraction, the extraction rate can reach 18.6% [18]. In another study of microwave-assisted extraction (MAE) of 13 different Arabica of green coffee beans, MAE could extract the amount which is in 10 minutes at 45°C, while Soxhlet extraction takes 4 hours. In addition, the space-time yield of MAE is six times of the Soxhlet method [18]. The extraction process of MAE needs to first set the microwave equipment for 10 minutes and 45°C. Next, mix the coffee powder with solvent (like petroleum ether) in a proportion and put it into the microwave. After the extraction of the microwave has finished, filter the extract. Finally, use high-performance liquid chromatography (HPLC) to analyze the diterpenoids [18].

All in all, coffee contains 1%-2% caffeine which can stimulate the nervous system, 6%-7% chlorogenic acid which offers antioxidant function and can reduce chronic disease risks, and a series of components like diterpenes that possess anticancer and liver protective functions, trigonelline, and so on [19,20].

3. Mechanism of bioactive ingredient

3.1. Antioxidant

Caffeine, chlorogenic acid, and other compounds in coffee have antioxidant activities. Chlorogenic acid which is a free radical scavenger can reduce intracellular reactive oxygen species (ROS) levels. Although the amount of caffeine will be reduced during digestion, it still has an antioxidant effect. Besides, the phenolic compounds in coffee can activate the pathway and promote the antioxidant enzymes (like HO-1). Therefore, coffee has antioxidant effects through these mechanisms [21,22].

3.1.1. Stroke

One research by searching Pubmed and EMbase databases and selecting 11 studies which include 479689 participants and 10003 stroke cases, has shown that there is a non-linear relationship between coffee consumption and stroke risk. Compared to people who do not consume coffee, the research found that the relative risk of stroke for people who consume two cups of coffee per day is 0.86. In

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corresponding, people who consume 3-4 cups per day, 6 cups per day, and 8 cups per day have a relative stroke risk of 0.83, 0.87, 0.93. The research also found that consuming coffee moderately (1-6 cups per day) was associated with a reduced risk of stroke [3]. However, when consuming coffee heavily (≥7 cups/day) was not associated with stroke risk. In addition, coffee consumption had similar effects on ischemic stroke (IS) and hemorrhagic stroke (HS).

3.1.2. Diabetes

A review of the correlation between coffee consumption and T2DM has shown that coffee consumption could decrease the risk of T2DM. This research contains 15 Rotterdam studies, 9 of which contain about 193473 participants and 8394 T2DM cases. The result shows that compared to people who drink 2 cups of coffee per day, people who consume 6 or even more cups per day have a lower risk of T2DM (decreased by about 35%). In addition, chlorogenic acid and other phenolic compounds in coffee can inhibit glucose absorption and increase insulin sensitivity by interfering with glucose transport. However, consuming too much caffeine is likely to harm glucose tolerance and reduce insulin sensitivity. Even though there are some disadvantages, it is much more beneficial to consume coffee in the long term [4]. By analyzing 18 studies that were published from 1966-2009, this review discussed the association between coffee, decaffeinated coffee intake, and the risk of developing T2DM. The research contains 457922 participants. The conclusion shows that there is a negative relation between coffee intake and T2DM. For each additional cup of coffee consumed per day, the relative risk of diabetes will be decreased by 7%. Besides, the consumption of decaffeinated coffee also showed a negative relation [5].

3.2. Anticancer

The caffeic acid (CGA) has an anticancer effect on human health. Because of its antioxidant effect, which can clear reactive oxygen species (ROS) in the human body and reduce the damage of oxidative stress to cells, it can reduce the risk of cancer. In addition, CGA can inhibit the increase and migration of tumor cells such as breast, colorectal, and liver cancers and induce them to die. Besides these two mechanisms, a series of processes all work together and bring coffee an anticancer function on human health [23].

3.2.1. HCC

One research which contains 110792 participants has shown that there is a negative association between coffee consumption and HCC. By sending questionnaires to 40-79-year-old participants, researchers can know their lifestyle, medical factors, and coffee consumption frequency. The result shows that people who consume coffee are less likely to have HCC (the risk of HCC is lower by 50%) than those who do not consume. In addition, among people with hepatitis C virus (HCV), coffee drinkers had a 69 percent lower risk of HCC [24]. Another research which contains 250 HCC patients (case group) and 500 patients hospitalized for non-tumor, non-liver, and non-alcohol-related (control group) also shows a similar result. Compared with people who do not drink coffee, there is a negative correlation was shown between coffee consumption and HCC. To be more specific, participants who drank 1-2 cups of coffee per day had a 20% lower risk of HCC; who consumed 3-4 cups per day had a 60% lower risk; and who drank 5 or more cups had a 70% lower risk [25].

3.2.2. The prevention of NDDs

Some studies have shown that caffeine can increase alertness and happiness, improve focus and mood, and reduce depression [26]. Eicosanoacyl-5-hydroxytryptamine (EHT) in coffee has a

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neuroprotective effect in MPTP models of Parkinson's disease. Therefore, consuming coffee in the long term is associated with protection against cognitive decline, PD, and AD [26].

Parkinson's disease (PD) is a pretty common NDD. There are several researches have shown that coffee intake is related to PD risk decrease. For example, one research that surveyed 4488 people concluding PD patients (case group) and healthy people (control group) found that Asians who carry a specific PD gene can reduce the risk of PD (four or eight times lower) by regularly consuming caffeine. To be more specific, people who carry the PD gene have 1.5 to 2 times that people do not carry, but caffeine intake could reduce this risk and even make it lower than non-caffeine users [7]. Besides, there is another example that can show that coffee intake is associated with Alzheimer's disease (AD). The experimental subject in this research is Alzheimer's mice, and the study found that caffeine and other components in coffee can increase the level of GCSF in the blood of mice. GCSF is one factor that promotes neurogenesis and synaptic plasticity. In this way, this research helps AD issues to have more solutions like consuming coffee [8].

4. Conclusion

This paper mainly talks about the potential benefits of coffee to human health and mainly analyzes the bioactive components in coffee and their mechanisms. In conclusion, caffeine, chlorogenic acid, diterpene, and so on have antioxidant, anti-inflammatory, and anti-cancer functions and can prevent NDDs. The main purpose of this paper is to provide the public with more scientific data and analysis about the relationship between coffee consumption and human health in different aspects. In addition, this paper also provides new ideas for the prevention and treatment of related diseases. Besides, this paper provides a reference for future research in many directions, like promoting deeper development about mechanisms of bioactive ingredients in coffee, helping future researchers to focus on the relationship between coffee consumption and the health of specific groups like people with chronic diseases, and encouraging more people to study different types of coffee. However, there are still some limitations in this paper. Firstly, the research in this review mainly relies on observational studies and meta-analysis. These research methods are not reliable since there are many confounding factors. In addition to that, the extraction methods and efficiency of bioactive ingredients in coffee are briefly introduced, and this could be improved by future study and analysis.

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