# Is Coffee and Green Tea Consumption Related to Serum Levels of Adiponectin and Leptin?

#### Abstract

Coffee and green tea are two of most usual consumed beverages in the world which have several benefit components. Coffee and green tea have significantly inverse correlation with obesity, diabetes, and cardiovascular diseases. Adiponectin and leptin are the adipokines mostly secreted from adipose tissue and play the important roles on the status of chronic diseases. In the present study, we aimed to review the evidence about relationship between these beverages and adiponectin and leptin levels. We searched in PubMed to January 2013 using several key words such as coffee, green tea, caffeine, leptin, adiponectin, and adipokines. Finally, most related articles were recruited in this regard. Several findings suggested the positive association between coffee and adiponectin level. Different studies showed contradictory results regarding green tea and adiponectin level. However, most of them reported the positive role of green tea in adiponectin concentration. Fewer studies are conducted about the association between these beverages and leptin, and their results are controversial. More longitudinal investigations should be conducted in this regard to declare these associations.

Keywords: Adipokine, adiponectin, caffeine, coffee, green tea, leptin

#### Introduction

Coffee is considered one of the most widely consumed hot beverages in the world. Several studies were conducted regarding the effects of coffee on health and prevention of chronic diseases. According to large body of evidence, coffee and its many components including caffeine, phenolic acid, and antioxidants display the protective roles on obesity, diabetes, and inflammation.<sup>[1-3]</sup>

Green tea is considered as one of the other hot consumed beverages, especially in Asian population which has the antioxidant properties. Green tea exerts cardioprotective effects and reduces the mortality from the cardiovascular diseases.<sup>[4-6]</sup> Several epidemiologic, experimental, and clinical trials examined the probable relationship between coffee and green tea consumption with changes of the serum levels of adiponectin and leptin.<sup>[2-7]</sup> The mechanism underlying these beverages' favorable actions against chronic diseases is not well known.

Adiponectin hormone is the adipose tissue-derived protein and acts as anti-obesity, anti-inflammation, and cardioprotective effects.<sup>[8]</sup> Leptin is another hormone mostly secreted from adipose tissue which is regulated by ob gene and plays an important role on appetite, energy expenditure, and thermogenesis, which may lead to weight loss.<sup>[9,10]</sup> Given the benefit roles of coffee and green tea on prevention of chronic diseases and also the important roles of these hormones on health status, we hypothesized that the association between these two beverages with prevention of chronic diseases is partly mediated through the changes of adiponectin and leptin. In this review, we aimed to focus on the correlation between coffee and green tea with adipokines.

#### Methods

We searched in PubMed search engine the related articles in this regard, to January 2013, using the following key words such as: ("coffee"[tiab] OR "coffee"[Mesh] OR "green tea" [tiab] OR "green tea" [Mesh] OR "caffeine" [Mesh] OR "caffeine" [tiab]) AND ("adiponectin"[tiab] OR "adipokines" [Mesh] OR "leptin" [tiab] OR "leptin" [Mesh] OR "adipocytokine" [tiab] OR "adipokines" [tiab] OR "adiponectin" [Mesh]). All 93 articles have been reviewed. Then, twenty papers of most related articles with cross-sectional,

How to cite this article: Izadi V, Larijani B, Azadbakht L. Is coffee and green tea consumption related to serum levels of adiponectin and leptin? Int J Prev Med 2018;9:106. Vajihe Izadi<sup>1,2</sup>, Bagher Larijani<sup>3</sup>, Leila Azadbakht<sup>1,2,4,5</sup>

<sup>1</sup>Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, <sup>2</sup>Department of Community Nutrition, School of Nutrition and Food Science. Isfahan University of Medical Sciences, Isfahan, Iran, <sup>3</sup>Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran, <sup>4</sup>Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences. Tehran, Iran, <sup>5</sup>Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Address for correspondence: Prof. Leila Azadbakht, Department of Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: azadbakht@hlth.mui. ac.ir



This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

experimental, and clinical trials were recruited in this review, and other articles were excluded owing to lack of direct relation with the present issue, lack of access the full text, or duplication. Studies regarding the relationship between coffee and green tea with adiponectin and leptin are shown in Table 1.

# Coffee, Green Tea, Major Components, and Beneficial Effects

Coffee contains several components like phenolic acids, coffeine, magnesium, N-methylnicotinic acid, quinidine, 3-caffeoylquinic acid (3-CQA) and several anti-oxidants which might have shown to have benefit effects on health.<sup>[11-14]</sup> Chlorogenic acid, the main phenolic acid of coffee, has anti-oxidant properties.<sup>[15]</sup> It can play an important role on reduction of inflammatory factors such as C reactive protein (CRP) which is closely related to obesity and metabolic syndrome.<sup>[2,16]</sup> Studies indicated the prevention effects of coffee on cardio-vascular diseases and cancer.<sup>[2,17]</sup> The constituents of coffee have the positive impact on glucose metabolism, reduce postprandial peak response of glucose and risk of type 2 diabetes can be decreased.<sup>[18,19]</sup>

Caffeine in coffee is well known to be associated with the reduction of body fat mass and it stimulates thermogenesis, lipid oxidation and lipolysis.[20] Additionally, caffeine in coffee leads to enhance satiety, increase thermic effect of food (TEF) and daily energy expenditure and hence it helps to weight loss.<sup>[21]</sup> Coffee consumption due to its caffeine and other components has protective effects on Alzheimer's disease.<sup>[22]</sup> Evidence suggested that decaffeinated coffee also may reduce hunger and elevate the level of satiety hormone PYY.<sup>[23]</sup> Findings from studies indicated that consumption of coffee and tea reduced the risk of cognitive decline especially among women.<sup>[24]</sup> Based on researches, coffee might be considered as a functional food.<sup>[25]</sup> Consumption of coffee independent of caffeine components can lead to lower blood pressure.[26] Moderate consumption of coffee has been recommended by Canadian government's Guildline. Based on this health eating recommendation, consumption of 3 cups of brewed caffeinated coffee (400-450 mg caffeine) is safe.<sup>[27]</sup>

Magnesium in coffee can lead to insulin sensitivity and reduced the risk of diabetes.<sup>[28]</sup> Consumption of  $\geq$ 4 cups/day of coffee was related to attenuate the risk of type 2 diabetes.<sup>[29]</sup> According to investigations, coffee

Table 1: Studies that investigated among association between coffee, green tea, and adipokines					
Study	Type of beverage	Type of hormone	Type of study	Study comments	Results
Rebello et al. <sup>[1]</sup>	Coffee	Adiponectin	Cross-sectional	Conducted among 4139 Asian population	No significant relationship
Imatoh <i>et al</i> . <sup>[46]</sup>	Coffee and green tea	Adiponectin	Cross-sectional	Conducted among 665 Japanese male	Dose response correlation between coffee and adiponectin, no relationship between green tea and adiponectin
Williams <i>et al</i> . <sup>[7]</sup>	Coffee	Adiponectin	Cross-sectional	Conducted among 982 diabetic and 1058 nondiabetic women of NHS study	20% higher level of adiponectin among women who consumed ≥4 cups/day of coffee
Kempf et al. <sup>[2]</sup>	Coffee	Adiponectin	Clinical trial	47 women and men in the age group of 54±9 years and BMI=29.2±4.6	Increase in adiponectin level up to 6% by consumption of 4 and 8 cups of coffee
Yamashita <i>et al.</i> <sup>[3]</sup>	Coffee	Adiponectin and leptin	Cross-sectional	Conducted among 2554 and 763 Japanese employee men and women	Direct and inverse association between consumption of coffee with adiponectin and leptin, respectively
Basu <i>et al</i> . <sup>[4]</sup>	Green tea	Lepton	Clinical trial	35 obese participants with metabolic syndrome in the age group of $42.5\pm1.5$ years	Any significant effect of green tea consumption with the level of leptin
Cho et al. <sup>[6]</sup>	Green tea (catechin)	Adiponectin	Experimental	Mice	Catechin in green tea significantly increased adiponectin
Bruno <i>et al</i> . <sup>[5]</sup>	Green tea	Adiponectin	Experimental	Mice	Extract of green tea could decrease weight, but it had not any significant impact on adiponectin
Sone et al. <sup>[12]</sup>	Green tea	Adiponectin	Randomized clinical trial	Conducted among 51 healthy individuals for 9 weeks	400 and 100 mg of green tea consumption both enhanced the adiponectin concentration

NHS=Nurses' Health Study, BMI=Body mass index

consumption was correlated with lower levels of triglyceride and higher levels of high density lipoprotein (HDL).<sup>[2,3,30]</sup> Based on evidence, coffee consumption is significantly associated with weight loss, amelioration of inflammation and oxidative stress.<sup>[31,32]</sup> In one cross sectional study, consumption of  $\geq$ 4 cups/days of coffee was related to lower levels of CRP and tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) and 20% higher level of adiponectin.<sup>[7]</sup> According to evidence, favorable effects of coffee may partly mediated though relationship with serum levels of adiponectin or leptin.

Green tea is the rich sources of polyphenolic flavonoids. Cathechin is considered as the main flavonoid of green tea which has several pharmacologic activities including antioxidant, anti-inflammation and anti-diabetes properties. Injection of cathechin into rat leads to reduce blood glucose and insulin levels.<sup>[6,33]</sup> According to one investigation, components of green tea could be able to increase glucose metabolism in adipocyte.[34] Habitual consumption of green tea has been correlated with reduced risks of CVD, obesity and dislipidemia.<sup>[4,35,36]</sup> According to epidemiologic studies, green tea consumption is inversely correlated with mortality from CVD and cerebral infarction.[5,37] Epigallocatechingallate (EGCG), bioactive polyphenol of green tea, is substantially attenuate features of metabolic syndrome and diabetes.<sup>[4]</sup> Evidence have indicated the probable beneficial effects of green tea consumption on protection against inflammation, hypertension and diabetes. Given the key role of adipocytokines on attenuate or augmentation of chronic disease, it seems that green tea may act on these metabolic effects mediated via the change of adipocytokines.

# **Functions of Adiponectin and Leptin**

Adiponectin is an adipokine secreted from adipose tissue and contains 244 amino acids, and it is account 0.01% of total plasma protein.<sup>[38]</sup> Obesity leads to reduced levels of adiponectin and increase risk of inflammation which is associated with metabolic syndrome.[38,39] High molecular weight of adiponectin is considered as the most important epimers of adiponectin.<sup>[40]</sup> Large body of evidence has suggested the close relationship between adiponectin and reduced risks of dyslipidemia, CVD, inflammation, and several types of cancer.<sup>[8,38]</sup> Diet-related factors including weight loss diet, healthy dietary pattern as well as protein and polyunsaturated fatty acids (PUFAs) play the important role on adiponectin levels.<sup>[8,38,41,42]</sup> Beside dietary pattern and macronutrients, some beverages such as coffee and green tea display a favorable role on adiponectin level, but it is still under debate.<sup>[3-7]</sup>

Leptin, another adipose tissue secreted hormone, is a 146 amino acid peptids. It has been reported to regulate appetite, energy expenditure, thermogenesis, and regulation of body weight.<sup>[10]</sup> Leptin also regulates food intake, insulin action, and oxidation of free fatty acids.<sup>[43]</sup> Obesity is positively related to increase of leptin. It seems that obesity

might lead to state of leptin resistance. It seems that leptin resistance is induced by the inactivation of leptin receptors which leads to reduce appetite and increase risk for obesity. Hence, any nutrition therapy that elevates leptin action in the central nervous system should decrease food intake, food mass, and concentration of circulating leptin.<sup>[44]</sup> Leptin concentration has been showed to be positively associated with insulin levels and insulin resistance.<sup>[9,10]</sup> According to evidence, diet affects the concentration of leptin. Low-calorie diet, high intake of omega-3 PUFA, and carbohydrate intake are associated with higher level of leptin or leptin sensitivity.<sup>[9,10,43]</sup>

### Adiponectin, Leptin, and Coffee Consumption

#### Coffee and adiponectin

Findings from several studies showed a positive relationship between coffee consumption and serum levels of adiponectin.<sup>[2,3,7]</sup> In a cross-sectional study among 665 male in Japan, those consuming more coffee were found to have higher levels of adiponectin either after adjustment for potential confounders ( $P_{\rm trend} < 0.05$ ). In addition, they observed a dose-response relationship between coffee consumption and adiponectin level.<sup>[45]</sup> Other cross-sectional study among 982 diabetic and 1058 nondiabetic women of Nurses' Health Study indicated that consumption of  $\geq$ 4 cups/day of coffee significantly related to 20% higher of adiponectin concentration (P = 0.04 for nondiabetic and P = 0.004 for diabetic women). However, decaffeinated coffee had no relationship with adiponectin level.<sup>[7]</sup> Other large cross-sectional study in Japan showed a positive correlation between coffee consumption and circulating level of adiponectin (P < 0.001).<sup>[3]</sup>

Association between coffee and adiponectin was suggested not only in observational studies but also in clinical trials.<sup>[2]</sup> In one interventional study conducted among 47 healthy individuals in the age of  $54 \pm 9$  years, consumption of 4 and 8 cups/day for 2 consecutive months was led to substantial increase of 6% in adiponectin concentration (P < 0.05).<sup>[2]</sup> However, in observational study on 4139 Asian participants, there was no relationship between consumption of this beverage and adiponectin after adjustment for several potential confounding factors ( $P_{trend} = 0.34$ ). Author stated that low amounts of coffee consumption in their population may be the reason for not observing the significant relationship in the study.<sup>[1]</sup>

#### Coffee and leptin

Fewer studies examined the roles of coffee on the concentration of leptin and contradictory results are found in this regard.<sup>[3,46,47]</sup> In one observational study there was no significant relationship between leptin and coffee consumption.<sup>[46]</sup> Result from one experimental study indicated that combination of choline, carnitine, and caffeine (the major coffee consumption) is able to reduce serum levels of leptin in rats.<sup>[47]</sup> In a cross-sectional study

among 2554 male and 763 female in Japan, consumption of coffee could reduce leptin concentration (P < 0.001) either after adjustment for potential confounders.<sup>[3]</sup>

To our best knowledge, there is no interventional study in this regard. More investigations (especially cohort and clinical trial) are suggested to clear this relationship.

# Role of Green Tea on Adipokines Levels

We found several studies with the design of experimental, cross-sectional, and clinical trial regarding the association between green tea consumption with adiponectin. Their results were controversial.<sup>[4-6,45,48]</sup> It seems that there is no strong correlation between green tea consumption and adipokines level.

In one randomized clinical trial among 51 healthy individuals, 9 weeks' consumption of green tea with two different dosages of catechin (100 and 400 mg) was enhanced the level of adiponectin in two interventional groups. However, there were no significant differences between two groups.<sup>[48]</sup> In the mentioned study, author stated more than half of participants followed the weight loss program. Although they prescribed two diverse dosages of catechin (the major component of green tea) low dosage of catechin might be sufficient to observe its beneficial effect on adiponectin.<sup>[48]</sup> Consumption of green tea for 8 weeks did not significantly affect on adiponectin and leptin in obese participants with metabolic syndrome.<sup>[4]</sup>

Results from one experimental study suggested that catechin in green tea displays an important role on upregulating of adiponectin expression in rats.<sup>[6]</sup> In contrast, in a cross-sectional study among a sample of male in Japan, no substantial correlation between consumption of green tea and adiponectin levels was found.<sup>[45]</sup> In addition, green tea extract led to weight loss in obese rats, without any significant effect on adiponectin level.<sup>[5]</sup>

# Discussion

Findings from numerous studies indicate that coffee is considered as an important dietary factor related to the elevation of adiponectin level. Coffee may also reduce the concentration of leptin; however, it is still under debate.

Coffee is considered as one of the food sources containing several antioxidants.<sup>[49]</sup> According to studies, dietary intakes play the key role on prevention or promotion of inflammation and obesity.<sup>[50-53]</sup> Beside dietary intakes, coffee may increase insulin sensitivity through the reduction of inflammation.<sup>[54]</sup> In addition, lower levels of adiponectin induce greater risks of inflammation and insulin resistance. It is possible that coffee reduces low-grade inflammation mediated through the elevation of adiponectin.

In one investigation, consumption of coffee enhanced concentration of adiponectin and attenuated level of  $TNF\alpha$  and CRP, and the link between coffee and adiponectin did

not attenuate after adjustment for these inflammatory factors. Author stated that individuals with higher consumption of coffee had significantly lower body mass index and greater level of physical activity.<sup>[7]</sup> Previous studies also indicated the relationship between coffee and CRP mediated through leptin and adiponectin concentration.<sup>[55,56]</sup> Findings suggested that leptin is positively associated with obesity and inflammatory factors which can stimulate the insulin resistance.<sup>[3]</sup> Higher consumption of coffee may have effect on leptin concentration.<sup>[3]</sup>

Caffeine in coffee favorably stimulates the peroxisome proliferator activated receptor  $\gamma$  (a group of nuclear receptor proteins that function as transcription factors regulating the expression of genes) expression. PPAR $\gamma$  positively elevates the adiponectin concentration.<sup>[57]</sup> Recent evidence found that coffee consumption has beneficial effects on increased adiponectin level with decreased levels of leptin as well as lipid profile. Hence, it seems that coffee improves the levels of blood lipids through influence of these adipokines.<sup>[3]</sup>

According to evidence, caffeine in coffee has been shown to cause greater thermogenesis, lipolysis, and lipid oxidation as well as weight loss.<sup>[58]</sup> One study suggested that consumption of 6 cups/day of coffee led to increase in energy expenditure (100 kcal/day).<sup>[59]</sup> In addition, coffee may increase satiety.<sup>[28]</sup>

To our best knowledge, there is no study which examines the possible roles of caffeine and coffee on increased thermogenesis and energy expenditure mediated through the adiponectin and leptin. It is possible that the beneficial effects of coffee on weight loss, improvement of glycemic indices and inflammation as well as reduces risk of CVD are mediated by adiponectin activities. Consumption of coffee among individuals with type 2 diabetes led to greater levels of adiponectin and HDL and decrease in inflammatory markers.<sup>[2]</sup> Given that, cross-sectional studies in this regard have to reach the contradictory results;<sup>[1,3,45]</sup> it seems that more investigations are needed regarding the association between coffee consumption and adiponectin, especially among different population with diverse ethnics and separate sexes because it is possible that other potential factors including genetic, environmental contribution and ethnic differences influence on this relationship.<sup>[60]</sup>

Studies examining the association between green tea and adiponectin are very controversial. Green tea may have relationship with adiponectin, and it is suggested in some observational and clinical trial studies.

Catechin in green tea reduced expression of Kruppel-like factor 7 (KLF7) protein. Evidence indicated that KLF7 inhibits the adiponectin, leptin, and PPARy.<sup>[6]</sup> Furthermore, overexpression of KLF7 suppresses catechin-stimulated adiponectin expression. Consumption of green tea through its catechin attenuates the expression of KLF7 and enhances PPARy and adiponectin expression and secretion.<sup>[6]</sup> Green tea enhances energy expenditure. It is also play the important roles on increase the sympathetic nervous system and elevate thermogenesis through the stimulating the norepinephrine secretion. Green tea and catechin display the key role on fatty acid oxidation and weight loss.<sup>[5,61,62]</sup> Adiponectin involves in fatty acid and glucose metabolism as well as insulin sensitivity and weight loss.<sup>[63]</sup> It is possible that green tea consumption beneficially affects metabolic pathways through increase in adiponectin.<sup>[5]</sup>

We suggested more investigations to examine relationship between coffee, adiponectin, and leptin. Regarding coffee and adipokines, there is no cohort study. Cross-sectional studies have reported positive roles of coffee on adiponectin concentration.<sup>[3,7]</sup> It is possible that coffee has diverse effects in different population.<sup>[60]</sup> In addition, the amount of coffee consumption which can improve levels of adiponectin is not clearly confirmed. The potential mechanism in this regard also is debated. It is affect adiponectin or it has favorable impact through the weight loss and improvement of metabolic effects.

To our knowledge, there is one study regarding the green tea and leptin. More studies should be conducted regarding green tea, leptin, and adiponectin. However, green tea may involve the changes in adiponectin concentration through weight loss.<sup>[5]</sup>

#### Conclusions

Fewer studies are conducted about the possible role of green tea and coffee with concentration of leptin. Based on several studies, coffee involves to increase the levels of adiponectin by the unknown mechanisms. Green tea because of its catechin and other components may beneficially influence on the circulation of adiponectin. However, more investigation should be conducted in future.

#### Financial support and sponsorship

The authors would like to thank Isfahan University of Medical Sciences, Isfahan, Iran.

#### **Conflicts of interest**

There are no conflicts of interest.

Received: 21 Jan 14 Accepted: 04 Jul 17 Published: 05 Dec 18

#### References

- 1. Rebello SA, Chen CH, Naidoo N, Xu W, Lee J, Chia KS, *et al.* Coffee and tea consumption in relation to inflammation and basal glucose metabolism in a multi-ethnic Asian population: A cross-sectional study. Nutr J 2011;10:61.
- Kempf K, Herder C, Erlund I, Kolb H, Martin S, Carstensen M, et al. Effects of coffee consumption on subclinical inflammation and other risk factors for type 2 diabetes: A clinical trial. Am J Clin Nutr 2010;91:950-7.
- 3. Yamashita K, Yatsuya H, Muramatsu T, Toyoshima H, Murohara T, Tamakoshi K, *et al.* Association of coffee

- 4. Basu A, Du M, Sanchez K, Leyva MJ, Betts NM, Blevins S, *et al.* Green tea minimally affects biomarkers of inflammation in obese subjects with metabolic syndrome. Nutrition 2011;27:206-13.
- 5. Bruno RS, Dugan CE, Smyth JA, DiNatale DA, Koo SI. Green tea extract protects leptin-deficient, spontaneously obese mice from hepatic steatosis and injury. J Nutr 2008;138:323-31.
- Cho SY, Park PJ, Shin HJ, Kim YK, Shin DW, Shin ES, et al. (-)-catechin suppresses expression of kruppel-like factor 7 and increases expression and secretion of adiponectin protein in 3T3-L1 cells. Am J Physiol Endocrinol Metab 2007;292:E1166-72.
- 7. Williams CJ, Fargnoli JL, Hwang JJ, van Dam RM, Blackburn GL, Hu FB, *et al.* Coffee consumption is associated with higher plasma adiponectin concentrations in women with or without type 2 diabetes: A prospective cohort study. Diabetes Care 2008;31:504-7.
- Izadi V, Farabad E, Azadbakht L. Serum adiponectin level and different kinds of cancer: A review of recent evidence. ISRN Oncol 2012;2012:982769.
- Cha MC, Jones PJ. Dietary fat type and energy restriction interactively influence plasma leptin concentration in rats. J Lipid Res 1998;39:1655-60.
- Kratz M, von Eckardstein A, Fobker M, Buyken A, Posny N, Schulte H, *et al.* The impact of dietary fat composition on serum leptin concentrations in healthy nonobese men and women. J Clin Endocrinol Metab 2002;87:5008-14.
- 11. Shearer J, Farah A, de Paulis T, Bracy DP, Pencek RR, Graham TE, *et al.* Quinides of roasted coffee enhance insulin action in conscious rats. J Nutr 2003;133:3529-32.
- 12. Rodríguez-Morán M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: A randomized double-blind controlled trial. Diabetes Care 2003;26:1147-52.
- Clifford MN. Chlorogenic acid and other cinnamates-nature, occurrence, dietary burden, absorption and metabolism. J Sci Food Agric 2000;80:1033-43.
- Ruiz-Crespo S, Trejo-Gabriel-Galan JM, Cavia-Saiz M, Muñiz P. Coffee component 3-caffeoylquinic acid increases antioxidant capacity but not polyphenol content in experimental cerebral infarction. Neurochem Res 2012;37:1085-90.
- 15. Tunnicliffe JM, Shearer J. Coffee, glucose homeostasis, and insulin resistance: Physiological mechanisms and mediators. Appl Physiol Nutr Metab 2008;33:1290-300.
- Hilpert KF, Kris-Etherton PM, West SG. Lipid response to a low-fat diet with or without soy is modified by C-reactive protein status in moderately hypercholesterolemic adults. J Nutr 2005;135:1075-9.
- Malerba S, Galeone C, Pelucchi C, Turati F, Hashibe M, La Vecchia C, *et al.* A meta-analysis of coffee and tea consumption and the risk of glioma in adults. Cancer Causes Control 2013;24:267-76.
- 18. Rodriguez de Sotillo DV, Hadley M. Chlorogenic acid modifies plasma and liver concentrations of: Cholesterol, triacylglycerol, and minerals in (fa/fa) zucker rats. J Nutr Biochem 2002;13:717-26.
- Johnston KL, Clifford MN, Morgan LM. Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: Glycemic effects of chlorogenic acid and caffeine. Am J Clin Nutr 2003;78:728-33.

- Astrup A, Toubro S, Cannon S, Hein P, Breum L, Madsen J, et al. Caffeine: A double-blind, placebo-controlled study of its thermogenic, metabolic, and cardiovascular effects in healthy volunteers. Am J Clin Nutr 1990;51:759-67.
- Westerterp-Plantenga MS, Lejeune MP, Kovacs EM. Body weight loss and weight maintenance in relation to habitual caffeine intake and green tea supplementation. Obes Res 2005;13:1195-204.
- 22. Cao C, Wang L, Lin X, Mamcarz M, Zhang C, Bai G, et al. Caffeine synergizes with another coffee component to increase plasma GCSF: Linkage to cognitive benefits in Alzheimer's mice. J Alzheimers Dis 2011;25:323-35.
- 23. Greenberg JA, Geliebter A. Coffee, hunger, and peptide YY. J Am Coll Nutr 2012;31:160-6.
- 24. Arab L, Khan F, Lam H. Epidemiologic evidence of a relationship between tea, coffee, or caffeine consumption and cognitive decline. Adv Nutr 2013;4:115-22.
- Dórea JG, da Costa TH. Is coffee a functional food? Br J Nutr 2005;93:773-82.
- Tse SY. Cholinomimetic compound distinct from caffeine contained in coffee. II: Muscarinic actions. J Pharm Sci 1992;81:449-52.
- Health Canada Food Program. Fact sheet—it's your health: Caffeine. Ottawa, Canada: Health Canada, 2006. Internet: Available from: http://www.hcsc. gc.ca/food-aliment/dg/e\_ caffeine.html. [Last accessed on 2006 Jul 26].
- Greenberg JA, Boozer CN, Geliebter A. Coffee, diabetes, and weight control. Am J Clin Nutr 2006;84:682-93.
- 29. van Dam RM, Hu FB. Coffee consumption and risk of type 2 diabetes: A systematic review. JAMA 2005;294:97-104.
- Lancaster T, Muir J, Silagy C. The effects of coffee on serum lipids and blood pressure in a UK population. J R Soc Med 1994;87:506-7.
- Lopez-Garcia E, van Dam RM, Qi L, Hu FB. Coffee consumption and markers of inflammation and endothelial dysfunction in healthy and diabetic women. Am J Clin Nutr 2006;84:888-93.
- Kono S, Shinchi K, Imanishi K, Todoroki I, Hatsuse K. Coffee and serum gamma-glutamyltransferase: A study of self-defense officials in japan. Am J Epidemiol 1994;139:723-7.
- Kao YH, Hiipakka RA, Liao S. Modulation of endocrine systems and food intake by green tea epigallocatechin gallate. Endocrinology 2000;141:980-7.
- Broadhurst CL, Polansky MM, Anderson RA. Insulin-like biological activity of culinary and medicinal plant aqueous extracts *in vitro*. J Agric Food Chem 2000;48:849-52.
- Wu CH, Lu FH, Chang CS, Chang TC, Wang RH, Chang CJ, et al. Relationship among habitual tea consumption, percent body fat, and body fat distribution. Obes Res 2003;11:1088-95.
- Imai K, Nakachi K. Cross sectional study of effects of drinking green tea on cardiovascular and liver diseases. BMJ 1995;310:693-6.
- Larsson SC, Männistö S, Virtanen MJ, Kontto J, Albanes D, Virtamo J, *et al.* Coffee and tea consumption and risk of stroke subtypes in male smokers. Stroke 2008;39:1681-7.
- Izadi V, Farabad E, Azadbakht L. Epidemiologic evidence on serum adiponectin level and lipid profile. Int J Prev Med 2013;4:133-40.
- Azadbakht L, Esmaillzadeh A. Red meat intake is associated with metabolic syndrome and the plasma C-reactive protein concentration in women. J Nutr 2009;139:335-9.
- Calle EE, Kaaks R. Overweight, obesity and cancer: Epidemiological evidence and proposed mechanisms. Nat Rev Cancer 2004;4:579-91.

- 41. Kratz M, Swarbrick MM, Callahan HS, Matthys CC, Havel PJ, Weigle DS, *et al.* Effect of dietary n-3 polyunsaturated fatty acids on plasma total and high-molecular-weight adiponectin concentrations in overweight to moderately obese men and women. Am J Clin Nutr 2008;87:347-53.
- 42. Fargnoli JL, Fung TT, Olenczuk DM, Chamberland JP, Hu FB, Mantzoros CS, *et al.* Adherence to healthy eating patterns is associated with higher circulating total and high-molecular-weight adiponectin and lower resistin concentrations in women from the nurses' health study. Am J Clin Nutr 2008;88:1213-24.
- Roberts CK, Berger JJ, Barnard RJ. Long-term effects of diet on leptin, energy intake, and activity in a model of diet-induced obesity. J Appl Physiol (1985) 2002;93:887-93.
- 44. Weigle DS, Cummings DE, Newby PD, Breen PA, Frayo RS, Matthys CC, *et al.* Roles of leptin and ghrelin in the loss of body weight caused by a low fat, high carbohydrate diet. J Clin Endocrinol Metab 2003;88:1577-86.
- 45. Imatoh T, Tanihara S, Miyazaki M, Momose Y, Uryu Y, Une H. Coffee consumption but not green tea consumption is associated with adiponectin levels in Japanese Male. Eur J Nutr 2011;50:279-89.
- Lagiou P, Signorello LB, Mantzoros CS, Trichopoulos D, Hsieh CC, Trichopoulou A, *et al.* Hormonal, lifestyle, and dietary factors in relation to leptin among elderly men. Ann Nutr Metab 1999;43:23-9.
- 47. Hongu N, Sachan DS. Caffeine, carnitine and choline supplementation of rats decreases body fat and serum leptin concentration as does exercise. J Nutr 2000;130:152-7.
- Sone T, Kuriyama S, Nakaya N, Hozawa A, Shimazu T, Nomura K, *et al.* Randomized controlled trial for an effect of catechin-enriched green tea consumption on adiponectin and cardiovascular disease risk factors. Food Nutr Res 2011;55. Doi: 10.3402/fnr.v55i0.8326.
- Tunnicliffe JM, Shearer J: Coffee, glucose homeostasis, and insulin resistance: physiological mechanisms and mediators. Appl Physiol Nutr Metab 2008;33:1290-300.
- 50. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC, *et al.* Fruit and vegetable intakes, C-reactive protein, and the metabolic syndrome. Am J Clin Nutr 2006;84:1489-97.
- Esmaillzadeh A, Azadbakht L. Legume consumption is inversely associated with serum concentrations of adhesion molecules and inflammatory biomarkers among iranian women. J Nutr 2012;142:334-9.
- 52. Azadbakht L, Haghighatdoost F, Karimi G, Esmaillzadeh A. Effect of consuming salad and yogurt as preload on body weight management and cardiovascular risk factors: A randomized clinical trial. Int J Food Sci Nutr 2013;64:392-9.
- 53. Miraghajani MS, Esmaillzadeh A, Najafabadi MM, Mirlohi M, Azadbakht L. Soy milk consumption, inflammation, coagulation, and oxidative stress among type 2 diabetic patients with nephropathy. Diabetes Care 2012;35:1981-5.
- Ndumele CE, Pradhan AD, Ridker PM. Interrelationships between inflammation, C-reactive protein, and insulin resistance. J Cardiometab Syndr 2006;1:190-6.
- 55. Hukshorn CJ, Lindeman JH, Toet KH, Saris WH, Eilers PH, Westerterp-Plantenga MS, *et al.* Leptin and the proinflammatory state associated with human obesity. J Clin Endocrinol Metab 2004;89:1773-8.
- 56. Sun H, Zhang Y, Gao P, Li Q, Sun Y, Zhang J, *et al.* Adiponectin reduces C-reactive protein expression and downregulates STAT3 phosphorylation induced by IL-6 in HepG2 cells. Mol Cell Biochem 2011;347:183-9.
- 57. Gressner OA, Lahme B, Rehbein K, Siluschek M,

Weiskirchen R, Gressner AM, *et al.* Pharmacological application of caffeine inhibits TGF-beta-stimulated connective tissue growth factor expression in hepatocytes via PPARgamma and SMAD2/3-dependent pathways. J Hepatol 2008;49:758-67.

- Astrup A, Breum L, Toubro S, Hein P, Quaade F. The effect and safety of an ephedrine/caffeine compound compared to ephedrine, caffeine and placebo in obese subjects on an energy restricted diet. A double blind trial. Int J Obes Relat Metab Disord 1992;16:269-77.
- Dulloo AG, Geissler CA, Horton T, Collins A, Miller DS. Normal caffeine consumption: Influence on thermogenesis and daily energy expenditure in lean and postobese human volunteers. Am J Clin Nutr 1989;49:44-50.
- 60. Kotani K, Fujiwara S, Hamada T, Tsuzaki K, Sakane N. Coffee

consumption is associated with higher plasma adiponectin concentrations in women with or without type 2 diabetes: Response to Williams *et al.* Diabetes Care 2008;31:e46.

- 61. Kao YH, Chang HH, Lee MJ, Chen CL. Tea, obesity, and diabetes. Mol Nutr Food Res 2006;50:188-210.
- Moon HS, Lee HG, Choi YJ, Kim TG, Cho CS. Proposed mechanisms of (-)-epigallocatechin-3-gallate for anti-obesity. Chem Biol Interact 2007;167:85-98.
- 63. Bahceci M, Gokalp D, Bahceci S, Tuzcu A, Atmaca S, Arikan S, et al. The correlation between adiposity and adiponectin, tumor necrosis factor alpha, interleukin-6 and high sensitivity C-reactive protein levels. Is adipocyte size associated with inflammation in adults? J Endocrinol Invest 2007;30:210-4.