NUTRITION REVIEWS 70 YEARS 1942-2012

Lead Article

Role of coffee in modulation of diabetes risk

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Coffee consumption has been associated with a lower risk of type 2 diabetes. This association does not depend on race, gender, geographic distribution of the study populations, or the type of coffee consumed (i.e., caffeinated or decaffeinated). This review discusses the strength of this relationship, examines the possibility that the pattern of coffee consumption could influence the association, and evaluates the possible relationship between coffee consumption and other risk factors associated with diabetes. Particular attention is paid to the identification, on the basis of the scientific evidence, of the possible mechanisms by which coffee components might affect diabetes development, especially in light of the paradoxical effect of caffeine on glucose metabolism. In addition to the role of coffee in reducing the risk of developing type 2 diabetes, the possible role of coffee in the course of the illness is explored. Finally, the possibility that coffee can also affect the risk of other forms of diabetes (e.g., type 1 diabetes and gestational diabetes) is examined.

INTRODUCTION

Brewed coffee is among the most widely consumed beverages in the world. Due to the broad consumption of coffee worldwide, several studies have examined the possibility of an association between coffee intake and health. Although coffee consumption has been correlated with a reduced risk of colon cancer[1] and Alzheimer's disease,[2] most of the evidence indicates a strong and clear inverse association between coffee consumption and diabetes.

As a brewed drink prepared from roasted seeds, coffee contains a number of bioactive molecules that are characteristic of fruits and vegetables. Generally, the principal health effects of coffee have been associated with its caffeine content. Caffeine, in fact, induces several pharmacological effects, mostly at the level of the central nervous system. A single cup of coffee can contain from 45 mg to 180 mg of caffeine, depending on the variety of coffee and the brewing method. Coffee, however, is not synonymous with caffeine; in fact, it contains several bioactive molecules (over 1,000 chemicals have been identified in roasted coffee), such as lipids, polysaccharides, phenolic compounds, melanoidins, soluble dietary fiber, and minerals, with caffeine representing only 2% of coffee's chemical profile.

Coffee is a very rich source of phenolic compounds, with the total content ranging from 200 mg to 550 mg per cup.[3] The main phenolic compound in coffee is chlorogenic acid.

Diabetes is recognized to be a syndrome, i.e., a collection of disorders sharing hyperglycemia and glucose intolerance as typical features. Insulin deficiency, impaired action of insulin, or a combination of these is responsible for the high blood glucose level that, if prolonged over time, can result in retinopathy, neuropathy, nephropathy, and atherosclerosis.

Diabetes has been classified as type 1 diabetes (T1D) (formerly known as juvenile diabetes), type 2 diabetes (T2D), and gestational diabetes. T1D results from an absolute deficiency in insulin secretion due to cell-mediated autoimmune destruction of pancreatic β-cells. T2D results from a combination of insulin resistance and inadequate insulin secretion. Finally, gestational diabetes is characterized by glucose intolerance during pregnancy.

Diabetes is the fourth leading cause of death in industrialized countries. About 177 million people in the

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Key words: bioactive molecules, coffee, diabetes

doi:10.1111/j.1753-4887.2012.00470.x

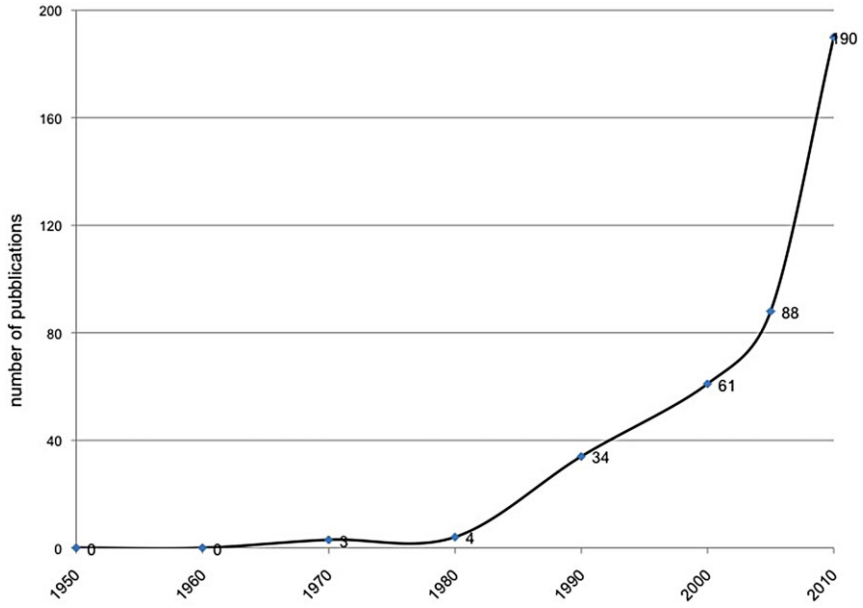

Figure 1 **Chronology of the number of publications appearing in Medline® between 1950 and 2010 with the key words "coffee" and "diabetes."**

world are affected by diabetes, and this number is expected to double by 2025. The number of deaths attributable to diabetes is around 4 million per year (World Health Organization estimates). T2D is the most common form of diabetes (about 90% of cases) and represents an important risk factor for cardiovascular disease.[4,5] Indeed, cardiovascular events (heart attack and stroke) are the major cause of premature deaths in diabetics.[6]

Given the high cost of the disease in terms of both human lives and healthcare costs (the total annual global health expenditure in 2010 is estimated to range between USD 376 and 672 billion[7]), prevention of diabetes is especially important. Although genetics plays an important role in the etiology of the disease,[8] there is increasing evidence that T2D is associated with several modifiable risk factors, including diet and physical activity. In recent years, a number of epidemiological studies have suggested that moderate and prolonged consumption of coffee is associated with a reduced risk of developing T2D.

COFFEE AND RISK OF TYPE 2 DIABETES

The literature documenting an association between coffee consumption and T2D is relatively recent (Figure 1). The first observations of the relationship between coffee consumption and plasma levels of glucose date back to the 1970s, when an experimental study demonstrated that an increase in coffee consumption reduced plasma levels of glucose.[9] This was confirmed by a Japanese study, which reported an inverse association between coffee consumption and plasma levels of fasting glucose.[10] The first epidemiological report indicating an inverse association between coffee consumption and T2D dates back to 2002.[11] Since then, the number of studies has steadily increased, so that a search in MEDLINE with the keywords "coffee" and "diabetes" today yields 439 scientific articles (PubMed 17 February 2012).

To date, about a dozen prospective studies and two meta-analysis studies indicate that regular and moderate consumption of coffee reduces the risk of T2D[12–16] and that the association does not depend on race, gender, or geographic distribution of the study population. In fact, the studies were conducted in different regions of the world and in different ethnic groups, including Europe (England,[17] Finland,[18] the Netherlands,[11,19] and Sweden[20]), the Americas (United States,[21,22] American Indians,[7,23] African Americans,[24] and Puerto Rico[25]), and Asia (Singapore[26] and Japan[27,28]). With few exceptions, all of these studies were carefully controlled for a large number of possible confounding factors and, among them, only three showed no association between coffee consumption and the development of diabetes.[17,29,30]

The first meta-analysis[31] (15 epidemiological studies, 9 prospective and 6 case-control, involving a total of about 200,000 participants) indicated that a higher consumption of coffee is consistently associated with a lower risk of disease. Compared with no consumption, consumption of four or more cups of coffee per day corresponded to a 35% reduction in the risk of T2D. The

second meta-analysis[32] (20 prospective studies involving a total of about 500,000 people with follow-up periods ranging from 2 to 20 years) indicated there is an inverse association between coffee consumption and the risk of T2D and that the association is dose dependent. In fact, an increase in coffee consumption decreased the risk, with a reduction of about 7% per cup of coffee consumed per day. The association was also valid in the case of decaffeinated coffee (analysis of 6 studies with a total of about 225,000 individuals), with the risk of developing T2D about one-third lower in people who drink three to four cups of decaffeinated coffee per day than in people who do not consume coffee.[32] Thus, the protective effect of coffee does not seem to depend on its caffeine content and, in one case, the association was even stronger for decaffeinated than for regular coffee.[22]

At present, the observations obtained through epidemiological studies have not been verified in experimental studies. Instead, the influence of coffee consumption on some indicators of the disease (hyperglycemia, hyperinsulinemia, etc.) has been tested in experimental studies.

Biomarkers of risk

Numerous epidemiological studies reported that coffee consumption is consistently associated with a lower prevalence of impaired glucose tolerance, hyperglycemia (fasting and after glucose load), hyperinsulinemia, and insulin sensitivity.[19,20,33,34] In some studies, coffee consumption reduced the risk of metabolic syndrome, a condition strongly related to diabetes,[35] but other epidemiological studies did not confirm these results.[36,37]

Recent epidemiological studies indicated that consumption of caffeinated coffee is positively associated with plasma adiponectin levels both in healthy and in diabetic women.[38,39] Adiponectin is a hormone that regulates the catabolism of glucose and insulin sensitivity. Adiponectin levels are reduced in diabetics, and thus adiponectin is considered protective against diabetes.[40] These findings, however, have not yet been confirmed in other population groups.[41]

Several epidemiological studies showed an inverse association between coffee consumption and markers of inflammation and endothelial dysfunction, such as soluble receptor of tumor necrosis factor-α, C-reactive protein, E-selectin, and soluble vascular cell adhesion molecule 1 in healthy,[42–44] diabetic,[38,43] and obese subjects.[45]

In conflict with these data, one study reported opposite results, showing a positive association between coffee consumption and markers of inflammation,[46] and another study reported no correlation between coffee consumption and markers of inflammation.[47]

A recent experimental study tried to clarify these contrasting indications.[48] Forty-seven healthy subjects at high risk of T2D participated in a single-blind experimental protocol. In the first month of the study, subjects had to refrain from drinking coffee, while in the second and third months, they drank four cups and eight cups per day of filtered coffee, respectively. After the consumption of eight cups of coffee per day, a significant decrease in plasma levels of proinflammatory cytokine (IL-18), but not of C-reactive protein, was observed, along with a significant increase in adiponectin levels. An experimental study conducted in an animal model confirmed that coffee consumption can reduce the production of proinflammatory adipocytokines in diabetic mice.[49]

Consumption patterns

The modality of coffee consumption varies greatly in different regions of the world. Even within the same population, individuals have very different consumption patterns. Apart from the frequency of consumption, in fact, the type and amount of coffee consumed, the time of consumption (i.e., after a meal or between meals), and the addition of sugar, other sweeteners, or milk could influence the capacity of coffee to affect the risk of diabetes.

A recent prospective study demonstrated that the pattern of coffee consumption may have an influence,[15] suggesting that consumption after lunch further reduces the risk of developing T2D. The positive effect was also evident for decaffeinated coffee, while the addition of milk to coffee annulled the protective effect. However, other studies seem to indicate that the addition of milk or cream does not have any effect on the risk of diabetes or on insulin sensitivity.[11,50] Finally, adding sugar to coffee did not seem to change the inverse association between coffee consumption and the risk of T2D,[11,15] although one study suggested that the addition of sugar can decrease insulin sensitivity.[50]

COFFEE AND RISK OF TYPE 1 DIABETES

Studies on the effects of coffee consumption on the development of T1D are very scarce, especially when compared with the number of studies on the development of T2D. This is not surprising, because the two diseases have a very different development. T1D usually develops in childhood or adolescence, probably because of exposure to early risk factors (perhaps even in the first months of life), that is, at a time when coffee consumption is rather limited. A cross-sectional study indicated that there is some association between the incidence of T1D in children between the ages of 0 and 14 years and the per capita

consumption of coffee in their countries.[51] The same authors warn, however, that their study must be interpreted with caution, as per capita consumption data are very poorly related to consumption in children.

In a study conducted in the early 1990s in 600 diabetic and 600 control children,[52] the risk of developing T1D was higher in children who consumed at least two cups of coffee or tea per day, while the consumption of coffee or tea by the mother during pregnancy had no influence on the risk. However, in that study, the increased sense of thirst in the prediabetic children probably acted as a confounder.

From the above, it is evident that further studies are needed to understand the association between coffee consumption and the risk of T1D.

COFFEE AND RISK OF GESTATIONAL DIABETES

Gestational diabetes can develop during pregnancy and, if not controlled, may result in serious consequences for the newborn. In most cases, this condition disappears with the end of pregnancy, although women who have had gestational diabetes have a greater risk of developing T2D. During pregnancy, the placenta secretes several hormones to increase the levels of circulating glucose; as a response, the maternal production of insulin increases. If the maternal pancreas cannot produce enough insulin to counteract the increased levels of circulating glucose, gestational diabetes develops.

The effect of prepregnancy consumption of coffee on the onset of gestational diabetes was examined in a single epidemiological study.[53] The study was conducted on a limited number of women ($n = 1,744$) and showed that women with moderate coffee consumption before pregnancy had a lower risk of developing gestational diabetes than women with null consumption. A reduction in risk was still observed in women who continued to drink coffee during pregnancy, but in this case the reduction was not statistically significant.

One experimental study showed that acute consumption of caffeine during pregnancy (i.e., after a single dose) had a negative effect on insulin sensitivity in women with gestational diabetes but had no effect on healthy women.[54]

Even in the case of gestational diabetes, then, it seems there are profound differences between occasional and regular consumption of coffee. In addition, the effect of coffee could vary widely depending on the timing of coffee consumption: prepregnancy consumption seems to be preventive, while consumption after the onset of gestational diabetes could be detrimental. Obviously, the scarcity of studies does not allow for recommendations to be made on the use of coffee during pregnancy to prevent gestational diabetes. In addition, the consumption of coffee during pregnancy may involve other health risks for both mother and child.[55]

THE NUTRIGENOMIC APPROACH: DIFFERENT RISKS FOR DIFFERENT PEOPLE

Epidemiological data indicate that the association of coffee consumption with the development of cardiovascular disease can vary according to the genetic characteristics of individuals. Polymorphisms in the CYP1A2 gene (a gene involved in the metabolism of caffeine) and in the COMT gene (a gene involved in the metabolism of catecholamines) are able to modify the association between coffee consumption and the risk of some pathological conditions, such as cardiovascular events[56,57] and hypertension.[58] A high level of coffee consumption was associated with an increased risk of these diseases only in individuals with a specific polymorphism (i.e., those with slow caffeine or catecholamine metabolism).

Currently, there are no similar studies on the association between coffee consumption and risk of T2D, but the possibility that coffee consumption is more protective against the development of T2D in some particular genotypes cannot be excluded. To date, one epidemiological study has indicated that the association between coffee consumption and the risk of T2D varies depending on the serum levels of the enzyme γ-glutamyl transferase.[18] In particular, the association appeared to be stronger in those individuals who had higher levels of the enzyme. This indication is particularly interesting because high levels of γ-glutamyl transferase are associated with risk factors closely related to diabetes (age, obesity, metabolic syndrome)[59–62] and with diabetes itself.[63,64] Thus, drinking coffee could better protect individuals at increased risk of developing diabetes.

PREVENTION VERSUS TREATMENT OF DIABETES

All of the studies mentioned above refer to the role that coffee can play in the primary prevention of diabetes. Few data are available on the possible influence of coffee consumption on the prognosis of diabetic patients. Some short-term studies have suggested that acute consumption of caffeine has a negative effect on glucose metabolism in T2D subjects through a transient decrease in insulin sensitivity and/or an increase in postprandial glucose levels.[65–68] One of these studies was conducted in free-living habitual coffee drinkers (not subjected to caffeine washout), and thus the authors hypothesized the absence of tolerance development,[9] but this hypothesis needs to be verified.

Studies conducted on T2D patients reported that coffee or caffeine can induce an increase of glucose

and/or insulin blood levels after a glucose load.[67,69] One epidemiological study, however, showed that coffee consumption is associated with a reduced risk of insulin resistance in patients with T2D.[20] To date, the risk of progression of diabetes in subjects with impaired glucose tolerance has been evaluated in a single epidemiological study, which reported that coffee consumption reduces the risk of T2D.[70]

The possibility that coffee consumption could modulate the risk of death due to cardiovascular disease in diabetics was also considered. The cardiovascular risk was three times greater in diabetic subjects than in healthy individuals; thus, any factor helping to control diabetes would have a greater effect on this group than on the general population.

A 20-year follow-up on about 4,000 diabetics indicated that in this group of patients there was an inverse association between habitual coffee consumption and death from cardiovascular disease.[33] Two more recent 20-year follow-up studies on about 10,000 subjects showed no association between habitual coffee consumption (with or without caffeine) and risk of death from cardiovascular disease (and for all causes) in men[23] and women.[71]

There is some evidence to suggest that intake of a single dose of caffeine causes a transient decrease in insulin sensitivity in individuals with T1D,[72] but even in this case, long-term studies are necessary to verify both the effect of coffee as a whole and the possible establishment of a tolerance mechanism. Moreover, there is evidence that acute consumption of caffeine can have positive effects on individuals with T1D. Experimental studies in patients with T1D have indicated that acute ingestion of moderate doses of caffeine and/or daily habitual consumption of caffeine helped to reinforce, and then helped patients to recognize, the warning signals of hypoglycemia and, at the same time, enhanced the hormonal response that counteracts the harmful effects of hypoglycemia.[73,74] Finally, in a study carried out in patients with T1D, regular caffeine consumption positively affected some cardiovascular risk factors.[75]

Although more studies are needed, it seems that drinking coffee is not contraindicated in diabetics (neither type 1 nor type 2), provided that habitual coffee consumption is moderate and inserted within the context of a healthy lifestyle.

POSSIBLE MECHANISMS OF ACTION

Coffee is a complex mixture of thousands of compounds, including caffeine, phenolic compounds, niacin, minerals (magnesium, potassium), and fiber. Many of these compounds may play a role in glucose metabolism and, thus, could affect the development of diabetes. To complicate matters, these different bioactive molecules may affect certain mechanisms, producing antagonistic, additive, and even synergistic effects.

Effects on glucose metabolism: can the paradoxical effect of caffeine be contrasted by phenolic compounds in coffee?

The vast amount of evidence on the protective role of coffee against the development of T2D is in contrast with several experimental observations indicating the adverse effect of caffeine on glucose metabolism. In fact, reduced insulin sensitivity and increased plasma levels of glucose were reported in healthy subjects after acute administration of caffeine (i.e., a single dose after an abstinence period).[76–80] Although one study conducted in the 1970s indicated no such effect,[81] the effect was observed in obese subjects[82] and diabetics.[65,68,83]

It has been hypothesized that a physiological tolerance to caffeine can develop as a result of habitual consumption. Experimental studies to test this hypothesis, however, provided conflicting results: a 5-day consumption of high doses of caffeine induced the development of tolerance toward plasma glucose levels,[84] while a 7-day consumption of caffeine reduced the sensitivity to insulin.[85] However, the duration of both studies was too short to give a conclusive indication, as the tolerance mechanism is induced after longer periods of consumption.[86]

A mechanism of tolerance would be consistent with the hypothesis that the effects of caffeine on glucose metabolism are mediated by the increased plasma concentrations of epinephrine. In fact, the effect of epinephrine on glucose metabolism is diametrically opposite to that of insulin, promoting the synthesis of glucose in the liver and inhibiting its uptake from peripheral tissues.[87] The effects of coffee on circulating levels of epinephrine disappear within a few days of caffeine consumption.[88]

Finally, the negative effect of caffeine on insulin sensitivity and glucose tolerance can be modified when caffeine is consumed within a complex mixture such as coffee. In a rather old study, coadministration of coffee with a glucose load reduced postprandial glucose response compared with placebo.[89] After the glucose load, the effect of caffeine (alone) on the plasma concentration of insulin was greater than that of coffee containing the same amount of caffeine; coffee (regular and decaffeinated) induced a lower response to glucose than did placebo.[90] Prolonged high consumption of coffee (4 weeks) induced a process of tolerance on fasting glucose levels but not on insulin,[86] and both regular and decaffeinated coffee reduced the serum concentration of insulin C-peptide (a marker of insulin secretion), suggesting a beneficial effect on insulin sensitivity.[91] Moreover, after glucose load, the glycemic curve was attenuated with

respect to placebo in subjects supplemented with chlorogenic-acid-enriched coffee (but not in those supplemented with regular coffee).[92] This result, added to the analysis of data obtained after consumption of decaffeinated coffee, suggests that other components of coffee may counteract the negative effect of caffeine. One study carried out on rats fed a high-fat diet showed that a 4-week consumption of decaffeinated coffee improved insulin sensitivity.[93] In humans, only one study reported that consumption of decaffeinated coffee adversely affected glucose metabolism, although the effect was less pronounced than that observed with caffeine,[94] while the majority of studies showed no effect[95,96] or even a reduction of glucose response to glucose load after both acute[90] and chronic[9] consumption.

Thus, other components of coffee might reduce or even antagonize the negative effects of caffeine on glucose metabolism. This hypothesis seems to be confirmed by epidemiological studies that demonstrated a lower prevalence of hyperinsulinemia,[19,33] an increased insulin sensitivity,[50,97] a reduced risk of insulin resistance,[20,98] and a lower plasma glucose level 2 h after glucose load[17,19,97,99] in regular consumers of coffee.

Some authors studied the possibility that phenolic compounds in coffee were responsible for the antagonistic effect against caffeine. In animal models, consumption of chlorogenic acid (and/or its derivatives) or plant extracts rich in chlorogenic acid reduced fasting plasma glucose,[100–102] increased sensitivity to insulin,[103] and slowed the appearance of glucose in circulation after glucose load.[96,104] In addition, it is known that some metabolites of chlorogenic acids (such as ferulic acid and isoferulic acid) also exert a hypoglycemic effect.[105,106]

Several mechanisms were proposed to explain how chlorogenic acid could affect glucose homeostasis. In an in vitro study conducted on vesicles of rat intestine membrane, chlorogenic acid reduced the intestinal absorption of glucose through inhibition of Na^+-dependent glucose transporter.[107] A study using the same experimental model demonstrated that caffeic acid has a weak inhibitory activity against sucrase activity (an enzyme involved in the digestion of carbohydrates).[107] In in vitro studies conducted on rat and human liver microsomes, chlorogenic acid was able to inhibit glucose 6-phosphatase, a key enzyme in the production of glucose in the liver.[108–110] Finally, in a cellular model, chlorogenic acid enhanced the uptake of glucose by myotubes through the increased expression of the glucose transporter GLUT 4.[111]

In humans, decaffeinated coffee modified the postprandial secretion of the gastrointestinal hormones secreted in response to glucose absorption and involved in its metabolism (glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1), suggesting that coffee may delay intestinal glucose uptake by shifting glucose absorption to a more distal region of the gastrointestinal tract.[95]

Thus, chlorogenic acid could slow complex carbohydrate catabolism, inhibit glucose absorption in the intestine, reduce the mobilization of glucose by the liver, and increase the uptake of glucose by the peripheral tissues. These effects may explain why coffee consumption has a greater effect on postload glucose concentration than on fasting levels.[34,86,99]

It should also be added that an increase in the secretion of glucagon-like peptide 1 might exert a trophic effect on pancreatic beta cells and thus may protect or reverse the beta-cell dysfunction observed in the development of T2D.[112] Finally, in an experimental study conducted in cellular and animal models, ferulic acid (a metabolite of chlorogenic acid) stimulated insulin secretion by pancreatic beta cells, and this effect influenced plasma glucose concentration.[113]

An effect on glucose metabolism was also suggested for two other coffee compounds: trigonelline and magnesium. Trigonelline is a precursor of vitamin B_3 and represents about 1% of the dry weight of roasted coffee beans[114]; its content in coffee ranges from 50 mg to 100 mg per cup.[96,115,116] An experimental study conducted in an animal model showed that trigonelline exerts a hypoglycemic effect.[117] However, these data have not been confirmed in human studies; in fact, supplementation with high doses of trigonelline in humans had no effect on glucose metabolism, except in the very short term (15 min after glucose load).[96]

Coffee is rather rich in magnesium (espresso, about 30 mg/cup; American coffee, 7 mg/cup) (US Department of Agriculture nutritional tables), although its contribution to the US recommended dietary allowance (RDA) is quite low (1 cup can contain from 2% to 8% of the RDA). Several studies showed that magnesium may have a positive effect on glucose metabolism by increasing insulin sensitivity.[118] However, this mechanism does not seem to be confirmed by epidemiological studies on the relationship between coffee and T2D; in fact, after adjusting for consumption of magnesium, the inverse association between coffee consumption and diabetes risk persists.[15,22,119]

Thermogenic effect

Some authors hypothesized that the protective effect of coffee could be due to the thermogenic effect of caffeine, which, by increasing the energy expenditure, indirectly could reduce the risk of obesity (a major risk factor for diabetes) (see Greenberg et al.[120] for a review). In animal models, caffeine intake increased the thermogenesis of brown adipose tissue (upregulating the expression of uncoupling protein).[121] In humans, the regular consump-

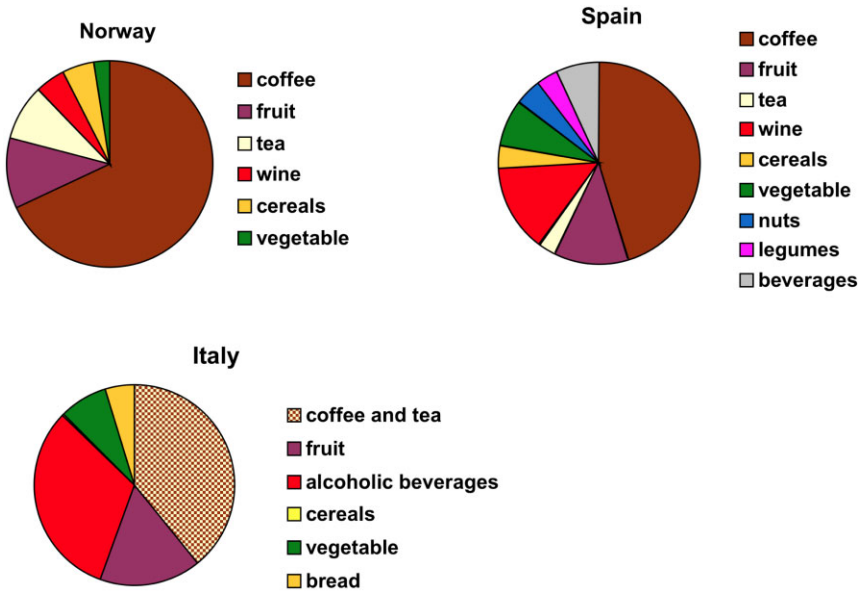

Figure 2 **Contribution of different food groups to dietary antioxidant intake.** Data from Svilaas et al. (Norway),[137] Pellegrini et al. (Italy),[138] and Saura-Calixto and Goñi (Spain).[139]

tion of caffeine increased energy expenditure and stimulated lipid oxidation.[122] Some studies in humans suggested that caffeine consumption stimulates lipolysis.[123,124] Finally, caffeine seems able to increase the sense of satiety.[125,126]

An inverse association between caffeine intake and body weight was observed in epidemiological studies, confirming this evidence.[127] The activation of energy metabolism could be promoted by induction of catecholamine release or by antagonism with the adenosine receptor.[120]

Coffee consumption can also stimulate thermogenesis in humans,[128] but the effect seems to depend on caffeine, because there was no effect when decaffeinated coffee was consumed.[129] However, some studies seem to indicate that the phenolic compounds in coffee might also have an effect on weight control. The phenolic compounds in coffee reduced diet-induced body weight gain and fat accumulation in C57BL/6J mice.[130] In overweight subjects, a chlorogenic-acid-rich supplement was significantly more effective than placebo in helping to reduce body weight,[131,132] and the consumption of coffee enriched with chlorogenic acid for 3 months resulted in a significant reduction in body weight and fat mass.[92]

Antioxidant effect

Coffee is extremely rich in antioxidants, particularly phenolic compounds (mainly chlorogenic acids) and melanoidins; in addition, caffeine shows a slight antioxidant activity.[133,134] Brewed coffee possesses a very high antioxidant capacity in vitro[135,136] and is one of the major contributors to the antioxidant capacity of the diet in many countries[137–139] (Figure 2). It is noteworthy that coffee antioxidants are bioavailable; in fact, several animal and human studies demonstrated that coffee consumption increases plasma antioxidant capacity.[140–142]

Oxidative stress induced by chronic hyperglycemia plays an important role in the process that leads to the dysfunction of pancreatic beta cells (followed by a reduced production and secretion of insulin),[143] a process that can be prevented by other antioxidants.[144] In epidemiological studies, the consumption of dietary antioxidants (especially vitamin E) was associated with increased protection against the risk of T2D,[145] but this effect was not confirmed by experimental studies.[146,147]

The antioxidants in coffee could protect pancreatic beta cells from oxidative stress. An experimental study conducted in an animal model showed that 24-day consumption of the lignan secoisolariciresinol diglucoside (a coffee antioxidant) can reduce by 75% the development of diabetes induced by streptozotocin.[148]

Anti-inflammatory effect

A state of subclinical inflammation is heavily involved in the pathogenesis of T2D; for this reason, substances with anti-inflammatory activity may putatively reduce the risk of T2D. There is much experimental evidence indicating that phenolic compounds can regulate the cellular processes that lead to inflammatory response. These observations are also valid for chlorogenic acid,[149] caffeic acid,[150,151] and ferulic acid,[152,153] the main phenolic compounds of coffee.

An excessive action of glucocorticoids seems to play an important role in the pathogenesis of diabetes and metabolic syndrome.[154] One experimental study conducted on a cellular model showed that coffee may inhibit the reactivation of glucocorticoids by inhibiting 11β-hydroxysteroid dehydrogenase.[155]

An anti-inflammatory role was also suggested for caffeine (see Horrigan et al.[156] for an extensive review), which, at high doses, can protect pancreatic beta cells from toxicity induced by streptozotocin in rats.[157]

Chelating effect

Polyphenols have a well-known chelating capacity and may therefore reduce the absorption of iron; some authors have suggested that coffee polyphenols may act through this mechanism.[158] Prospective studies showed that high iron stores are associated with an increased risk of T2D independently of other known risk factors for diabetes.[159,160] However, although there are indications that coffee can transiently reduce iron absorption when consumed with a meal,[161] there is no evidence that a prolonged and habitual consumption of coffee reduces iron stores in the body.

CONCLUSION

The studies conducted thus far provide a clear indication that healthy, habitual coffee drinkers are more protected from the risk of contracting diabetes than individuals who do not drink coffee. The protective effects of coffee are not likely due to caffeine, as there is strong evidence that decaffeinated coffee offers protective benefits as well. This, obviously, does not justify recommending an increase in coffee consumption as a strategy to prevent diabetes, since high consumption of coffee may have other effects on health (some of which remain to be elucidated). As highlighted in this review, some aspects of the relationship between coffee and diabetes are not yet clarified and warrant further investigation, such as the role of coffee consumption in the prevention of T1D and gestational diabetes; the role of coffee consumption in the prognosis of T2D, T1D, and gestational diabetes; and the mechanisms through which coffee prevents T2D.

The study of the relationship between diet and health in humans needs to consider dietary habits overall and should not be limited to the direct effect of a single food. For these reasons, the influence of coffee consumption on diabetes should always be studied within the context of healthy eating habits and lifestyle: the best way to prevent diabetes remains to combat overweight and obesity and ensure an adequate level of physical activity.

Acknowledgment

Declaration of interest The authors have no relevant interests to declare.

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