The Relationship Between Caffeinated Coffee and CVD Risk as well as Blood Pressure

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Abstract. Aspects around cardiovascular disease (CVD), especially its predisposing factors, have been studied for a long period. Recent studies have largely concentrated on coffee intake by elderly individuals with type 2 diabetes and its association with CVDs. Others have looked at the potential of coffee and tea in preventing CVD. The association between intake of caffeinated coffee with heart valve disease among the elderly has been another area of interest. However, there is still a gap in research in this area, explaining why this review was conducted to explore the effects of caffeinated coffee on human cardiovascular function as well as the association between coffee consumption and the blood pressure level. The review concludes that Caffeinated coffee consumption is associated with a lower risk of CVD. However, the association between caffeinated coffee intake and blood pressure needs further study.

Keywords: CVD, Coffee, Blood pressure.

1. Introduction

The association between the intake of coffee and the occurrence of CVD and blood pressure in populations has been a subject of interest for researchers for many years. Despite the extent of research, there are multiple knowledge gaps that require examination, especially due to contradictory or unspecified research findings on the topics. This paper explores both aspects of the relationship of coffee intake to CVD and blood pressure. CVD is a leading cause of death globally and its risk factors include hypertension, smoking, high cholesterol levels, diabetes, inactivity, and family history of CVD. From the current research, coffee is not a known risk factor for CVD.

An examination of coffee consumption patterns reveals that Europe and the Americas prefer coffee while the other parts of the world consume more tea than coffee. The major component of coffee, caffeine, is known to cause an increase in alertness and attention, reduce the risk of contracting diabetes, and increases the metabolic rate. Caffeine also causes addiction, anxiety, diuresis, and reduced control of fine motor movements. However, there is no evidence that caffeine increases the risk of CVD. Other key components of coffee such as antioxidants, diterpenes, and various minerals do not increase the risk of CVD. Studies also show that coffee intake can cause a short-term rise in blood pressure but the effect subsides as coffee concentration declines in the body.

2. CVD risk factors

The term cardiovascular diseases (CVDs) are used to refer to a collection of disorders of the blood vessels and the heart. They include but are not limited to coronary heart disease, peripheral arterial disease, cerebrovascular disease, rheumatic heart disease, deep vein thrombosis, and congenital heart disease. Being among the top 3 leading causes of death, CVD needs to be monitored and analyzed to decrease its risk in the community. The global cases of CVD increased from 271 million in 1990 to over 523 million in 2019, indicating the high prevalence of the diseases. The figures represent a 93% increase in CVD cases over a 20-year period. Further, there were over 18.6 million CVD-related deaths in 2019. Coffee remains one of the most popular drinks in the modern world hence can be associated with the risk of CVD. Therefore, it is crucial to find out the association between these two factors.
High blood pressure or hypertension is the main risk factor for CVD. Very high blood pressure can damage an individual's blood vessels thereby causing one or more of the CVDs. Smoking has also been described as a major risk factor for CVD. The nicotine and other harmful substances contained in tobacco have the potential to cause the narrowing of blood vessels thereby damaging them. High levels of cholesterol, a fatty substance contained in a person's blood, can increase the risk of CVD. Cholesterol is associated with narrowing blood vessels, a situation that increases the likelihood of developing a blood clot, which can cause a stroke. Diabetes is known to be an important CVD risk factor, although the biology behind the relationship between the two disorders is highly complex. The effect of diabetes on heart muscles that later causes diastolic and systolic heart failure is the main cause of CVD in diabetic individuals. High blood sugar linked to diabetes causes damage to the inner lining of blood vessels. In response, the body deposits plague along the injured vessels leading to the narrowing of the blood vessels.

Inactive individuals are at high risk of suffering from CVD. People who do not engage in regular exercise are likely to have high levels of cholesterol, high blood pressure, and be overweight. A high body mass index of over 25, worsens CVD risk factors such as blood pressure, blood sugar, and inflammation in individuals. Although still under investigation, researchers have suggested that individuals with a family history of CVD are likely to develop one of the CVDs in their life, indicating some genetic factors may fall into play. A genetic predisposition to CVD increases the likelihood of suffering from the diseases irrespective of other factors. Additional CVD risk factors include older age, gender, unhealthy diet, alcohol consumption, and impaired kidney function. An unhealthy diet and alcohol can lead to an increase in body weight as well as cholesterol levels. Men are also more likely to suffer from CVD compared to women.

The impairment of the renal function increases the risk of CVD two to four times. There is a close relationship between CVD and kidney disease and the occurrence of disease in either organ increases the probability of dysfunction in the other organ. CVD is a leading cause of mortality for end-stage kidney disease patients. The occurrence of CVD in kidney disease patients is linked to disturbances in mineral and vitamin D metabolism. The Fibroblast Growth Factor 23 hormone responsible for vitamin D synthesis is a key factor in the occurrence of CVD in kidney disease patients. Moreover, the occurrence of CVD in patients with kidney diseases can be attributed to the release of kidney hormones, cytokines, and enzymes that cause changes in the blood vessels. Besides, hemodynamic alterations and chronic kidney disease mediators can cause cardiac malfunctions. The general information about CVD risk factors indicates that those interested in reducing their risk should avoid tobacco, consume less fat and salt in their diet, consume more fruits and vegetables, and exercise regularly. The figure 1 below shows the prevalence of CVD globally.

![CVD deaths per 100,000 people](image)

**Figure 1.** Prevalence of CVD per 100,000 people in several countries
3. Coffee consumption patterns

Coffee is a popular beverage across the globe. In the year 2020/2021 over 166 million 60kg bags of coffee were consumed globally. Researchers have found that the average caffeine intake in a day is 240 mg, which translates to about 150 ml of instant coffee. One-third of the world's population consumes this or more every day and can be described to be caffeine dependent. Some studies report that coffee consumption patterns remain similar in all genders and ages, although others note that younger individuals consume more coffee than older persons as the latter consumer more tea. Coffee is the preferred drink in the Americas and Europe while tea is the preferred drink in other parts of the world. Finland, Sweden, Iceland, Norway, and Denmark are the top five consumers of coffee as shown in figure 2 below.

As evident from figure 2, a single person in Finland consumes 12kgs of coffee every year. These figures stand at 9.9kgs in Norway and 9kgs in Iceland. The figures are lower in the USA and the UK, where the average consumption per person is 4.2 kg and 2.8kg respectively. Overall, there is higher consumption in Europe compared to North America. The consumption differences are due to stronger coffee culture in Europe than in America. In Europe, coffee consumption is a highly social activity that often happens in roadside cafes. In the USA, most people consume coffee as a habitual process of stimulating the mind rather than as a social activity. In the United States, over 70% of the people drink coffee weekly while 62% consume coffee daily. The average consumption is 3 cups per day and most people prefer to get coffee from drive-through stores rather than preparing it at home. Further, the most preferred coffee beverages are expresso, lattes, cappuccinos, and flat whites. The consumption of coffee is the United States is integrated into the busy work culture in comparison to the extended coffee breaks that are common in Europe.

Caffeinated coffee contains a range of compounds that contribute to the physiological effects associated with coffee as well as its unique flavor. Below is figure 3 that shows the common compounds that are available in the coffee products.

Though as indicated in figure 3 numerous compounds are within the coffee product, only a few of the compounds have a significant effect on individuals. Caffeine is the main pharmacologically active component in coffee and is known to stimulate the central nervous system. Most of the other components are destroyed during the roasting process.

Caffeine consumed in beverages is absorbed quickly from the gastrointestinal tract and released into body water. Further, the liver does not filter out caffeine as it passes from the intestinal tract to the blood circulatory system. It has been noted that caffeine reversibly binds to plasma proteins and protein-bound caffeine amounts to 10-30% of all caffeine in the plasma. Caffeine is hydrophilic and moves freely in the intracellular tissue water. The average distribution volume of caffeine in the body is 0.7L/kg. moreover, caffeine is lipophilic which enables it to pass through biological membranes. The body eliminates caffeine through first-order kinetics. Caffeine metabolism occurs in the liver and the process is catalyzed by microsomal enzyme systems. The products of metabolism include uric acids, uracil derivatives, dimethylxanthines, and trimethylallantoin. The primary metabolite in humans is paraxanthine, which is excreted through urine. Paraxanthine and caffeine cause an increase in the concentration of epinephrine in plasma, high diastolic blood pressure, and free fatty acids. Caffeine is usually metabolized completely and very little amounts are excreted in urine.

Caffeine causes an increase in alertness and attention, reduces fatigue, lowers the risk of contracting diabetes, and increases the metabolic rate. Further, caffeine helps to regulate body weight by increasing energy usage while decreasing energy intake. Caffeine also promotes weight maintenance through fat oxidation and thermogenesis. An average cup of coffee contains about 75-100 mg of caffeine.

Research shows that intake of up to 400mg of caffeine a day has no safety issues in non-pregnant adults. However, pregnant and breastfeeding mothers are advised to take a maximum of 200mg of caffeine per day. Caffeine can readily cross the placenta and reach similar concentrations in the fetus as is in the mother’s body. Research implications show that excessive consumption of coffee among pregnant women can result in impaired fetus growth and spontaneous abortion. Caffeine has multiple
negative effects on adults. The effects include addiction and increased anxiety, higher stimulation of urination, reduced control of fine motor movements, and higher vasoconstriction. Caffeine inhibits fine motor movements by affecting the sodium-potassium-adenosine triphosphate pump activity, which leads to decreased potassium concentrations in the plasma. As a result, it affects the depolarization-repolarization process leading to reduced fine motor coordination. Ceasing the usage of caffeine causes various withdrawal symptoms that include irritability, headache, nervousness, and energy reduction. Caffeine causes a slight reduction in calcium absorption in the intestinal tract. The substance inhibits the uptake and storage of calcium in striated muscles and increases the translocation of calcium ions through the plasma membrane. Among the elderly, the consumption of a maximum of 2-3 cups of coffee a day coupled with regular intake of calcium and vitamin D may help to reduce incidences of osteoporosis and bone fractures. In children, caffeine can cause nervousness and anxiety. Therefore, the recommended maximum coffee consumption for children is 2.5mg/kg of body weight/day. The fatal oral dose of caffeine is 10-14g/kg body weight. Oral dosages of up to 150mg cause vomiting, convulsions and recovery occurs within 6 hours. Dosages of 1g can also cause nervousness, restlessness, irritability, emesis, delirium, neuromuscular tremors, increased respiration, and tachycardia.

Antioxidants are another key component of coffee and they include melanoidins, caffeic acid, and chlorogenic acids, and they help to deactivate oxidants. Studies have concluded that there is an increase in the level of antioxidants in the blood every time a person consumes coffee. These antioxidants have diverse effects on the body and research is still on about the potential roles of these antioxidants. Chlorogenic acids influence lipid and glucose metabolism and are also anti-inflammatory, anti-carcinogenic, and anti-obesity. Moreover, the degree of roasting determines the level of antioxidant activity in coffee. Medium-roasted coffee has the maximum level of antioxidant activity.

![Top Five Coffee Consumers](image)

**Figure 2.** Top five countries with individuals who consume the highest quantity of coffee annually

Diterpenes are a naturally occurring compound in the oil found in coffee. A high intake of diterpenes (cafestol and kahweol) can cause an increase in low-density lipoprotein cholesterol (bad cholesterol). However, using paper filters eliminates diterpenes in coffee thus reducing the incidence of serum cholesterol. Cafestol and kahweol have anticarcinogenic properties and they help to inhibit the activity of aflatoxin BA in the body cells. The diterpenes also help to reduce the genotoxicity of multiple carcinogens and they also cause apoptosis by controlling the expression of certain proteins in malignant pleural cancer. Additional compounds are found in coffee and are said to form during the storage process of coffee. They include but are not limited to furan, acrylamide, and Ochratoxin A. Other components in coffee include phenols, potassium, lactones, niacin, and the vitamin B3
precursor trigonelline. Overall, coffee contains over 1,000 phytochemicals in varying quantities. Coffee has minimal energy content due to the low amount of carbohydrates, fat, or proteins in its composition. However, it contains many vitamins and minerals. Some of the minerals include manganese, iron, sulfates, lanthanum, cesium, bromine, calcium, Sodium, magnesium, copper, zinc, strontium, barium, nickel, cobalt, lead, cadmium, scandium, rubidium, and phosphorus. Some of the amino acids in coffee include amino acids such as glutamic acid, arginine, alanine, cysteine, asparagine, isoleucine, glycine, histidine, leucine, proline, lysine, serine, methionine, phenylalanine, tyrosine, threonine, and valine. In general, coffee consumption has an inverse relationship with the occurrence of various diseases such as Alzheimer’s, liver damage, Parkinson’s, and various cancers. Coffee consumption increases endurance in long physical activities and reduces suicide risk by 13% for every cup consumed. Evidently, coffee has multiple benefits for its consumers.

Figure 3. Chemical compounds of coffee product

4. Association between caffeinated coffee consumption and CVD

A 2012 systematic review coupled with a dose-response meta-analysis of several prospective studies concluded that there is a J-shaped association between coffee intake and heart failure. When compared with individuals who did not consume coffee, the most significant inverse relationship was observed at four cups per day and higher risks were reported for those consuming more than four cups a day. There is a significant inverse relationship between intake of coffee and the risk of CVD mortality, particularly in women. However, a study by Liu et al. concluded that there is a positive relationship between coffee intake and mortality rate in adults below 55 years of age. Another study by Rebello and van Dam explains that there is no association between coffee intake and risk of coronary heart disease. They add that there is a weak relationship between coffee intake and a lower risk of heart failure and stroke. The same study concluded that coffee intake has no association with increased risk of fatal cardiovascular incidences.

Individuals who consume 3-5 cups of caffeinated coffee reduce their risk of CVD by 15%. The study by Rodríguez-Artalejo and López-García concluded that those who consume more than 3-5 cups have no elevated risk of CVD. Another study indicated that consumption of coffee regularly lowers the risk of cardiovascular death as well as a myriad of adverse cardiovascular outcomes, such as stroke, congestive heart failure, and coronary heart disease. Again, habitual intake of 3-4 cups of coffee every day was not associated with positive or negative effects on hypertension and arrhythmias. Voskoboinik, Koh, and Kistler argue that moderate consumption of tea and coffee can have beneficial effects on different cardiovascular conditions, such as arrhythmias, heart failure, and coronary heart disease.
5. Association between caffeinated coffee consumption and Blood Pressure

Geleijnse concluded that there is a U-shaped or linear relationship between habitual intake of coffee and blood pressure in diverse populations. Although further investigation is needed to confirm the results, it is suggested that coffee intake has protective effects against hypertension, especially in women who take at least four cups per day. It is not yet clear whether abstainers are associated with a higher or lower risk of hypertension than people who take one or two cups per day. When randomized control studies were used, it was concluded that those who take about five cups every day may experience a slight increase in blood pressure in comparison with those who take decaffeinated coffee or those who abstain from coffee intake. Intake of 200-300mg of caffeine is said to lead to an 8.1mmHg increase in the systolic blood pressure and a 5.7mmHg in the diastolic blood pressure. The increase is observed within one hour of caffeine intake and is found to last for about 3 hours. Caffeine causes an increase in coronary blood flow in the heart as well as provides anti-asthmatic effects through activating the relaxation of the smooth muscles in the lungs and dilation of the bronchi. Caffeine is a well-known natural alkaloid methylxanthine. Methylxanthines stimulate the heart and kidney functioning, excite the central nervous system, act as bronchodilators, and promote the psychical and physic activities of organisms. Around 99% of the caffeine in coffee is absorbed after ingestion and the blood concentration peaks after 60 minutes. The half-life of caffeine in human adults is 3-6 hours. Studies following participants for at least two weeks found that there was no significant increase in blood pressure. Caffeine causes an increase in blood flow and renin secretion. Rennin hormone causes an increase in blood pressure. The conclusion was that coffee intake can cause a temporary increase in the blood pressure of hypertensive individuals. Besides, caffeinated coffee is associated with a higher increase in blood pressure than decaffeinated coffee. Caffeinated coffee induces a higher concentration of adrenaline leading to high blood pressure. However, the effect is only noted in people who do not take coffee regularly and not in habitual coffee consumers.

6. Future directions

There is a lot of information in the public domain about the possible association of specific factors with the risk of CVD. However, some of this information is not grounded on any scientific study hence should be consumed with caution. Most studies have associated tobacco intake, lack of regular exercise, and high levels of cholesterol with increased levels of CVD risk. Thus, it is necessary to consider such pre-disposing factors when making effort to reduce the risk of CVD. It should be noted that research is still on about the link between these factors and CVD.

7. Conclusion

Recent studies have indicated that caffeinated coffee consumption is associated with a lower risk of CVD, especially for those consuming about 5 cups per day. However, the association between caffeinated coffee intake and blood pressure needs further study because there are unclear associations and conflicting results in current studies. As one of the most popular drinks in the modern world, coffee plays an important role in regulating the risk of CVD, which is one of the leading causes of death in China, as well as blood pressure. Results from the consulted studies are not conclusive hence further studies are needed to explore the effects of caffeinated coffee consumption on blood pressure and CVD.

References

[1] G.A. Roth, G.A. Mensah, C.O. Johnson, G. Addolorato, E. Ammirati, L.M. Baddour, V. Fuster. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update from the GBD 2019 Study. Journal of the American College of Cardiology, 2020, 76(25). Retrieved from https://doi.org/10.1016/j.jacc.2020.11.010
[2] G.V. De Melo Pereira, D.P. de Carvalho Neto, A.I.M. Júnior, F.G do Prado, M.G.B. Pagnoncelli, S.G. Karp, & C.R. Soccol. Chemical composition and health properties of coffee and coffee by-products. In Advances in food and nutrition research (Vol. 91, pp. 65-96). (2020). Academic Press.

[3] G.V. De Melo Pereira, D.P. de Carvalho Neto, A.I.M. Júnior, F.G. do Prado, M.G.B. Pagnoncelli, S.G. Karp & C.R. Soccol. Chemical composition and health properties of coffee and coffee by-products. In Advances in food and nutrition research (Vol. 91, pp. 65-96). (2020). Academic Press.

[4] R. Amani & N. Sharifi. Cardiovascular disease risk factors. The Cardiovascular System - Physiology, Diagnostics, and Clinical Implications. 2012. doi:10.5772/34374

[5] S. Said & G.T. Hernandez. The link between chronic kidney disease and cardiovascular disease. Journal of Nephropathology, 3(3), (2014), 99.

[6] M. Liu, X.C. Li, L. Lu, Y. Cao, R.R. Sun, S. Chen, & P.Y. Zhang. Cardiovascular disease and its relationship with chronic kidney disease. Eur Rev Med Pharmacol Sci, 18(19), (2014), 2918-2926.

[7] J. Jankowski, J. Floege, D. Fliser, M. Böhm & N. Marx. Cardiovascular disease in chronic kidney disease. Circulation, 143(11), (2021), 1157-1172. doi:10.1161/circulationaha.120.050686

[8] World Life Expectancy. Coronary heart disease death rate by country. (2021) https://www.worldlifeexpectancy.com/cause-of-death/coronary-heart-disease/by-country/

[9] J. Conway. Coffee consumption worldwide from 2012/13 to 2020/21 (in million 60kg bags). (2021) Retrieved from https://www.statista.com/statistics/292595/global-coffee-consumption/

[10] S.A. Kim & S. Shin. The association between coffee consumption pattern and prevalence of metabolic syndrome in Korean adults. Nutrients, 11(12), (2019), 2992.

[11] E. Lopez-Garcia, R.M. van Dam, T.Y. Li, F. Rodriguez-Artalejo & F.B. Hu. The relationship of coffee consumption with mortality. Annals of internal medicine, 148(12), (2008), 904-914; R.M. Van Dam & E.J. Feskens. Coffee consumption and risk of type 2 diabetes mellitus. The Lancet, 360(9344), (2002), 1477-1478.

[12] S.A. Kim & S. Shin. The association between coffee consumption pattern and prevalence of metabolic syndrome in Korean adults. Nutrients, 11(12), (2019), 2992.

[13] G, M., Zanella & V. Monda. The beneficial effects of coffee in human nutrition. Biology and Medicine, 07(04). (2015), doi:10.4172/0974-8369.1000240

[14] National Coffee Association. NCA releases 2020 national coffee data trends, the "Atlas of American coffee". (2020). Retrieved from https://www.ncausa.org/Newsroom/NCA-releases-Atlas-of-American-Coffee.

[15] Institute of Medicine. Caffeine for the Sustainment of Mental Task Performance: Formulations for Military Operations. Retrieved from National Academies Press (US) (2001), website: https://www.ncbi.nlm.nih.gov/books/NBK223808/

[16] Institute of Medicine. Caffeine for the Sustainment of Mental Task Performance: Formulations for Military Operations. (2001). Retrieved from National Academies Press (US) website: https://www.ncbi.nlm.nih.gov/books/NBK223808/

[17] Institute of Medicine. Caffeine for the Sustainment of Mental Task Performance: Formulations for Military Operations. (2001). Retrieved from National Academies Press (US) website: https://www.ncbi.nlm.nih.gov/books/NBK223808/

[18] G.V. De Melo Pereira, D.P. de Carvalho Neto, A.I.M. Júnior, F.G. do Prado, M.G.B. Pagnoncelli, S.G. Karp & C.R. Soccol. Chemical composition and health properties of coffee and coffee by-products. In Advances in food and nutrition research (Vol. 91, pp. 65-96). 2020. Academic Press.

[19] J. Bae, J. Park, S. Im & D. Song. Coffee and health. Integrative Medicine Research, 3(4), (2014), 189-191. doi:10.1016/j.imr.2014.08.002

[20] G, M., Zanella & V. Monda. The beneficial effects of coffee in human nutrition. Biology and Medicine, (2014), 07(04). doi:10.4172/0974-8369.1000240

[21] J. Bae, J. Park, S. Im & D. Song. Coffee and health. Integrative Medicine Research, 3(4), (2014), 189-191. doi:10.1016/j.imr.2014.08.002

[22] J. Bae, J. Park, S. Im & D. Song. Coffee and health. Integrative Medicine Research, 3(4), (2014), 189-191. doi:10.1016/j.imr.2014.08.002
[23] L. Bresciani, L. Calani, R. Bruni, F. Brighenti & D. Del Rio. Phenolic composition, caffeine content, and antioxidant capacity of coffee silverskin. Food Research International, 61, (2014), 196-201.

[24] H. L. Wachamo. Review on health benefit and risk of coffee consumption. Medicinal & Aromatic Plants, 06(04), (2017). doi:10.4172/2167-0412.1000301

[25] J. Bae, J. Park, S. Im & D. Song. Coffee and health. Integrative Medicine Research, 3(4), (2014), 189-191. doi:10.1016/j.imr.2014.08.002

[26] M. Zuhaier Mohd Zain. Composition and health properties of coffee bean. European Journal of Clinical and Biomedical Sciences, 3(5), (2017), 97. doi:10.11648/j.ejecs.20170305.13

[27] J. Bae, J. Park, S. Im & D. Song. Coffee and health. Integrative Medicine Research, 3(4), (2014), 189-191. doi:10.1016/j.imr.2014.08.002

[28] E. Mostofsky, M.S. Rice, E.B. Levitan & M.A. Mittleman. Habitual coffee consumption and risk of heart failure: a dose-response meta-analysis. Circulation: Heart Failure, 5(4), (2012), 401-405

[29] S. Malerba, F. Turati, C. Galeone, C. Pelucchi, F. Verga, C. La Vecchia & A. Tavani. A meta-analysis of prospective studies of coffee consumption and mortality for all causes, cancers, and cardiovascular diseases. 2013.

[30] J. Liu, X. Sui, C.J. Lavie, J.R. Hebert, C.P. Earnest, J. Zhang & S.N. Blair. Association of coffee consumption with all-cause and cardiovascular disease mortality. In Mayo clinic proceedings (Vol. 88, No. 10, pp. 1066-1074). 2013. Elsevier.

[31] S.A. Rebello & R.M. van Dam. Coffee consumption and cardiovascular health: getting to the heart of the matter. Current cardiology reports, 15(10), (2013), 403.

[32] F. Rodriguez-Artalejo & E. Lopez-Garcia. E. Coffee consumption and cardiovascular disease: A condensed review of epidemiological evidence and mechanisms. Journal of agricultural and food chemistry, 66(21), (2017), 5257-5263.

[33] J.H. O'Keefe, J.J. DiNicolantonio & C.J. Lavie. Coffee for cardioprotection and longevity. Progress in cardiovascular diseases, 61(1), (2018), 38-42.

[34] A. Voskoboinik, Y. Koh & P.M. Kistler. Cardiovascular effects of caffeinated beverages. Trends in cardiovascular medicine, 29(6), (2019), 345-350.

[35] J.M. Geleijnse. Habitual coffee consumption and blood pressure: an epidemiological perspective. Vascular health and risk management, 4(5), (2008), 963.

[36] I. Guessous, C.B. Eap & M. Bochud. Blood pressure in relation to coffee and caffeine consumption. Current hypertension reports, 16(9), (2014), 468.

[37] A.E. Mesas, L.M. Leon-Muñoz, F. Rodriguez-Artalejo & E. Lopez-Garcia. The effect of coffee on blood pressure and cardiovascular disease in hypertensive individuals: a systematic review and meta-analysis. The American journal of clinical nutrition, 94(4), (2011), 1113-1126.

[38] E.Y. Andreeva, S.G. Dmitrienko & Y.A. Zolotov. Methylxanthines: Properties and determination in various objects. Russian Chemical Reviews, 81(5), (2012), 397-414. doi:10.1070/rc2012v081n05abeh004220.

[39] Z. Zhang, G. Hu, B. Caballero, L. Appel & L. Chen. Habitual coffee consumption and risk of hypertension: a systematic review and meta-analysis of prospective observational studies. The American journal of clinical nutrition, 93(6), (2011), 1212-1219.

[40] L.K. Pourshahidi, L. Navarini, M. Petracco & J. Strain. A comprehensive overview of the risks and benefits of coffee consumption. Comprehensive Reviews in Food Science and Food Safety, 15(4), (2016), 671-684. doi:10.1111/1541-4337.12206.