Review Article

Effect of Decaffeinated Coffee-enriched Chlorogenic Acid on Blood Glucose Levels in Healthy Controls: A Systematic Review

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Abstract

As an important group of health problems, glucose metabolism disorders are associated with a number of diseases as well as mortality rate. Recently, studies have demonstrated that the consumption of decaffeinated coffee-enriched chlorogenic acid (CGA) can reduce the risk of diabetes and blood glucose rise, while the results of some previous studies have shown an opposite effect. Hence, a systematic search was conducted based on literature search and appropriate keywords through PubMed, Google Scholar, Web of Knowledge, Science direct, Medline, Cochrane, and Scopus databases from 2003 to 2018. After searching, 1593 articles were found. Then, we excluded papers based on the duplication and relevant for title and abstract, whereas 25 relevant articles remained for checking eligibility criteria. Since only randomized clinical trials studies (RCTs) could be included in the current study, six RCTs remained in end-stage for qualitative synthesis. The results of reviewed studies showed no significant effect of decaffeinated coffee-enriched CGA on blood glucose concentration. Although recent studies have suggested the effectiveness of decaffeinated coffee-enriched CGA on blood glucose in animals, and there are various mechanisms for this effect, and the result of our review showed that there is not sufficient evidence for this claim in healthy humans. Hence, further research in this area seems necessary.

Keywords: *Blood glucose, chlorogenic acid, coffee, decaffeinated coffee, diabetes mellitus*

Introduction

According to recent clinical studies, there is a link between blood glucose levels and mortality rate among hospitalized patients with hyperglycemia than patients with normal blood glucose levels, in particular.[1] Accordingly, the problems due to glucose metabolic disorders have a significant effect on health-care systems worldwide.[2] Glucose homeostasis disorders can independently increase the risk of other diseases.[3] One of the major problems of hyperglycemia is the chronic complications it causes. Recently, evidence has shown that the prevalence of diabetic neuropathy and diabetic nephropathy is 17.8% and 10.7%, respectively. Furthermore, studies have indicated the prevalence of diabetic retinopathy as 21.9%.[4]

The Previous studies have shown a link between decaffeinated coffee and reduction in the risk of type 2 diabetes.[5,6] Decaffeinated coffee is a major source of chlorogenic acid (CGA). CGA is a polyphenol compound known as active phenolic groups in each extract of green coffee bean such as coffee and decaffeinated coffee.[7-9] Based on recent findings, there are many biological properties for CGA such as antibacterial, antioxidant, anticarcinogenic, and especially blood glucose lowering effect in animals.[8,10-12] Several mechanisms have been suggested for the effects of CGA on glucose metabolism. One of these mechanisms is inhibition of α-glucosidase and glucose-6-phosphate translocase 1, which leads to elevated glucagon-like peptide 1 (GLP-1) secretion and delayed intestinal glucose uptake, eventually resulting in altered blood glucose level.[13] In addition, CGA can reduce hepatic glucose output and gluconeogenesis by decreasing the glucose-6-phosphatase activity.[14,15] Considering a lack of sufficient systematic reviews in this area, we investigated the acute effect of decaffeinated coffee-enriched CGA on blood glucose levels in healthy humans.

Materials and Methods

To do this review, we followed the preferred reporting items for systematic reviews and meta-analyses.[16]

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Eligibility criteria

This systematic review included studies examining the effect of decaffeinated coffee-enriched CGA on blood glucose levels in healthy humans. In this study, inclusion criteria involved studies as follows: (1) with healthy human subjects (men and women); (2) conducted through randomized control trial design; (3) with described information about the issue, method of study, analysis method of the outcomes, and subject characteristics; and (4) that have full text. On the other hand, the exclusion criteria involved studies as follows: (1) performed on nonhuman subjects; (2) whose design was not randomized controlled design; (3) with unclear data about the issue, method of study, and subject characteristics; and (4) that have no full text. Overall, all potentially related studies were assessed for eligibility by the author.

Search strategy

Search strategy was limited to randomized clinical trials, and literature search was performed through PubMed, Google Scholar, Web of knowledge, Science direct, Medline, Cochrane, and Scopus databases. It was then by publisher databases such as Springer link, Elsevier, and Wiley online from January 2003 to May 2018 for studies illustrating the effect of decaffeinated coffee-enriched CGA on blood glucose levels. In addition, the reference lists of suitable articles were reviewed for the supplementary data. No language restriction was applied in the literature search, and if the supplementary information was needed, the corresponding author would be contacted. The key words used for searching in PubMed database were as follows: "Decaffeinated Coffee," "CGA," "Green coffee," "Coffee," "Green coffee bean extract," "Glucose," "Glycemic markers," "Diabetes mellitus," "Blood Glucose Self-Monitoring," "Blood sugar," "Fasting blood sugar," "Oral glucose tolerance test," "Fasting blood glucose," and "2-Hour Post-Prandial Blood Glucose." The data terms were searched as medical subject headings (Mesh) terms or abstract of trial studies.

Study selection

Overall, the findings gained from searching the databases were sorted based on the title and abstract of papers. The studies which did not match the purposes of the current review were removed. The chosen studies analysis of method and those which did not meet the appointed criteria were eliminated. Studies were included if they met the following criteria: participants who had not been previously identified with diabetes; consumption of decaffeinated coffee versus a control; and assessment of the effects of decaffeinated coffee on blood glucose. The inclusion criteria were evaluated by assessing the relevant study protocol. If necessary, supplementary data were requested from the study's authors. Clinical trial studies were removed after being assessed as irrelevant to the participant type, outcomes of interest, duplicate publications, and unsuitable design of studies.

Method of quality assessment

Quality of studies was evaluated by JADAD scale tables that included score of quality. This table included the following three items: randomization, blinding, and dropouts in the course of study. The score of randomization and blinding is between 0 and 2 depending on whether the method of randomization and blinding has clear descriptions or not. Furthermore, the score of dropout is 0 or 1, 0 for studies with dropout and 1 for studies lacking dropout in the course of study. Overall, the JADAD score is between 0 for low-quality studies and 5 for high-quality studies.[17]

Results

Search results

Overall, after searching according to literature search in databases, 1593 articles were found, 81 articles of which were duplicated and removed. In the next step, we excluded articles based on relevancy for title and abstract, where 25 relevant articles remained for checking eligibility criteria such as study design, type of study design, and availability of full text. Finally, six articles remained in the end for qualitative synthesis and 19 articles were excluded for not meeting the eligibility criteria. Figure 1 displays the stages of search.

Quality assessment

Following quality assessment of included studies, based on JADAD scale, randomization was mentioned in all studies which included qualitative synthesis, while randomization method was described in only three of them.[18-20] Blinding had been performed in four studies; however, its method was described only in two of them.[9,18,19,21] However, two of the studies have dropouts in duration and the analysis stage of study.[19,20] Finally, Wedick study gained the top score (five), while Greenberg study obtained the lowest score (zero) according to JADAD scale.[19,22] JADAD score of studies are provided in Table 1.

Study characteristics

Included studies involved 101 healthy participants with a mean age of 36.42 years and body mass index ≤35 kg/m^2. Among them, 61 persons (60%) were male and 40 were female (40%). The publication year of studies was from 2003 to 2012 and their countries were as follows: the USA (n = 3),[9,19,22] England (n = 1),[21] the Netherlands (n = 1),[18] and Japan (n = 1).[20] The design of studies was randomized controlled trial of crossover and parallel type, and the follow-up time range of studies was from 120 to 180 min to 16 weeks. In addition, the total isomers of CGA were 3, 4, 5 Caffeoylquinic which was mentioned in three studies. The characteristics of the studies are presented in Table 1.

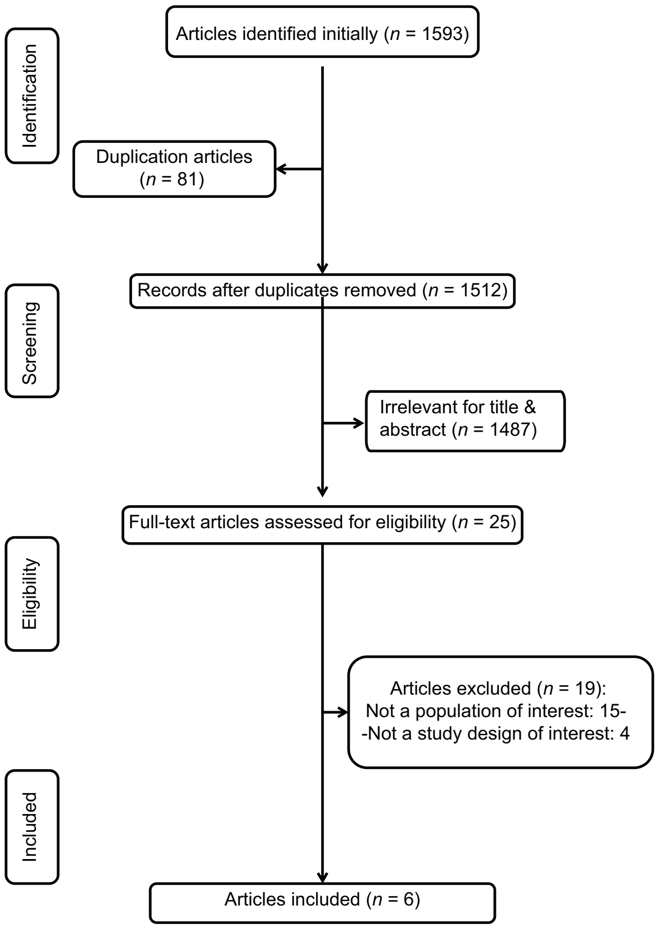

Figure 1: Flowchart of study selection

Outcomes

Considering the evaluation of the results of studies qualifying for the qualitative synthesis, we investigated the acute effect of decaffeinated coffee-enriched CGA arm on blood glucose level compared with control for 0–120 and 180 min of the area under the curve in each of studies. In general, no significant effect was observed for consumption of decaffeinated coffee on blood glucose levels throughout the time period ($P > 0.05$). The mean area under the curve of blood glucose (mmol/l), compared with control, was as follows: Thom study: 818 ± 10.9 compared with 778 ± 10.2, Van Dijk study: 958 ± 134 compared with 962 ± 134, Greenberg study: 4.1 ± 0.67 compared with 4.35 ± 1.01, Wedick study: 14.32 ± 1.32 compared with 13.85 ± 1.23, Ohnaka study: 0.3 ± 3.3 compared with 0.3 ± 1.6, and Johnston study: no reported data. The details of studies are shown in Table 1.

Discussion

This systematic review was done to explore the effect of decaffeinated coffee-enriched CGA on blood glucose levels from January 2003 to May 2018. Overall, according to the search based on search strategy and eligibility criteria, six studies were found on evaluating the effects of decaffeinated coffee-enriched CGA on blood glucose in healthy humans. The results of these studies demonstrated that the consumption of this compound has no significant effect on blood glucose concentration in healthy controls [Table 1].

About the recent evidence, regulation of blood glucose concentration may be affected by different factors. The concentration of blood glucose changes after food consumption. Consumed foods enter the beginning of small-bowel and are absorbed in the area. In response to it, some hormones related to the glucose metabolism regulation (e.g., insulin, Gastric inhibitory polypeptide [GIP], and GLP-1) increase in blood and change the level of blood glucose.[23-26]

Coffee and decaffeinated coffee are known as a compound rich in CGA which decreases the risk of diabetes by affecting the metabolism of glucose, insulin, GIP, and GLP-1.[15,27] Furthermore, with regards to the conducted studies and their results, although the effect of CGA as a group of polyphenols cannot be associated with the regulation of glucose, insulin, GIP, and GLP-1 hormones in healthy individuals, the mechanisms mentioned in the studies are also considerable.[9,13] However, the results of conducted studies indicate counter acute effects of CGA on glucose concentration and metabolism of hormones intervening the pathophysiology of glucose regulation between human and animals.[9,19,28-30] Today, the results of studies conducted on animals suggest that the consumption of decaffeinated coffee has a significant lowering effect on blood glucose concentration and the risk of diabetes. The results of a study conducted by Tunnicliffe *et al.* showed that consumption of CGA in laboratory animals has no effect on plasma insulin and secretion of GLP-1; however, it can decrease plasma levels of glucose and GIP after eating.[30] In addition, the study of Bassoli *et al.* demonstrated that ingestion of CGA leads to reduced blood glucose level in rats.[12] Another study revealed that the consumption of coffee and decaffeinated coffee reduced the risk of type 2 diabetes in humans.[31] However, the results of studies reviewed in the current systematic review demonstrated that the consumption of decaffeinated coffee has no significant effect on blood glucose levels in healthy humans.

Overweight participants were included in three included studies.[18-20] Obesity and high body mass index can cause insulin resistance. Due to it, blood glucose level increases in obese people compared to people with normal weight. One of the roles of decaffeinated coffee-enriched CGA is the reduction of glucose absorption in small intestine.[21] Even though the consumption of decaffeinated coffee could not change glucose concentration in these studies, the pathophysiology of blood glucose is abnormal in individuals with high body mass index.[21] As a result, it seems that the regulation of blood glucose requires higher

Table 1: Characteristics of the studies included in the qualitative synthesis

Study	Publication (year)	Location	Sample size of study	Gender ration	Age (year)	BMI (kg/m²)	Design	Jadad score	DCC group	Dose of DCC	Dose of CGA in DCC	Total isomers of CGA	Control group	Duration	Glucose (AUC)
Johnston *et al*.[9]	2003	USA	9 healthy controls (4 males and 5 females)	44% men 56% women	22.8-29.2 Mean: 26	<25	Cross over RCT	2	DCC + glucose	400 ml	2.5 mmol	3-CQA, 4-CQA, 5-CQA	Glucose	180 min	No significant
Thom[21]	2007	England	12 healthy controls (6 males and 6 females)	50% men 50% women	21-27.4 Mean: 24.2	<25	Cross over RCT	3	DCC + sucrose	10 g	350 mg	3-CQA, 4-CQA, 5-CQA	Sucrose	120 min	No significant
van Dijk *et al*.[18]	2009	Netherlands	15 healthy males	100% men	23.4-56.4 Mean: 39.9	25-35	Cross over RCT	3	DCC	12 g	264 mg	NR	Mannitol	120 min	No significant
Greenberg *et al*.[22]	2010	USA	11 healthy males	100% of men	NR	NR	Crossover RCT	0	DCC	57 g	NR	NR	Placebo (hot water)	180 min	No significant
Wedick *et al*.[19]	2011	USA	41 healthy controls (12 males and 29 females)	29% men 71% women	27.5-53.7 Mean: 40	25-35	Parallel RCT	5	DCC	5 cups (885 ml)/day	216 mg	NR	Placebo beverage (no coffee)	8 weeks	No significant
Ohnaka *et al*.[20]	2012	Japan	13 males (over weight)	100% men	40-64 Mean: 52	25-30	RCT	3	DCC	5 cups of DCC/day	NR	NR	Placebo beverage (no coffee)	16 weeks	No significant

AUC=Area under the curve, NR=No reported, DCC=Decaffeinated coffee, CGA=Chlorogenic acid, CQA=Caffeoylquinic acid, RCT=Randomized clinical trial, BMI=Body mass index dosage of decaffeinated coffee in these subjects compared to normal weight counterparts.

Overall, some following hypotheses can be considered: (i) the reviewed studies have had different follow-up times and sample sizes which may affect their results. In addition, systematic conclusion for studies with a homogeneous follow-up time and sample size has greater validity; (ii) since there is no standard dosage of decaffeinated coffee to change blood glucose levels, and given the use of different dosages of decaffeinated coffee in the included studies, it is possible that the consumption of decaffeinated coffee at another dosage (e.g., higher or lower) alters the blood glucose concentration significantly. Hence, further studies seem to be necessary.

Limitations

Overall, due to the qualitative assessment of studies, based on the JADAD table, one study acquired the highest score for describing the method of randomization, blinding, and dropouts in the course of study, while the other articles were not able to gain the complete score of JADAD items.[9,18-22]

Conclusion

Even though some animal studies have indicated the blood glucose lowering effect of decaffeinated coffee, our findings do not approve the previous findings in healthy humans. Therefore, it seems that decaffeinated coffee does not have the preventive effect on the risk of diabetes in healthy individuals. Hence, further studies are suggested to be performed in the future for confirming this conclusion.

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Conflicts of interest

There are no conflicts of interest.

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