

## Coffee Consumption and Cardiovascular Diseases – Has the Time Come to Change Dietary Advice? A Mini Review

Regina Wierzejska

Department of Nutrition and Dietetics with Clinic of Metabolic Diseases and Gastroenterology,  
National Food and Nutrition Institute, Powsińska St. 61/63, 02–903 Warsaw, Poland

**Key words:** coffee, cardiovascular diseases; cholesterol, polyphenols

The question whether coffee has a negative or a positive impact on human health has been the topic of much heated debate for years. Nevertheless, recent studies have not only failed to confirm earlier concerns, but in fact suggested a positive effect of coffee intake. Latest studies revealed that people who drink at least 3 cups of coffee per day are at a lower risk for type 2 diabetes, as well as liver and colon cancer. The reports on a possible correlation between coffee drinking and heart diseases have also generated optimistic results. No adverse associations between coffee consumption and coronary heart disease, stroke, and hypertension have been found. What is more, some authors demonstrated that coffee drinking may prevent cardiovascular diseases. Composition of coffee is determined by the strength of the brew and brewing methods. Unfiltered coffee is rich in cholesterol-raising diterpenes, therefore patients with dyslipidemia should be advised to drink filtered rather than non-filtered coffee. On the other hand coffee contains polyphenols which act as antioxidants, and these compounds are probably responsible for the suggested beneficial effect of coffee on health. This article summarizes the current literature reports on this controversial topic.

### INTRODUCTION

Coffee consumption is associated with diverse health effects. Owing to its widespread popularity, the effects of coffee on health, including cardiovascular diseases, cancer, osteoporosis, diabetes and neurological diseases, have been extensively studied for many years. Two and three decades ago consumption of coffee was predominantly reported to constitute a risk factor and the impact of coffee on health remains controversial until today. However, recent research has suggested that coffee consumption has no adverse effects and may even help prevent several chronic diseases, including type 2 diabetes mellitus, liver cancer and Parkinson's disease [Akash *et al.*, 2014; Butt & Sultan, 2011; Floegel *et al.*, 2012; Higdon & Frei, 2006; Lopez-Garcia *et al.*, 2011; Sudano *et al.*, 2005]. For example, data from Finland indicates lower mortality and morbidity rates among coffee drinkers as compared to non-drinkers with regard to many common chronic diseases [Tuomilehto, 2013].

### COFFEE AND CARDIOVASCULAR HEALTH

Longitudinal studies have generated conflicting data about the effects of coffee consumption on the cardiovascular system. Meta-analysis of case-control studies conducted

in the 90s revealed that people who consumed  $\geq 5$  cups of coffee per day were at a 60% higher risk of coronary heart disease than their non-drinking peers [Kawachi *et al.*, 1994]. Recent publications have been more optimistic and most of them suggest that coffee consumption not only does not constitute a cardiovascular risk factor, and may in fact be beneficial to health [Akash *et al.*, 2014; Corti *et al.*, 2005; Higdon & Frei, 2006; Lopez-Garcia *et al.*, 2011; Sudano *et al.*, 2005].

Case-control and cohort studies have brought inconsistent results. The former have mostly demonstrated an increased risk of cardiovascular diseases (CVD) among regular coffee consumers [Kawachi *et al.*, 1994; Riksen *et al.*, 2009; Sofi *et al.*, 2007], whereas the latter have found no evidence of a detrimental effect of coffee [Higdon & Frei, 2006; Lopez-Garcia *et al.*, 2011; Silletta & Marchioli, 2008], and reported a lower risk of coronary heart disease to be correlated with coffee consumption [de Koning *et al.*, 2010; Kleemola *et al.*, 2000; Woodward & Tunstall-Pedoe, 1999].

Numerous studies conducted by Lopez Garcia *et al.* have provided strong evidence against the hypothesis that coffee consumption increases the risk of cardiovascular diseases [Lopez-Garcia *et al.*, 2006, 2011]. They found that long-term coffee consumption (even 6 cups/day) does not increase the risk of coronary heart disease, stroke, and premature death due to cardiovascular diseases. Woodward and Tunstall-Pedoe [1999] revealed that an intake of 3–4 cups of coffee per day is associated with a lower risk of cardiovascular diseases among men but not among women. Three

\* Corresponding Author: Tel.: +4822 550 97 47; Fax: +4822 842 11 03  
E-mail: [rwierzejska@izz.waw.pl](mailto:rwierzejska@izz.waw.pl) (R. Wierzejska)

meta-analyses of prospective cohort trials concerning this matter have recently been published. A meta-analysis by Wu *et al.* [2009] suggested that moderate coffee consumption (>1–2 cups/day) may decrease a long-term risk of coronary heart disease by 13%. Ding *et al.* [2014] concluded that moderate coffee consumption was inversely associated with CVD risk, with the lowest risk at 3–5 cups of coffee per day, and that heavy coffee consumption was not associated with elevated CVD risk. In turn, Mostofsky *et al.* [2012] reported an inverse association between moderate coffee consumption and risk of heart failure, with the strongest inverse association (11% decrease) observed for 4 servings of coffee a day. According to a scientific statement of the American Heart Association, coffee consumption is a minor clinical risk factor for heart failure [Schocken *et al.*, 2008].

Similar conclusions concern a potential correlation between coffee and stroke. Meta-analysis of the prospective studies, as well as epidemiologic studies published in 2011 and 2012, found that coffee consumption was not associated with a higher risk of stroke and that habitual moderate coffee consumption may even have a protective effect on stroke [Larsson & Orsini, 2011; Kim *et al.*, 2012].

Some authors also examined the impact of coffee drinking on the risk of atherosclerosis. One study has shown an inverse association [van Woudenberg *et al.*, 2008], whereas the second study provided no evidence that coffee has either beneficial or harmful impact on coronary and carotid atherosclerosis [Reis *et al.*, 2010].

Studies on the association between coffee consumption and mortality in patients with CVD have generated conflicting results. Some researchers found that heavy coffee consumption was significantly related to a higher risk of sudden cardiac death, but other studies found no association or lower risk of CVD events [Lopez-Garcia *et al.*, 2011]. A cohort study conducted by Bidel *et al.* [2006] revealed that drinking >2 cups of coffee per day is associated with reduced CVD mortality among patients with type 2 diabetes mellitus.

Mixed results of the above mentioned studies may be conditioned by inadequate adjustment for many confounding factors, such as smoking, diet, variation in cup sizes and brewing methods [Silletta & Marchioli, 2008].

#### **IMPACT OF COFFEE ON BLOOD LIPIDS AND HOMOCYSTEINE CONCENTRATIONS**

Coffee is a complex mixture of many biologically active substances that may have either beneficial or harmful impact on health [Silletta & Marchioli, 2008]. To a large extent, the components found in coffee depend on the brewing method. Unfiltered coffee is rich in cholesterol-raising diterpenes, including cafestol and kahweol [Cano-Marquina *et al.*, 2013; O’Keefe *et al.*, 2013; van Dam, 2008], whereas filtered coffee has by far lower concentrations of these compounds, because of the shorter contact with hot water and retention of diterpenes by the filter paper [Higdon & Frei, 2006; O’Keefe *et al.*, 2013].

The literature indicates a strong relationship between unfiltered coffee consumption and elevated cholesterol and tri-

glyceride levels, whereas paper-filtered coffee has been less frequently reported to raise the levels of these lipids [Dworzański *et al.*, 2011; Ranheim & Halvorsen, 2005]. A positive association between unfiltered coffee drinking and plasma cholesterol concentration has been revealed, especially by a study from Scandinavia, where coffee grounds are traditionally boiled without filtering [Weusten-Van der Wouw *et al.*, 1994; Urgert & Katan, 1996]. Studies from the United States and the United Kingdom, where filtered coffee is extremely popular, did not report a significant association [Riksen *et al.*, 2009]. In contrast, Corrêa *et al.* [2013], in a randomized clinical trial found that drinking 3–4 cups of paper-filtered coffee per day for 4 weeks increased total cholesterol concentration and low-density lipoprotein-cholesterol by 10–12% and 12–14%, respectively.

The conclusions of meta-analyses from 2001 and 2012, that consumption of unfiltered coffee increases serum lipids levels, have not changed despite over a 10-year period between the two papers [Cai *et al.*, 2012; Jee *et al.*, 2001]. In the first meta-analysis, Jee *et al.* [2001] concluded that consumption of 6 cups of coffee per day was significantly associated with a mean increase in total cholesterol (11.8 mg/dL), LDL cholesterol (6.5 mg/dL), and triglyceride (5.9 mg/dL) level, but not with HDL cholesterol level. Filtered coffee resulted in very little change in serum cholesterol [Jee *et al.*, 2001]. Both meta-analyses revealed that patients with hyperlipidemia were more sensitive to the lipid-raising effect of coffee.

Also, coffee consumption has been adversely associated with plasma homocysteine concentration [Higdon & Frei, 2006; van Dam, 2008; Verhoef & Groot, 2005]. Hyperhomocysteinaemia is considered to be a risk factor for the development of cardiovascular diseases [van Oijen *et al.*, 2007]. A randomized study performed in the Netherlands suggested that drinking 1 L of unfiltered coffee per day for two weeks increases mean plasma homocysteine by 10% [Grubben *et al.*, 2000]. However, a study in the Norwegian population showed a strong dose-response relationship between coffee intake and total homocysteine levels, irrespective of the type of coffee (filtered, boiled, instant). Heavy coffee consumption ( $\geq 9$  cups/day) was associated with a mean increase in homocysteine concentration by 18% and 29% for men and women, respectively [Nygard *et al.*, 1997]. Plasma homocysteine concentration may also depend on the dietary intake of methionine, vitamins B-12 and B-6, and folic acid. However, in both of the above mentioned reports concentrations of homocysteine appear to have been independent of the intake of these compounds.

In contrast, other studies showed no changes in the concentration of homocysteine after consumption of 3–4 cups of paper-filtered coffee per day [Corrêa *et al.*, 2013]. Also, abstinence from filtered coffee for six weeks was demonstrated to be associated with a 10%-decrease in homocysteine concentration in consumers of approximately 4 cups of coffee per day [Christensen *et al.*, 2001].

In conclusion, some authors are of the opinion that patients with dyslipidemia should be advised to drink filtered rather than non-filtered coffee [O’Keefe *et al.*, 2013]. Consumption of filtered coffee was not associated with CVD or all-cause mortality in women with CVD [Lopez-Garcia *et al.*, 2011].

## COFFEE AND BLOOD PRESSURE

Coffee consumption has been related to acute increases of blood pressure in non-coffee drinkers, but not in habitual coffee drinkers [Bidel *et al.*, 2006; Cano-Marquina *et al.*, 2013; Steffen *et al.*, 2012]. Caffeine is one of the main compounds of coffee which have a well-documented acute pressor effect. A 200–300 mg dose of caffeine, equivalent to the amount in 2–3 cups of coffee, has been found to increase systolic blood pressure by 3–14 mm Hg and diastolic blood pressure by 4–13 mm Hg in normotensive persons [Nurminen *et al.*, 1999]. However, after a few days of caffeine intake people develop a complete or partial tolerance to caffeine effects. Therefore, habitual coffee consumers may be less sensitive to the effects of coffee on blood pressure [Lopez-Garcia *et al.*, 2011; Mostofsky *et al.*, 2012; O’Keefe *et al.*, 2013; Riksen *et al.*, 2009; Silletta & Marchioli, 2008; Zhang *et al.*, 2011]. Meta-analyses of randomized controlled trials, as well as cohort studies, support the theory of neutral effects of chronic coffee intake on blood pressure. Clinical trials showed statistically insignificant mean changes in systolic (0.55 mmHg) and diastolic (0.45 mmHg) blood pressure in coffee drinkers as compared to abstaining controls, whereas cohort studies demonstrated a pooled risk ratio for developing hypertension of 1.03 (95% CI: 0.98–1.08) [Steffen *et al.*, 2012]. However, these authors noticed that, due to low-quality evidence, no general recommendations can be issued with regard to blood pressure and hypertension *versus* coffee consumption.

As far as patients with hypertension are concerned, a recently published systematic review and meta-analysis of controlled trials failed to deliver evidence justifying avoidance of habitual coffee consumption in well-controlled hypertensive patients [Mesas *et al.*, 2011].

In conclusion, according to the Guidelines for the management of arterial hypertension of the European Society of Hypertension and of the European Society of Cardiology, a firm recommendation for or against coffee consumption cannot to be issued due to insufficient quality of most studies [Mancia *et al.*, 2013]. In the United States restricted coffee consumption is no longer advised according to the recent Evidence-Based Guideline for the Management of High Blood Pressure in Adults [James *et al.*, 2014].

## BENEFICIAL COMPOUNDS OF COFFEE AND THEIR SUGGESTED ACTION IN THE BODY

Coffee contains potentially beneficial and harmful ingredients, which may interact in their physiological effects. Apart from caffeine and diterpenes, coffee contains polyphenols (which act as antioxidants), potassium, magnesium, and niacin. These constituents can be responsible for the suggestive beneficial effects of coffee and they can balance the negative action of other ingredients [Bøhn *et al.*, 2012]. In some populations coffee contributes to a large share of the consumption of polyphenols. In Finland, Spain, and Norway coffee is their primary source, whereas in Poland and Japan coffee is one of the most important sources of these compounds [Zujko *et al.*, 2015; Fukushima *et al.*, 2009].

Composition of coffee is determined by strength of the brew and brewing methods. Stronger brews may have higher levels of caffeine, antioxidants and other compounds [Mostofsky *et al.*, 2012]. Caffeine concentration per cup ranges from 28 to 322 mg, depending on the type of coffee and volume of serving [Crozier *et al.*, 2012; Jarosz *et al.*, 2012; O’Keefe *et al.*, 2013]. According to the Polish nutrient databases, a cup of coffee (160 mL) provides 201 mg of potassium, 19 mg of magnesium, and 1.1 mg of niacin, which could amount to 4%, 5%, and 7% of the recommended dietary allowance for these nutrients, respectively [Kunachowicz *et al.*, 2005].

It remains unclear which compounds are responsible for the potential health-promoting properties of coffee, but they are mainly attributed to polyphenols [Bøhn *et al.*, 2012; Butt & Sultan, 2011]. Chlorogenic acid is one of the major and well-known polyphenols of coffee [Higdon & Frei, 2006; O’Keefe *et al.*, 2013]. A single serving of coffee provides between 20 and 675 mg of this compound [Cano-Marquina *et al.*, 2013]. The mechanism of beneficial effects of chlorogenic acid on the cardiovascular system is mainly associated with improved antioxidant status of the body, which protects it from the hazardous effect of free radicals and prevents endothelial damage [Butt & Sultan, 2011; Zujko *et al.*, 2015]. As far as antioxidant potency of caffeine is concerned, some studies have suggested both strong antioxidant ability of caffeine [Devasagayam *et al.*, 1996], and weak anti-radical activity of this substance [Zhao *et al.*, 2015]. However the study by Buscemi *et al.* has shown that caffeinated coffee had only 15% higher anti-oxidant capacity than decaffeinated coffee [Buscemi *et al.*, 2010].

Consumption of coffee appears to have favourable effects on some markers of subclinical inflammation. One study found that drinking 8 cups of coffee per day decreased the concentrations of proinflammatory interleukin-18 [Kempf *et al.*, 2010], whereas another reported an inverse correlation between the consumption of  $\geq 1$  cups of coffee per day and the level of C-reactive protein [Kotani *et al.*, 2008].

## CONFOUNDING FACTORS OF THE HEALTH EFFECTS OF COFFEE

It is important to stress that lifestyle-related factors may modify the influence of coffee on health. Heavy coffee consumption tends to be strongly associated with cigarette smoking and with other unhealthy behaviours [Floegel *et al.*, 2012; Higdon & Frei, 2006; Lopez-Garcia *et al.*, 2006]. The Hordaland Homocysteine Study in Norway showed that combination of cigarette smoking and high coffee intake was associated with particularly high homocysteine concentration [Nygard *et al.*, 1997]. Another study also found that smoking combined with high coffee consumption has a particularly unfavourable effect on acute myocardial infarction [D’Avanzo *et al.*, 1993]. Nevertheless, the literature reports suggest that increased rates of coronary heart diseases in smokers who drink much coffee occur as a result of cigarette smoking, not coffee consumption [Harland, 2000]. A study by Lopez-Garcia *et al.* [2006] revealed that detrimental effects of smoking on coronary heart diseases were the same among coffee drinkers and non-drinkers.

Interindividual differences in relation between coffee and health might also be conditioned by genetic factors [Cano-Marquina *et al.*, 2013; Dworzański *et al.*, 2011]. There is substantial evidence that the CYP1A2 genotype of cytochrome P450, which accounts for 95% of the primary metabolism of caffeine, modifies the association between coffee consumption and cardiovascular risk [Dworzański *et al.*, 2011; Mostofsky *et al.*, 2012]. Some study revealed that an intake of 4 cups of coffee per day may increase the risk of non-fatal myocardial infarction only among individuals with the variant CYP1A2\*1F allele who are 'slow' caffeine metabolizers, but not among CYP1A2\*1A allele carriers who are 'rapid' caffeine metabolizers [Cornelis *et al.*, 2006].

## CONCLUSIONS

Recent research has indicated that habitual moderate coffee intake does not pose a health threat and may even be associated with beneficial effects on the cardiovascular health. According to some experts, coffee can become a part of a healthy diet for the general public and also for those with cardiovascular risk or cardiovascular diseases [Cano-Marquina *et al.*, 2013; O'Keefe *et al.*, 2013].

Recommendation to reduce coffee consumption as means of lowering the risk of coronary heart disease is not required [van Dam, 2008]. However, it is important to note that strong brews of coffee contain a lot of caffeine, which is a psychoactive substance. Caffeine is also present in other popular products in the diet, *i.e.* tea, cola drinks, chocolate, and energy drinks. High intake of caffeine may cause a wide range of adverse effects, including psychomotor agitation, insomnia, gastrointestinal complaints and tachycardia. Therefore, one should exercise caution when encouraging high consumption of coffee as a preventive measure for cardiovascular diseases.

## ACKNOWLEDGEMENTS

This work was supported by statutory action of National Food and Nutrition Institute.

## REFERENCES

1. Akash M.S., Rehman K., Chen S., Effects of coffee on type 2 diabetes mellitus. *Nutrition*, 2014, 30, 755–763.
2. Bidel S., Hu G., Qiao Q., Jousilahti P., Antikainen R., Tuomilehto J., Coffee consumption and risk of total and cardiovascular mortality among patients with type 2 diabetes. *Diabetologia*, 2006, 49, 2618–2626.
3. Bøhn S.K., Ward N.C., Hodgson J.M., Croft K.D., Effects of tea and coffee on cardiovascular disease risk. *Food Funct.*, 2012, 3, 575–591.
4. Buscemi S., Batsis J.A., Arcoleo G., Verga S., Coffee and endothelial function: a battle between caffeine and antioxidants? *Eur. J. Clin. Nutr.*, 2010, 64, 1242–1243.
5. Butt M.S., Sultan M.T., Coffee and its consumption: benefits and risk. *Crit. Rev. Food Sci. Nutr.*, 2011, 51, 363–373.
6. Cai L., Ma D., Zhang Y., Liu Z., Wang P., The effect of coffee consumption on serum lipids: a meta-analysis of randomized controlled trials. *Eur. J. Clin. Nutr.*, 2012, 66, 872–877.
7. Cano-Marquina A., Tarfín J.J., Cano A., The impact of coffee on health. *Maturitas*, 2013, 75, 7–21.
8. Christensen B., Mosdol A., Retterstol L., Landaas S., Thelle D.S., Abstention from filtered coffee reduces the concentrations of plasma homocysteine and serum cholesterol - a randomized controlled trial. *Am. J. Clin. Nutr.*, 2001, 74, 302–307.
9. Cornelis M.C., El-Sohemy A., Kabagambe E.K., Campos H., Coffee, CYP1A2 genotype, and risk of myocardial infarction. *JAMA*, 2006, 295, 1135–1141.
10. Corrêa T.A., Rogero M.M., Miotto B.M., Tarasoutchi D., Tuda V.L., César L.A., Torres E.A., Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: a clinical trial. *Nutrition*, 2013, 29, 977–981.
11. Corti R., Sudano I., Spieker L., Binggeli C., Hermann F., Tonenz D., Coffee – poison or medicine? *Ther. Umsch.*, 2005, 62, 629–663.
12. Crozier T.W., Stalmach A., Lean M.E., Crozier A., Espresso coffees, caffeine and chlorogenic acid intake: potential health implications. *Food Funct.*, 2012, 3, 30–33.
13. D'Avanzo B., La Vecchia C., Tognoni G., Franceschi S., Franzosi M.G., Nobili A., Coffee consumption and risk of myocardial infarction in Italian males. *Ann. Epidemiol.*, 1993, 3, 95–600.
14. de Koning Gans J.M., Uiterwaal C.S., van der Schouw Y.T., Boer J.M., Grobbee D.E., Verschuren W.M., Beulens J.W., Tea and coffee consumption and cardiovascular morbidity and mortality. *Arterioscler. Thromb. Vasc. Biol.*, 2010, 30, 1665–1671.
15. Devasagayam T.P., Kamat J.P., Mohan H., Kesavan P.C., Caffeine as an antioxidant: inhibition of lipid peroxidation induced by reactive oxygen species. *Biochim. Biophys. Acta*, 1996, 1282, 63–70.
16. Ding M., Bhupathiraju S.N., Satija A., van Dam R.M., Hu F.B., Long-term coffee consumption and risk of cardiovascular disease: A systematic review and dose-response meta-analysis of prospective cohort studies. *Circulation*, 2014, 129, 643–659.
17. Dworzański W., Burdan F., Szumiło M., Jaskólska A., Anielska E., Coffee and caffeine - enemies or allies of a cardiologist? *Kardiol. Pol.*, 2011, 69, 173–176 (in Polish: English abstract).
18. Floegel A., Pischon T., Bergmann M.M., Teucher B., Kaaks R., Boeing H., Coffee consumption and risk of chronic disease in the European Prospective Investigation into Cancer and Nutrition (EPIC) – Germany study. *Am. J. Clin. Nutr.*, 2012, 95, 901–908.
19. Fukushima Y., Ohie T., Yonekawa Y., Yonemoto K., Aizawa H., Mori Y., Watanabe M., Takeuchi M., Hasegawa M., Taguchi C., Kondo K., Coffee and green tea as a large source of antioxidant polyphenols in the Japanese population. *J. Agric. Food Chem.*, 2009, 57, 1253–1259.
20. Grubben M., Boers G.H., Blom H.J., Broekhuizen R., de Jong R., van Rijt L., de Ruijter E., Swinkels D.W., Nagengast F.M., Katan M.B., Unfiltered coffee increases plasma homocysteine concentrations in healthy volunteers: a randomized trial. *Am. J. Clin. Nutr.*, 2000, 71, 480–484.
21. Harland B., Caffeine and nutrition. *Nutrition*, 2000, 16, 522–526.
22. Higdon J.V., Frei B., Coffee and health: A review of recent human research. *Crit. Rev. Food Sci. Nutr.*, 2006, 46, 101–123.
23. James P.A., Oparil S., Carter B.L., Cushman W.C., Dennison-Himmelfarb C., Handler J., Lackland D.T., LeFevre M.L., MacKenzie T.D., Ogedegbe O., Smith S.C., Svetkey L.P., Taler S.J., Townsend R.R., Wright J.T., Narva A.S., Ortiz E., 2014 ev-

- idence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*, 2014, 311, 507–520.
24. Jarosz M., Wierzejska R., Siuba M., Maternal caffeine intake and its effect on pregnancy outcomes. *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2012, 160, 156–160.
  25. Jee S.H., He J., Appel L.J., Whelton P.K., Suh I., Klag M.J., Coffee consumption and serum lipids: a meta-analysis of randomized controlled clinical trials. *Am. J. Epidemiol.*, 2001, 153, 353–362.
  26. Kawachi I., Colditz G.A., Stone C.B., Does coffee drinking increase the risk of coronary heart disease? Results from a meta-analysis. *Br. Heart J.*, 1994, 72, 269–275.
  27. Kempf K., Herder C., Erlund I., Kolb H., Martin S., Carstensen M., Koenig W., Sundvall J., Bidel S., Kuha S., Tuomilehto J., Effects of coffee consumption on subclinical inflammation and other risk factors for type 2 diabetes: a clinical trial. *Am. J. Clin. Nutr.*, 2010, 91, 950–957.
  28. Kim B., Nam Y., Kim J., Choi H., Won C., Coffee consumption and stroke risk: a meta-analysis of epidemiologic studies. *Korean J. Fam. Med.*, 2012, 33, 356–365.
  29. Kleemola P., Jousilahti P., Pietinen P., Vartiainen E., Tuomilehto J., Coffee consumption and the risk of coronary heart disease and death. *Arch. Intern. Med.*, 2000, 160, 3393–3400.
  30. Kotani K., Tsuzaki K., Sano Y., Maekawa M., Fujiwara S., Hamada T., Sakane N., The relationship between usual coffee consumption and serum C-reactive protein level in a Japanese female population. *Clin. Chem. Lab. Med.*, 2008, 46, 1434–1437.
  31. Kunachowicz H., Nadolna I., Przygoda B., Iwanow K., Food Composition Tables. 2005, PZWL, Warsaw, p. 634 (in Polish).
  32. Larsson S.C., Orsini N., Coffee consumption and risk of stroke: a dose-response meta-analysis of prospective studies. *Am. J. Epidemiol.*, 2011, 174, 993–1001.
  33. Lopez-Garcia E., Rodrigues-Artalejo F., Li T.Y., Mukamal K.J., Hu F.B., van Dam R.M., Coffee consumption and mortality in women with cardiovascular disease. *Am. J. Clin. Nutr.*, 2011, 94, 218–224.
  34. Lopez-Garcia E., van Dam R.M., Willett W.C., Rimm E.B., Manson J.E., Stampfer M.J., Rexrode K.M., Hu F.B., Coffee consumption and coronary heart disease in men and women. A prospective cohort study. *Circulation*, 2006, 113, 2045–2053.
  35. Mancia G., Fagard R., Narkiewicz K., Redón J., Zanchetti A., Böhm M., Christiaens T., Cifkova R., Backer G., Dominiczak A., Galderisi M., Grobbee D., Jaarsma T., Kirchhof P., Kjeldsen S., Laurent S., Manolis A., Nilsson P., Ruilope L., Schmieder R., Sirnes P., Sleight P., Viigimaa M., Waeber B., Zannad F., 2013 ESH/ESC Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of the Hypertension (ESH) and of the European Society of Cardiology (ESC). *J. Hypertens.*, 2013, 31, 1281–1357.
  36. Mesas A.E., Leon-Muñoz L.M., Rodrigues-Artalejo F., Lopez-Garcia E., The effect of coffee on blood pressure and cardiovascular disease in hypertensive individuals; a systematic review and meta-analysis. *Am. J. Clin. Nutr.*, 2011, 94, 1113–1126.
  37. Mostofsky E., Rice M.S., Levitan E.B., Mittleman M.A., Habitual coffee consumption and risk of heart failure: a dose-response meta-analysis. *Circ. Heart Fail.*, 2012, 5, 401–405.
  38. Nurminen M.L., Niittynen L., Korpela R., Vapaatalo H., Coffee, caffeine and blood pressure: a critical review. *Eur. J. Clin. Nutr.*, 1999, 53, 831–839.
  39. Nygard O., Refsum H., Ueland P.M., Stensvold I., Nordrehaug J.E., Kvale G., Vollset S.E., Coffee consumption and plasma total homocysteine: The Hordaland Homocysteine Study. *Am. J. Clin. Nutr.*, 1997, 65, 136–143.
  40. O’Keefe J.H., Bhatti S.K., Patil H.R., DiNicolantonio J.J., Lucan S.C., Lavie C.J., Effects of habitual coffee consumption on cardiometabolic disease, cardiovascular health, and all-cause mortality. *J. Am. Coll. Cardiol.*, 2013, 62, 1043–1051.
  41. Ranheim T., Halvorsen B., Coffee consumption and human health - beneficial or detrimental? Mechanism for effects of coffee consumption on different risk factors for cardiovascular disease and type 2 diabetes mellitus. *Mol. Nutr. Food Res.*, 2005, 49, 274–284.
  42. Reis J.P., Loria C.M., Steffen L.M., Zhou X., Coffee, decaffeinated coffee, caffeine, and tea consumption in young adulthood and atherosclerosis later in life: the CARDIA study. *Arterioscler. Thromb. Vasc. Biol.*, 2010, 30, 2059–2066.
  43. Riksen N.P., Rongen G.A., Smits P., Acute and long-term cardiovascular effects of coffee: implications for coronary heart disease. *Pharmacol. Ther.*, 2009, 121, 185–191.
  44. Schocken D.D., Benjamin E.J., Fonarow G.C., Krumholz H.M., Levy D., Mensah G.A., Narula J., Shor S., Young J.B., Hong Y., A scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Clinical Cardiology, Cardiovascular Nursing, and High Blood Pressure Research; Quality of Care and Outcomes Research Interdisciplinary Working Group; and Functional Genomics and Translational biology Interdisciplinary Working Group. *Circulation*, 2008, 117, 2544–2565.
  45. Silletta M.G., Marchioli R., Coffee and cardiovascular disease risk: yin and yang. *Recenti. Prog. Med.*, 2008, 99, 533–537.
  46. Sofi F., Conti A.A., Gori A.M., Eliana Luisi M.L., Casini A., Abbate R., Gensini G.F., Coffee consumption and risk of coronary heart disease: a meta-analysis. *Nutr. Metab. Cardiovasc. Dis.*, 2007, 17, 209–223.
  47. Steffen M., Kuhle C., Hensrud D., Erwin P.J., Murad M.H., The effect of coffee consumption on blood pressure and the development of hypertension: a systematic review and meta-analysis. *J. Hypertens.*, 2012, 30, 2245–2254.
  48. Sudano I., Binggeli C., Spieker L., Lüscher T.F., Ruschitzka F., Noll G., Corti R., Cardiovascular effects of coffee: is it a risk factor? *Prog. Cardiovasc. Nurs.*, 2005, 20, 65–69.
  49. Tuomilehto J., Coffee and health. *Duodecim*, 2013, 129, 1398–1405.
  50. Urgert R., Katan M.B., The cholesterol-raising factor from coffee beans. *J. R. Soc. Med.*, 1996, 89, 618–623.
  51. van Dam R.M., Coffee consumption and coronary heart disease: paradoxical effects on biological risk factors versus disease incidence. *Clin. Chem.*, 2008, 54, 1418–1420.
  52. van Oijen M.G., Laheij R.J., Jansen J.B., Verheugt F.W., The predictive value of vitamin B12 concentrations and hyperhomocysteinaemia for cardiovascular disease. *Neth. Heart J.*, 2007, 15, 291–294.
  53. van Woudenberg G.J., Vliegthart R., van Rooij F.J., Hofman A., Oudkerk M., Witteman J.C., Geleijnse J.M., Coffee consumption and coronary calcification: the Rotterdam Coronary

- Calcification Study. *Arterioscler. Thromb. Vasc. Biol.*, 2008, 28, 1018–1023.
54. Verhoef P., de Groot L.C., Dietary determinants of plasma homocysteine concentrations. *Semin. Vasc. Med.*, 2005, 5, 110–123.
55. Weusten-Van der Wouw M.P., Katan M.B., Viani R., Huggett A.C., Liardon R., Lund-Larsen P.G., Thelle D.S., Ahola I., Aro A., Meyboom S., Beynen A.C., Identity of the cholesterol-raising factor from boiled coffee and its effects on liver function enzymes. *J. Lipid Res.*, 1994, 35, 721–733.
56. Woodward M., Tunstall-Pedoe H., Coffee and tea consumption in the Scottish Heart Health Study follow up: conflicting relations with coronary risk factors, coronary disease, and cause mortality. *J. Epidemiol. Community Health*, 1999, 53, 481–487.
57. Wu J.N., Ho S.C., Zhou C., Ling W.H., Chen W.Q., Wang C.L., Chen Y.M., Coffee consumption and risk of coronary heart disease: a meta-analysis of 21 prospective cohort studies. *Int. J. Cardiol.*, 2009, 137, 216–225.
58. Zhang Z., Hu G., Caballero B., Appel L., Chen L., Habitual coffee consumption and risk of hypertension: a systematic review and meta-analysis of prospective observational studies. *Am. J. Clin. Nutr.*, 2011, 93, 1212–1219.
59. Zhao E.H., Ergul B., Zhao W., Caffeine's antioxidant potency optically sensed with double-stranded DNA-encased single-walled carbon nanotubes. *J. Phys. Chem. B.*, 2015, 119, 4068–4075.
60. Zujko M.E., Witkowska A.M., Wańkiewicz A., Piotrowski W., Terlikowska K.M., Dietary antioxidant capacity of the patients with cardiovascular disease in a cross-sectional study. *Nutr. J.*, 2015, 14, art. no. 26, doi: 10.1186/s12937-015-0005-4.

Submitted: 9 February 2015. Revised: 25 July 2015. Accepted: 27 August 2015. Published on-line: 21 January 2016.