



## Review article

## Coffee and metabolic impairment: An updated review of epidemiological studies

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## ABSTRACT

**Background:** Coffee is one of the most consumed beverages worldwide. In the last years, coffee consumption has been associated with a number of beneficial effects against metabolic impairment. The aim of this narrative review was to report the most updated and comprehensive evidence from epidemiological and experimental studies as well as mechanisms of action of coffee on metabolic impairment.

**Methods:** A search in electronic databases (PUBMED and EMBASE) was performed to retrieve systematic and pooled analyses on coffee and diabetes, hypertension, and dyslipidemia. Furthermore, the most accredited hypotheses and mechanisms of action of coffee have been described.

**Results:** Coffee consumption has been associated with reduced risk of diabetes in observational studies. However, the effect seems not to be mediated by caffeine. Contrasting results have been found in pooled analyses of observational studies on hypertension, despite short- and long-term follow-ups that have been demonstrated to influence the outcome. Poor or little effect on plasma lipids has been reported in studies on acute administration of coffee, yet depending on the type of coffee preparation. The main beneficial effects of coffee consumption seem to rely on the content of antioxidant and anti-inflammatory compounds (i.e., polyphenols). Among the most important, chlorogenic acids have demonstrated direct anti-hypertensive action through beneficial effect on endothelial function, and significant improvement in glucose and insulin metabolism. Also, diterpenes and melanoidins are major candidates as antioxidant compounds showing the capacity to inhibit the production of inflammatory mediators. However, caffeine and diterpenes may also exert negative effects, such as acute rise in blood pressure and serum lipids.

**Conclusion:** In light of the most recent evidence, coffee consumption seems to be favorably related with health and to protect by metabolic impairment.

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## 1. Introduction

Metabolic disorders, such as obesity, dysregulated glucose homeostasis, dyslipidemia, and abnormal elevation of systolic and diastolic blood pressure are important risk factors for cardiovascular disease (CVD) and are among the major contributors for overall mortality [1]. Overweight and obese population have rapidly increased worldwide leading to a concomitant rise of type 2 diabetes incidence, especially in the highest income regions [2]. Hypertension and dyslipidemia affect 20%–40% of the population, showing a significant association with elevated BMI, waist circumference, and fasting blood glucose [3]. Altogether, these conditions represent a major public health issue that could potentially be reduced by the adoption of a healthier lifestyle. Besides well-known risk factors, such as sedentary and smoking habits, dietary habits show a crucial impact toward metabolic disorders. Several investigations pointed out the important role of certain dietary patterns, such as the Mediterranean diet or the Dietary Approach to Stop Hypertension (DASH), as significant protective factors against metabolic disorders and CVD risk factors [4–7]. Cohort studies demonstrated positive effects of these dietary patterns in both Mediterranean and non-Mediterranean countries [8,9]. However, their application in non-Mediterranean areas is somehow limited and some important foods have not been taken into account when considering such dietary patterns. In the last ten years, research on coffee drinking has increased dramatically suggesting that coffee consumption is not as negative as it was hypothesized in earlier studies [10]. In a recent State-of-the-Art review, a moderate coffee consumption (2 to 3 cups per day) has shown potential benefits on cardiometabolic disease, cardiovascular health, and all-cause mortality [11]; although in other studies, high coffee consumption (>4 cups per day) could have adverse effects [12]. The findings recently published pointed out convincing hypotheses on its beneficial effects in preventing metabolic impairment and laboratory research on its components provided biological plausibility for its action [13]. In this narrative review, we report the most important epidemiological evidence on coffee consumption and metabolic impairment, showing the inconsistency between epidemiological and experimental studies as a result of the biological differences between short- versus long-time consumption. Furthermore, the most accredited hypotheses and mechanisms of action have been described.

## 2. Epidemiological versus experimental evidence

### 2.1. Diabetes mellitus, glucose tolerance, and insulin sensitivity

Two recent systematic reviews and meta-analyses analyzing the specific association between coffee (data from 28 studies with information on 1,109,272 participants) [14], and decaffeinated coffee (10 studies, 491,485 participants) [15] on incidence of type 2 diabetes found a nonlinear dose–response relationship between coffee intake and subsequent risk of type 2 diabetes, with a decrease of about 8% of risk for every 1 cup/day increment in coffee intake after adjustment for potential confounding factors (Table 1). Since similar results were shown for decaffeinated coffee, it is likely that the protective effect may exist aside from the influence of caffeine intake. Another systematic review including 13 cohort studies with 9473 type 2 diabetes cases and 47,387 participants, found a reduction in type 2 diabetes incidence in those subjects who consumed 4 or more cups per day compared with less than 2 cups drinkers [16] (Table 1). Advantage emerged comparing intake of filtered coffee over pot boiled and decaffeinated coffee over caffeinated coffee. However, by analyzing single studies reporting inconclusive results, a relation with factors that could explain such results (i.e., type of coffee or country) could not be found. In addition to the previous systematic reviews, more recent observational studies are in line with the hypothesis that coffee intake may be linked to a lower risk of diabetes [17–21], reduced risk of deterioration of glucose metabolism [22,23], and insulin resistance [24–27].

Generally, results from randomized controlled trials (RCT) exploring the effect of coffee consumption on glucose metabolism and biological risk factors for type 2 diabetes widely contrasted those from observational studies. A recent meta-analysis of RCT in people with type 2 diabetes reported substantial negative effect of caffeine intake on blood glucose control [28] (Table 1). As expected, a major limitation of the trials included in the pooled analysis was the short period of study. Indeed, the beneficial effects of caffeinated and decaffeinated instant coffee on glucose metabolism were found in a recent study that lasted 16 weeks [29], but studies exploring the acute effects following the meal reported opposite or inconclusive results. An experimental study conducted on healthy volunteers resulted in an increasing insulin response and decreased insulin sensitivity index after a 75 g oral glucose tolerance test, compared to water [30]. While in another RTC on healthy subjects, coffee consumption increased glucose concentration and lowered insulin concentrations in the first 30 min after a standardized meal [31]. Caffeinated coffee, after either a high or low glycemic index meal, significantly impaired acute blood glucose management and insulin insensitivity compared with ingestion of decaffeinated coffee [32,33], despite these effects being stronger after a lipid-rich meal [34]. Moreover, coffee consumption during a carbohydrate meal seems to decrease the insulin sensitivity of a second carbohydrate meal, even without an additional coffee intake [35]. Some other experimental studies reported poorly significant results of caffeinated coffee on postprandial glycemic tolerance and insulin sensitivity [36,37] or increase of coffee-derived compounds but no changes of markers of glucose metabolism at an oral glucose tolerance test were found [38].

### 2.2. Hypertension

Epidemiological studies exploring the role of coffee consumption on the development of hypertension showed inconclusive results. Among the several pooled analysis that have been conducted during last 10 years, the most recent meta-analysis of epidemiological studies, including 6 prospective cohorts with a total of 172,567 participants and 37,135 incident cases of hypertension, concluded that the summary relative risks (RRs) for hypertension was 1.09 (95% confidence interval (CI): 1.01, 1.18) for consumption of 1–3 cups per day, whereas no significant risk was found for higher categories (>3 cups/day) [39] (Table 1). A meta-analysis of experimental and observational epidemiological studies on coffee consumption and hypertension reported low-quality evidence, unable to show any statistically significant effect of coffee consumption on blood pressure or the risk of hypertension [40] (Table 1). Another meta-analysis investigating the role of coffee/caffeine intake in hypertensive subjects results in an acute increment of BP for  $\geq 3$ , without any long-term association between coffee intake and BP [41] (Table 1). These findings seem to confirm the results of a previous meta-analysis of RCT conducted with regard to the intake of both coffee and caffeine [42] (Table 1). They reported a significant rise of 2.04 mmHg (95% CI: 1.10, 2.99) in systolic blood pressure and 0.73 mmHg (95% CI: 0.14, 1.31) in diastolic blood pressure for pooled analysis of coffee and caffeine trials. When coffee trials and caffeine trials were analyzed separately, blood pressure elevations appeared to be significant only for caffeine but not for coffee, suggesting that despite the biochemical mechanism of action of caffeine supporting the biological plausibility that acute ingestion of such compounds may increase blood pressure, when ingested through coffee, the blood pressure effect of caffeine was somehow attenuated. It is noteworthy that most recent investigations found a significantly reduced risk of hypertension evaluated in both cross-sectional and prospective design only when analysis was stratified by smoking status [43,44].

### 2.3. Dyslipidemia and lipid metabolism

The early epidemiological studies published in the 1980s demonstrated a significant association between coffee consumption and

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