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Review

Effects of coffee on type 2 diabetes mellitus

Muhammad Sajid Hamid Akash Ph.D. [a,b], Kanwal Rehman B.Pharm., M.Phil. [a], Shuqing Chen Ph.D. [a,*]

[a] Institute of Pharmacology, Toxicology and Biochemical Pharmaceutics, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, China

[b] College of Pharmacy, Government College University Faisalabad, Faisalabad, Pakistan

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ABSTRACT

This review provides the epidemiologic and research evidences documenting the effects of coffee consumption on type 2 diabetes mellitus (T2DM). We summarize the literature concerning the effects of coffee consumption on different mechanistic factors involving in pathogenesis of T2DM, such as glucose tolerance, insulin sensitivity, insulin resistance, glucose-6-phosphatase, intestinal glucose absorption, antioxidant activity, inflammatory biomarkers, nuclear factor-κB inhibition, glucose uptake, glucose homeostasis, glucose metabolism, and insulin secretion. These factors play a crucial role in influencing the normal levels of glucose in blood. Overall, the experimental and epidemiologic evidences presented here elucidate the protective effects of coffee consumption on T2DM, involving multiple preventive mechanisms. Despite the firm evidences available through a growing literature base, it is still uncertain whether the use of coffee should be recommended to patients with diabetes and/or any patient who might be at the risk of T2DM as a supplementary therapy to prevent further progression of T2DM.

Introduction

Coffee is among the most widely used beverages worldwide. It contains several substances that may affect glucose uptake and metabolism and is obtained from tealeaves, guarana, and cola plant seeds [1]. Numerous epidemiologic, clinical, experimental, or a combination of all three, studies have been conducted to investigate the effects of coffee on cardiovascular diseases [2,3], cancers [4], cholelithiasis [5], neurologic disorders [6], endocrine disorders [7–9], kidney stones, [10] and T2DM [11–13].

Diabetes mellitus is an autoinflammatory syndrome that is a collection of many disorders such as hyperglycemia, dyslipidemia, insulin resistance, impaired β-cell functioning, and insulin secretion [14–17]. It is considered among the major life-threatening diseases worldwide, particularly in developing countries. There are various ways to treat T2DM such as medication, lifestyle modification, and dietary supplementation. Traditional antidiabetic agents may cause some potential adverse events [14,18]; however, there are some naturally occurring anti-inflammatory agents that may have anti-diabetic effects against T2DM [19–22] but these agents have some limitations because of short biological half-life [14,22–24]. Dietary supplements are one of the best choices known to have natural properties against T2DM [25–29].

The purpose of this article is to explore and summarize the current scientific literature on the potential effects of coffee consumption on T2DM. PubMed, Medline, ScienceDirect, and/or Scopus were searched using the following key words: Coffee, caffeine, diabetes mellitus, insulin sensitivity, glucose-6-phosphatase, inflammatory biomarkers, glucose metabolism, chlorogenic acid, and *oxidative stress*.

General properties of coffee

Coffee is a mixture of many chemicals such as carbohydrates, lipids, vitamins, nitrogenous compounds, isoflavonoids, and micronutrients. The major components of coffee are caffeine, cafestol and kahweol, chlorogenic acid (CGA), and micronutrients [30]. Caffeine is rapidly absorbed from the gastrointestinal tract and distributes rapidly [31] in all tissues including brain. Pharmacologically, caffeine exhibits its antagonistic effects via *A1* and $A2_A$ subtype adenosine receptors [32] that are responsible for stimulatory effects.

Coffee exhibits its beneficial effects in both former coffee drinkers and/or irregular coffee drinkers by improving mood,

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* Corresponding author. Tel.: +86 15 5581 71291; fax: +86 57 1882 0841.
E-mail address: Chenshuqing@zju.edu.cn (S. Chen).

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cognitive performance, and endurance during prolonged and exhaustive exercise [33,34]. Coffee is used as an ergogenic aid in sports and is also useful for competitive and recreational athletes who perform resistance training. Significant improvements have been seen in athletic performance after coffee consumption [35,36]. Coffee consumption also increases the subjective alertness, improves reaction time for both visual and auditory stimuli, and enhances the performance of manual tasks such as driving and encoding of new information [37]. Several components of coffee may ameliorate the symptoms of T2DM by affecting glucose regulation. These may include the effects of CGA on glucose-6-phosphatase, the antioxidant activity of polyphenols on α-glucosidase, and the effects of caffeine on insulin secretion [38].

Epidemiologic studies of coffee consumption on T2DM

Various epidemiologic studies have been conducted to investigate the hypoglycemic effects of coffee on T2DM. The first study was conducted to investigate the effects of coffee consumption on T2DM [39] and found that increased coffee consumption reduced glucose plasma levels. The results of the study were confirmed by another trial conducted with a Japanese population [40]. To date, many meta-analysis and prospective studies have demonstrated that regular coffee intake may reduce the risk for T2DM [14,38,41–44]. Many epidemiologic studies related to coffee consumption have been conducted in different regions of the world with different ethnic groups, including European [14,38,45–50], American [51–56] and Asian populations [57–61]. With the exception of a few studies [45,48,57], it has been concluded that there is an inverse association between coffee consumption and risk for T2DM. On the basis of these epidemiologic studies, it has been demonstrated that high consumption of coffee over the long term may reduce the risk for T2DM more significantly compared with short-term, low coffee consumption [62,63]. On the basis of these findings, another study was conducted to differentiate the significant effects between coffee and caffeine [53]. This study demonstrated that the protective effects of coffee did not depend on caffeine intake and the association was stronger with decaffeinated coffee than with nondecaffeinated coffee. The hypoglycemic effects were the result of several other components that make up coffee, along with caffeine.

Effects of coffee consumption on T2DM risk factors

T2DM is the collection of various risk factors that together provoke progression of the disease [14,16,17,64]. Results from various studies have found that coffee consumption reduces the risk for T2DM by directly affecting the risk factors discussed here.

Effects on impaired glucose tolerance and insulin sensitivity

Impaired glucose tolerance (IGT) is a condition of hyperglycemia in which resistance to insulin sensitivity is increased within peripheral tissues in response to glucose [19,20]. Several studies have investigated the effects of short- and long-term administration of coffee and/or caffeine on glucose tolerance. Some studies found that glucose tolerance was impaired after short-term ingestion of coffee [34] and/or caffeine [65,66]; but several studies demonstrated that coffee has the ability to increase glucose tolerance [34,67–71]. Short-term administration of coffee may impair insulin resistance and glucose tolerance by blocking the effects of adenosine *A1* receptor relating glucose uptake in skeletal muscles [45]; however, results from several epidemiologic studies show that long-term and habitual use of coffee may help maintain normal glucose tolerance and improve insulin sensitivity [53,67–71].

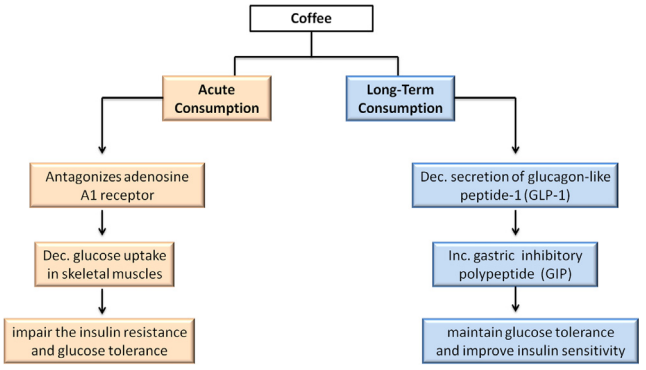

Fig. 1. Short- and long-term effects of coffee on glucose tolerance and insulin sensitivity. Short-term coffee consumption blocks the effects of adenosine *A1* receptor decreasing glucose uptake in skeletal muscles, which may result in insulin resistance and impaired glucose tolerance. However, long-term and habitual coffee consumption can modulate the secretions of gastrointestinal hormones that may result in maintaining normal glucose tolerance and improvements in insulin sensitivity.

Decreased insulin sensitivity in response to short-term doses of coffee [72–74] may be the result of caffeine-induced antagonism of adenosine receptors with increased epinephrine levels [12]. On the contrary, several epidemiologic studies have found that long-term administration of coffee prevents the symptoms of diabetes and improves insulin sensitivity [13,38,40,42,43,47,75]. The short-term effects of coffee may suppress insulin sensitivity, whereas regular consumption of coffee can induce glucose tolerance and insulin sensitivity [69,76–79]. Habitual consumption of caffeine within a complex mixture such as coffee changes the negative effect of caffeine to a positive one on insulin sensitivity and glucose tolerance (Fig. 1).

Effects on inflammatory biomarkers of T2DM

Because T2DM is correlated with and influenced by the activation of various pro-inflammatory cytokines and chemokines [14,16,17], suppression of these markers with a suitable agent having anti-inflammatory properties may stop the overall inflammation in T2DM [14,16,19,20]. Coffee contains a complex mixture of components other than caffeine such as CGA, cafestol, trigonelline, and kahweol. These components have strong anti-inflammatory properties.

Components of coffee that are usually absorbed after intake have varying effects on different pro-inflammatory and anti-inflammatory biomarkers of T2DM (Table 1). Various studies conducted on humans and different animals have demonstrated that habitual consumption of coffee may significantly reduce the levels of pro-inflammatory biomarkers such as interleukin (IL)-1 β, IL-6, tumor necrosis factor α, C-reactive protein, monocyte chemotactic protein 1, vascular cell adhesion molecule 1, C-peptides, endothelial-leukocyte adhesion molecule 1, and IL-18 [69,80–89]. Similarly, in some other studies, regular intake of coffee significantly increased the levels of various anti-inflammatory biomarkers such as adiponectin, IL-4, and IL-10 [82,87,90]. Habitual intake of coffee assertively blocks the activation of these pro-inflammatory markers, whereas the levels of anti-inflammatory markers that validate the protective effects of coffee consumption in T2DM are significantly increased (Fig. 2).