WEP
Warwick
Evans
Publishing

Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 1
FBB 2023

(Poly)phenol-rich food and cardio-metabolic health

Yu Hu
University of British Columbia, Vancouver, V6T1Z2, Canada

Abstract. Due to the changes in people's diet structure caused by economic development, cardio-metabolic disease has also become a concernthat more people care about or need to alleviate. (Poly)phenols, a chemical widely found in natural plants or fruits, such as, berries and tea, are thought to play an important role in alleviating cardiometabolic disease. As a result, (poly)phenols rich foods can offer positive effects in general cardiovascular system, and multiple evidence present in helping improve glycemic control, blood pressure and blood lipid level. However, controversy remains , especially in their effects on relieving metabolic syndrome, and the effects of (poly)phenol-rich foods on the cardiovascular system could be differed based on origin, for example, quercetin is associated with blood pressure, but cannot contribute to blood glucose problem as much as they provide in hypertension, while anthocyanins signally relieve glycemic disorder. Meanwhile, details such as the daily intake of (poly)phenols with health benefits remains to be explored.

Key words: (poly)phenols, cardio-metabolic diseases, hypertension, atherosclerosis, type 2 diabetes.

1. Introduction

Cardio-metabolic diseases, including heart attack, diabetes, stroke, insulin resistance, and so on, typically being a series of high prevalence diseases and widely concerns. The number of cases has increased widely and reached 14.4% in USA in 2018 (Cheng et al. 2022). Cardio-metabolic diseases are multifactorial disorders that may involve several different factors, including changes in diet, lifestyle, and genetic factors. Modifying daily diet is one of the most common ways to ameliorate or prevent cardio-metabolic disease. It has been found that various nutrients can impact the risk of cardio-metabolic diseases, like saturated fatty acids, which could raise the risk, and (poly)phenols, in opposite, can improve the symptoms (López-Jaramillo et al., 2018).

According to previous studies, (poly)phenols, a series of compounds that naturally occurs largely in plant food products, such as, tea, coffee, and cocoa, are able to help effectively prevent chronic diseases and decrease the risk of cardio-metabolic diseases (Giacco et al., 2019).

Polyphenols, as a large class of heterogeneous phytochemicals containing phenolic rings, their abundant sources have led to diverse structures, and are roughly divided into four categories: flavonoids, phenolic acids, styrines and lignans. Flavonoids include flavones, flavonols flavanols, flavanones, isoflavones, and anthocyanins, mostly of which are relatively common polyphenols. Other high-profile (poly)phenols, such as, resveratrol, the most studied stilbene compound in grapes, grape products and red wine (Manach et al., 2004). The richest source of lignans is flaxseed, mainly in the form of isoresinol (Manach et al., 2004), and the most common phenolic acids refer to caffeic acid and ferulic acid found in grains (Manach et al., 2004). Different structures or functional groups can also lead to differences in health effects, for example, some polyphenols may have nitrogen-containing functional substituents as polyphenolic amides, like capsaicinoids in chili peppers, which have been found to have significant antioxidant and anti-inflammatory properties (Davis et al., 2007).

In this review, we present evidence focus on the effect of (poly)phenol-rich foods on cardio-metabolic disease risk, including reducing blood pressure and blood lipid incidence, improving glycemic control and other metabolic syndromes. For each following section, we searched and summarized different papers, including meta-analysis, randomised control trials, cohort studies and case-controlled studies, and based on different associated factors as evidence for the important role of (poly)phenol-rich foods in theimprovement of cardio-metabolic diseases.

2. Method

This is a review of the current literature on the (poly)phenols and cardio-metabolic disease risk, the literature search was performed in PubMed included the following keywords combined: cardio-metabolic health, (poly)phenol, type 2 diabetes, cardiovascular disease, metabolic syndrome, blood pressure, coffee, tea, cocoa, type 2 diabetes, cardiovascular diseases, blood pressure. The inclusion criteria were peer-reviewed human studies, meta-analyses and systematic reviews from 2004 to May 31st 2023, so that the focus is (poly)phenol-rich foods on associations with cardio-metabolic health.

3. Result

(Poly)phenol-rich food and cardiovascular disease

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality globally, accounting for 44% of all non-communicable disease deaths and 32% of all causes of deaths (GBD, 2018). For CVD, the common comprehensive criteria used to assess cardiovascular health generally includetriglyceride(TG) level , systolic blood pressure (>130mmHg), total cholesterol(>4.1mmol/L) , low-density lipoprotein cholesterol (LDL-C)(>3.5mmol/L), or high-density lipoprotein cholesterol (HDL-C) levels (<1.19mmol/L)base on the Framingham Risk Scope(FRS) and Cardiovascular Life Expectancy Model (CLEM)(Province of BC, 2021; Anderson et al., 2016)while (poly)phenols showed benign interference with multiple factors that influence cardiovascular disease, such as, lowering blood pressure and lipids levels, as well as assisting endothelial dysfunction. A study conducted in 2015 focused on the effect of quercetin on improving blood pressure and endothelial function (Brüll et al., 2015). In this double-blind, placebo-controlled crossover trial, 70 participants were randomized to receive 162 mg/day of quercetin, an onion peel extract, or placebo, for a 6-week treatment period and another 6-week washout period. As a result, in the subgroup of hypertensive participants, quercetin significantly reduced systolic blood pressure (SBP) by 3.6 mmHg ($p = 0.022$) comparing with placebo group (mean difference in treatment was -3.9 mmHg; $p = 0.049$), and the improvement in blood pressure was considering to be secondary to the improvement in endothelial function.

Hypertension and dyslipidemia are also part of the more concerned conditions in CVD and will be discussed further in the following sections. In general, multiple evidence has proven that (poly)phenols could improve CVD by reducing blood pressure, lipids and endothelial dysfunction, however, controversy remains, and the result may be affected by exact (poly)phenols bioavailability or intake level (Potì et al., 2019).

(Poly)phenol-rich food, body weight, and metabolic syndrome

Overweight or obesity is a common concern across the world recently, which could lead to hypertension, altered lipidlevels, and inflammation. Metabolic syndrome had an average prevalence of 31% and was associated with a two-fold increased risk of coronary heart disease, cerebrovascular disease, and a 1.5-fold increased risk of all-cause death (Engin, 2017). Obesity, especially abdominal obesity, is considered to be associated with increased risk of type 2 diabetes and cardiovascular diseases (Engin, 2017). For metabolic syndrome, the main treatment strategy is still weight loss, in addition, pharmacotherapy and nutritional treatment are proven to have beneficial effectiveness (Mitjavila et al., 2013). In the field of obesity and metabolic syndrome, the more concerned (poly)phenols are resveratrol and curcumin. Interestingly, even if they belong to different structure group (resveratrol is a stilbene and curcumin is phenolic acid) with different metabolism pathway, they showed similar physiological characteristics in the same field Curcumin, a (poly)phenols found mostly in ginger, has been proven to reducing angiogenesis and lipogenesis by inhibiting the expression of a specific enhancer (CCAAT) binding protein alpha and peroxisome proliferators-activated receptors (PPAR) and lowering cholesterol levels, as well as modulating the expression of glucose transporters to stimulate insulin secretion (Jabczyk et al., 2021), as seen in a randomized double-blind clinical trial in 2021 investigating the effects of curcumin nanoparticles on metabolic syndrome patients. The study showed that supplementation with 80 mg/day of curcumin nanomicelles for 12 weeks significantly reduced plasma TG levels ($p = 0.03$) and homeostasis model-assessed ß-cell dysfunction (HOMA-ß) compared with placebo (Bateni et al., 2021). Resveratrol, which is a natural (poly)phenols found widely in plants, fruits and wine, can reduce fat production in a variety of ways, such as inhibiting PPARγ in fat cells to promote lipolysis and fat loss, or inhibiting CAMP-specific phosphodiesterase to regulate sugar and lipid metabolism and protein synthesis (Chaplin, Carpéné & Mercader, 2018). However, the research on resveratrol is controversial, and lack of latest experiment data. Most of the experiments focus on rodents have shown that resveratrol is able to inhibit the accumulation of fat in the liver (Wang et al., 2015; Alberdi et al., 2011), while the results in human experiments is more diverse, and many experiments have failed to prove the effect of resveratrol on fat inhibition (Poulsen et al., 2013), and meanwhile, some have confirmed its beneficial effect (Méndez-del Villar et al., 2014).

In summary, more studies, especially in human studies, are needed to draw further conclusions about the association between (poly)phenols foods and obesity and metabolic syndrome.

(Poly)phenol-rich food and glycemic control

Type 2 diabetes(T2D) , as a chronic metabolic disorder mainly characterized by abnormal glucose metabolism, is usually accompanied by cardiovascular diseases, retinopathy, nephropathy, neuropathy and other complications, the prevalence is rising so rapidly that it is expected to reach 592 million by 2035 (Guariguata et al., 2014). Therefore, the alleviation method of T2D and its related diseases has become a vital point of research, while multiple (poly)phenols have been considered to be associated with glycemic control and able to lower the risk of T2D, such as flavonoids and phenolic acids. The hypoglycemic mechanism of (poly)phenols is related to decreasing carbohydrate digestion and glucose absorption and stimulating insulin secretion by inhibiting small intestinal brush salivarium and pancreatic α-amylase and α-glucosidase (Kim, Keogh & Clifton, 2016), as well as improving glucose uptake in surrounding tissues (Hanhineva et al., 2010). Phenolic acids, most commonly come from tea and coffee, have been highly anticipated, but the consequence is diverse. A meta-analysis of seven randomized controlled trials on green tea or green tea extracts shows tea intake did not affect the glucose level (Wang et al., 2014), while another set of meta-analyses (Zheng et al., 2013) indicated that green tea catechins with or without caffeine reduced fasting blood glucose (-1.48 mg/dL; 95% CI −2.57 ~−0.40 mg/dL).However, fasting insulin, glycated hemoglobin (HbA1c) or homeostasis model assessment of insulin resistance (HOMA–IR) index were not affected. Its subgroup analyses also found that the hypoglycemic effect of green tea intake was observed when the median follow-up time was more than 12 weeks, indicating that longer trials may be needed obtain more definitive (poly)phenol health effects. In addition to phenolic acids, anthocyanins, as a common type of flavonoids, have a significant association with T2D as higher anthocyanin intake is associated with a lower risk of T2D (Wedick et al., 2012). A randomized controlled trial was carried out in pregnant women with obese to explore the dietary intervention on the risk of gestational diabetes (Basu et al., 2021). In this study, participants in the dietary intervention group were provided frozen blueberries and soluble fiber as supplement for 18 weeks. As a result, the level of blood glucose (100 ± 33 mg/dL compared with 131 ± 40 mg/dL, $p < 0.05$), maternal weight (mean ± SD: 6.8 ± 3.2 kg compared with 12.0 ± 4.1 kg, $p= 0.001$) and C-reactive protein (baseline: 6.1 ± 4.0 compared with 6.8 ± 7.2 mg/L; midpoint: 6.1 ± 3.7 compared with 7.5 ± 7.3 mg/L; end: 5.5 ± 2.2 compared with 9.5 ± 6.6 mg/L, respectively, $p = 0.002$) were significantly lower in the dietary intervention than in the control group, while another study found the similar trend through the intake of apples, pears and blueberries (Wedick et al., 2012). However, besides anthocyanins, other part of the flavonoids, such as flavanones, flavonols, or even the total flavonols level, though previously considered to be anti-diabetic (Sun et al., 2015), subsequent studies have contradicted the previous conclusions (Sun et al., 2015) (Song et al., 2005), indicating their effect is unclear. The cyanidin3-O-β-glucoside (C3G) and metabolite protocatechuic acid (PCA) from anthocyanins are thought to lead to the unique effect that most other flavins do not have. Experiments by Scazzocchio et al. treated human retinal fat cells and mouse cells with 50μmol/L C3G and 100μmol/L PCA, after which both experimental compounds were observed to counteract the decline in glucose uptake and reverse defective GLUT4 translocation with insulin in both treated and untreated cells (Scazzocchio et al., 2011).

In summary, evidence is present to indicate that (poly)phenol-rich food can lead to improved glycemic control, while the type and origin of (poly)phenols maybe limited, and more study is needed to make more specific conclusion.

(Poly)phenol-rich food and blood pressure

Blood pressure control problems may cause serious cardiovascular disorders, becoming one of the most concerned symptoms of CVD extension. In the United States, antihypertensive medications (Lindsley, 2015) were the most prescribed (698 million) in 2012 and 2013. Blood pressure is thought to be influenced by a variety of factors, such as cardiac output, vascular compliance (representing the elasticity), total blood volume, nervous control system, or the renin-angiotensin system that regulates vascular resistance and blood volume. Among them, the antioxidant and anti-inflammatory effects of (poly)phenols plays an important role in alleviating hypertension. (poly)phenols have anti-inflammatory effects by inhibiting the activity and/or production of inflammation-inducing enzymes (Endale et al., 2013); In addition, (poly)phenols also have antioxidant ability by binding to antioxidant enzymes, increasing the free radical scavenging capacity of various antioxidant enzymes, and controlling redox regulation of cytoprotective enzyme genes through sulfhydryl modification (Ishii et al., 2009). Meanwhile, there is also growing evidence indicated that (poly)phenols also regulate ion transporters and channels, which in turn regulate total blood volume dependent on fluid volume or regulate vascular compliance (represent elasticity) and resistance (Marunaka et al., 2017). It is still the flavonoids that have been widely studied. Quercetin, for example, a flavonol and flavonoid, has been verified to play a certain role in resisting hypertension, but the difference between the results of their resistance effect exists. According to a randomized, double-blind, placebo-controlled, cross-over study, taking 730mg/day of quercetin for 4 weeks reduced systolic and diastolic blood pressure in patients with stage 1 hypertension. However, no effect on systolic and diastolic blood pressure were observed in patients with prehypertension (Edwards et al., 2007). Meanwhile, another double-blind randomized clinical trial (Zahedi et al., 2013) in 72 women with type 2 diabetes showed that consuming 500 mg/d quercetin for 10 weeks significantly reduced systolic blood pressure, but diastolic blood pressure was not significantly affected by quercetin intake. A meta-analysis of several randomized controlled trials concluded that quercetin intake >500 mg/ day for 8 weeks, but not ≤500 mg/ day, significantly reduced systolic and diastolic blood pressure (Serban et al., 2016). Besides quercetin, an increase in serum cGMP was observed in patients with hypercholesterolemia after supplementation with 320 mg of purified anthocyanins for 12 weeks as well (Zhu et al., 2011), which was paralleled by an increase in flow-mediated vasodilation (FMD) ($r = 0.428$, $p < 0.05$), another study revealed the decrease in neutrophil NADPH oxidase activity (Rodriguez-Mateos et al. 2013). Furthermore, anthocyanins can improve endothelial function and alleviate hypertensive disorder as well. However, further experiments are required to prove this statement.

In summary, multifarious evidence are present to indicate that (poly)phenol, especially flavonoids, have positive effects on hypertension, while their metabolic pathway is complicated, more research are needed to explore the actions of blood pressure, and may not all (poly)phenols are effective.

(Poly)phenol-rich food and blood lipids

Other than causing hyperlipidemia, excess blood lipid may also lead to atherosclerosis, a disease caused by the accumulation of lipids in the walls of the arteries (Garcia, C., & Blesso, C. N., 2021). Lipoprotein metabolism, oxidative stress, and inflammation play an interplay in the development of cardiovascular disease and considered key targets for the prevention and treatment of cardiovascular disease, such as, reducing serum low-density lipoprotein (LDL) abundance or LDL-cholesterol (LDL-C) and high-density lipoprotein (HDL) oxidation, increasing of HDL-cholesterol (HDL-C) level (Garcia, C., & Blesso, C. N., 2021). Excess level of LDL-C can gradually damage the artery wall as lipids become trapped in blood vessel, causing cholesterol crystals to oxidize, accumulate, and eventually deposit in the lining of the artery and in the smooth muscle underneath, while too much LDL exposure to the artery wall accelerates oxidation, leading to the appearance of more oxidized LDL (oxLDL) and stimulating the inflammatory response (Ference et al., 2017). Meanwhile, chronic inflammation may also lead to the oxidation of high-density lipoprotein (HDL), impeding its ability to perform cholesterol reverse transport (RCT) and protect lipoprotein and endothelial cells from oxidation (Pan et al., 2013). Therefore, various antioxidant and anti-inflammatory effects making (poly)phenols receiving great attention in CVD studies. As mentioned in previous section, anthocyanins, for example, growing evidence have indicated their abilities in affecting redox activities and reduced CVD risk. According to previous studies, the effect of anthocyanins on HDL-C, especially in adults with CVD-related symptoms such as dyslipidemia (Qin et al., 2009) and hypercholesterolemia (Zhu et al., 2014), has confirmed that an increase in HDL-C level can be observed after supplementation of anthocyanins for 12-24 weeks. Besides anthocyanins, various (poly)phenols are expected to have beneficial effects on blood lipid disorders. In a previous study (Sahebkar et al., 2015), no significant effect was observed in the subgroups in the first given curcumin <6 weeks (WMD: 0.75U /mL, 95%CI: -0.566-2.05, $p = 0.26$), but a significant increase in SOD activity was found at ≥6 weeks of supplementation (WMD: 1.46 U/mL, 95%CI: 0.60-2.32, $p = 0.0009$) as well as decreased serum lipid peroxides (WMD:−6.35 nmol/mL, 95%CI:−11.06 ~−1.64, $p = 0.008$) , increased GSH concentration (WMD: 5.39 μg /mL, 95%CI: 1.17-9.60, $p = 0.01$) and catalase activity (WMD: 51.78 U/mL, 95%CI: 15.71-87.85, $p = 0.005$). Tea (poly)phenols such as theabrownins were also indicated having the ability to reduce hepatic cholesterol and lipogenesis (Huang et al., 2019).

In summary, evidence has proven that various (poly)phenols have beneficial effect on alleviating blood lipid problems, further details, such as the specific pathway and target molecule of a particular (poly)phenol, may require more research.

4. Conclusion

The positive effect of (poly)phenols on cardio-metabolic health is worthy of recognition. However, in terms of diverse aspects (such as blood pressure vs. blood lipid), the effect or mechanism of action brought by different (poly)phenols may be different while the underlying mechanism is complicated, the obtained results would be different as well. In addition, the bioavailability and dietary intake of (poly)phenols are not significant in many regions, more detailed studies on cardio-metabolic system are required to obtain more accurate results.

References

[1] López-Jaramillo, P., Otero, J., Camacho, P. A., Baldeón, M., & Fornasini, M. (2018). Reevaluating nutrition as a risk factor for cardio-metabolic diseases. Colombia medica, 49(2), 175-181.

[2] Cheng, X., Ma, T., Ouyang, F., Zhang, G., & Bai, Y. (2022). Trends in the Prevalence of Cardiometabolic Multimorbidity in the United States, 1999-2018. International journal of environmental research and public health, 19(8), 4726. https://doi.org/10.3390/ijerph19084726

[3] Giacco, R., Costabile, G., Fatati, G., Frittitta, L., Maiorino, M. I., Marelli, G., ... & Vitale, M. (2020). Effects of (poly)phenols on cardio-metabolic risk factors and risk of type 2 diabetes. A joint position statement of the Diabetes and Nutrition Study Group of the Italian Society of Diabetology (SID), the Italian Association of Dietetics and Clinical Nutrition (ADI) and the Italian Association of Medical Diabetologists (AMD). Nutrition, Metabolism and Cardiovascular Diseases, 30(3), 355-367.

[4] Manach, C., Scalbert, A., Morand, C., Rémésy, C., & Jiménez, L. (2004). Polyphenols: food sources and bioavailability. The American journal of clinical nutrition, 79(5), 727–747. https://doi.org/10.1093/ajcn/79.5.727

[5] GBD 2017 Mortality Collaborators (2018). Global, regional, and national age-sex-specific mortality and life expectancy, 1950-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet (London, England), 392(10159), 1684–1735. https://doi.org/10.1016/S0140-6736(18)31891-9

[6] Province of British Columbia (2021). Cardiovascular disease - primary prevention. Province of British Columbia. https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/cardiovascular-disease, Accessed August 17, 2023.

[7] Anderson, T. J., Grégoire, J., Pearson, G. J., Barry, A. R., Couture, P., Dawes, M., ... & Ward, R. (2016). 2016 Canadian Cardiovascular Society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in the adult. Canadian Journal of Cardiology, 32(11), 1263-1282.

[8] Brüll, V., Burak, C., Stoffel-Wagner, B., Wolffram, S., Nickenig, G., Müller, C., Langguth, P., Alteheld, B., Fimmers, R., Naaf, S., Zimmermann, B. F., Stehle, P., & Egert, S. (2015). Effects of a quercetin-rich onion skin extract on 24 h ambulatory blood pressure and endothelial function in overweight-to-obese patients with (pre-)hypertension: a randomised double-blinded placebo-controlled cross-over trial. The British journal of nutrition, 114(8), 1263–1277. https://doi.org/10.1017/S0007114515002950

[9] Potì, F., Santi, D., Spaggiari, G., Zimetti, F., & Zanotti, I. (2019). (poly)phenols Health Effects on Cardiovascular and Neurodegenerative Disorders: A Review and Meta-Analysis. International journal of molecular sciences, 20(2), 351. https://doi.org/10.3390/ijms20020351

[10] Engin A. (2017). The Definition and Prevalence of Obesity and Metabolic Syndrome. Advances in experimental medicine and biology, 960, 1–17. https://doi.org/10.1007/978-3-319-48382-5_1

[11] Mitjavila, M. T., Fandos, M., Salas-Salvadó, J., Covas, M. I., Borrego, S., Estruch, R., Lamuela-Raventós, R., Corella, D., Martínez-Gonzalez, M. Á., Sánchez, J. M., Bulló, M., Fitó, M., Tormos, C., Cerdá, C., Casillas, R., Moreno, J. J., Iradi, A., Zaragoza, C., Chaves, J., & Sáez, G. T. (2013). The Mediterranean diet improves the systemic lipid and DNA oxidative damage in metabolic syndrome individuals. A randomized, controlled, trial. Clinical nutrition (Edinburgh, Scotland), 32(2), 172–178. https://doi.org/10.1016/j.clnu.2012.08.002

[12] Jabczyk, M., Nowak, J., Hudzik, B., & Zubelewicz-Szkodzińska, B. (2021). Curcumin in Metabolic Health and Disease. Nutrients, 13(12), 4440. https://doi.org/10.3390/nu13124440

[13] Bateni, Z., Rahimi, H. R., Hedayati, M., Afsharian, S., Goudarzi, R., & Sohrab, G. (2021). The effects of nano-curcumin supplementation on glycemic control, blood pressure, lipid profile, and insulin resistance in patients with the metabolic syndrome: A randomized, double-blind clinical trial. Phytotherapy research : PTR, 35(7), 3945–3953. https://doi.org/10.1002/ptr.7109

[14] Wang, S., Liang, X., Yang, Q., Fu, X., Rogers, C. J., Zhu, M., Rodgers, B. D., Jiang, Q., Dodson, M. V., & Du, M. (2015). Resveratrol induces brown-like adipocyte formation in white fat through activation of AMP-activated protein kinase (AMPK) α1. International journal of obesity (2005), 39(6), 967–976. https://doi.org/10.1038/ijo.2015.23

[15] Alberdi, G., Rodríguez, V. M., Miranda, J., Macarulla, M. T., Arias, N., Andrés-Lacueva, C., & Portillo, M. P. (2011). Changes in white adipose tissue metabolism induced by resveratrol in rats. Nutrition & metabolism, 8(1), 29. https://doi.org/10.1186/1743-7075-8-29

[16] Poulsen, M. M., Vestergaard, P. F., Clasen, B. F., Radko, Y., Christensen, L. P., Stødkilde-Jørgensen, H., Møller, N., Jessen, N., Pedersen, S. B., & Jørgensen, J. O. (2013). High-dose resveratrol supplementation in obese men: an investigator-initiated, randomized, placebo-controlled clinical trial of substrate metabolism, insulin sensitivity, and body composition. Diabetes, 62(4), 1186–1195. https://doi.org/10.2337/db12-0975

[17] Méndez-del Villar, M., González-Ortiz, M., Martínez-Abundis, E., Pérez-Rubio, K. G., & Lizárraga-Valdez, R. (2014). Effect of resveratrol administration on metabolic syndrome, insulin sensitivity, and insulin secretion. Metabolic syndrome and related disorders, 12(10), 497–501. https://doi.org/10.1089/met.2014.0082

[18] Chaplin, A., Carpéné, C., & Mercader, J. (2018). Resveratrol, Metabolic Syndrome, and Gut Microbiota. Nutrients, 10(11), 1651. https://doi.org/10.3390/nu10111651

[19] Guariguata, L., Whiting, D. R., Hambleton, I., Beagley, J., Linnenkamp, U., & Shaw, J. E. (2014). Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes research and clinical practice, 103(2), 137–149. https://doi.org/10.1016/j.diabres.2013.11.002

[20] Sun, Q., Wedick, N. M., Tworoger, S. S., Pan, A., Townsend, M. K., Cassidy, A., Franke, A. A., Rimm, E. B., Hu, F. B., & van Dam, R. M. (2015). Urinary Excretion of Select Dietary (poly)phenols Metabolites Is Associated with a Lower Risk of Type 2 Diabetes in Proximate but Not Remote Follow-Up in a Prospective Investigation in 2 Cohorts of US Women. The Journal of nutrition, 145(6), 1280–1288. https://doi.org/10.3945/jn.114.208736

[21] Song, Y., Manson, J. E., Buring, J. E., Sesso, H. D., & Liu, S. (2005). Associations of dietary flavonoids with risk of type 2 diabetes, and markers of insulin resistance and systemic inflammation in women: a prospective study and cross-sectional analysis. Journal of the American College of Nutrition, 24(5), 376–384. https://doi.org/10.1080/07315724.2005.10719488

[22] Scazzocchio, B., Varì, R., Filesi, C., D'Archivio, M., Santangelo, C., Giovannini, C., Iacovelli, A., Silecchia, G., Li Volti, G., Galvano, F., & Masella, R. (2011). Cyanidin-3-O-β-glucoside and protocatechuic acid exert insulin-like effects by upregulating PPARγ activity in human omental adipocytes. Diabetes, 60(9), 2234–2244. https://doi.org/10.2337/db10-1461

[23] Kim, Y., Keogh, J. B., & Clifton, P. M. (2016). (poly)phenols and Glycemic Control. Nutrients, 8(1), 17. https://doi.org/10.3390/nu8010017

[24] Hanhineva, K., Törrönen, R., Bondia-Pons, I., Pekkinen, J., Kolehmainen, M., Mykkänen, H., & Poutanen, K. (2010). Impact of dietary polyphenols on carbohydrate metabolism. International journal of molecular sciences, 11(4), 1365–1402. https://doi.org/10.3390/ijms11041365

[25] Wang, X., Tian, J., Jiang, J., Li, L., Ying, X., Tian, H., & Nie, M. (2014). Effects of green tea or green tea extract on insulin sensitivity and glycaemic control in populations at risk of type 2 diabetes mellitus: a systematic review and meta-analysis of randomised controlled trials. Journal of human nutrition and dietetics : the official journal of the British Dietetic Association, 27(5), 501–512. https://doi.org/10.1111/jhn.12181

[26] Zheng, X. X., Xu, Y. L., Li, S. H., Hui, R., Wu, Y. J., & Huang, X. H. (2013). Effects of green tea catechins with or without caffeine on glycemic control in adults: a meta-analysis of randomized controlled trials. The American journal of clinical nutrition, 97(4), 750–762. https://doi.org/10.3945/ajcn.111.032573

[27] Wedick, N. M., Pan, A., Cassidy, A., Rimm, E. B., Sampson, L., Rosner, B., Willett, W., Hu, F. B., Sun, Q., & van Dam, R. M. (2012). Dietary flavonoid intakes and risk of type 2 diabetes in US men and women. The American journal of clinical nutrition, 95(4), 925–933. https://doi.org/10.3945/ajcn.111.028894

[28] Basu, A., Feng, D., Planinic, P., Ebersole, J. L., Lyons, T. J., & Alexander, J. M. (2021). Dietary Blueberry and Soluble Fiber Supplementation Reduces Risk of Gestational Diabetes in Women with Obesity in a Randomized Controlled Trial. The Journal of nutrition, 151(5), 1128–1138. https://doi.org/10.1093/jn/nxaa435

[29] Lindsley, C. W. (2015). 2013 Trends and statistics for prescription medications in the United States: CNS highest ranked and record number of prescriptions dispensed. ACS Chemical Neuroscience, 6(3), 356-357.

[30] Endale, M., Park, S. C., Kim, S., Kim, S. H., Yang, Y., Cho, J. Y., & Rhee, M. H. (2013). Quercetin disrupts tyrosine-phosphorylated phosphatidylinositol 3-kinase and myeloid differentiation factor-88 association, and inhibits MAPK/AP-1 and IKK/NF-κB-induced inflammatory mediators production in RAW 264.7 cells. Immunobiology, 218(12), 1452–1467. https://doi.org/10.1016/j.imbio.2013.04.019

[31] Ishii, T., Ishikawa, M., Miyoshi, N., Yasunaga, M., Akagawa, M., Uchida, K., & Nakamura, Y. (2009). Catechol type (poly)phenols is a potential modifier of protein sulfhydryls: development and application of a new probe for understanding the dietary (poly)phenols actions. Chemical research in toxicology, 22(10), 1689–1698. https://doi.org/10.1021/tx900148k

[32] Marunaka, Y., Marunaka, R., Sun, H., Yamamoto, T., Kanamura, N., Inui, T., & Taruno, A. (2017). Actions of Quercetin, a (poly)phenol, on Blood Pressure. Molecules (Basel, Switzerland), 22(2), 209. https://doi.org/10.3390/molecules22020209

[33] Edwards, R. L., Lyon, T., Litwin, S. E., Rabovsky, A., Symons, J. D., & Jalili, T. (2007). Quercetin reduces blood pressure in hypertensive subjects. The Journal of nutrition, 137(11), 2405–2411. https://doi.org/10.1093/jn/137.11.2405

[34] Zahedi, M., Ghiasvand, R., Feizi, A., Asgari, G., & Darvish, L. (2013). Does Quercetin Improve Cardiovascular Risk factors and Inflammatory Biomarkers in Women with Type 2 Diabetes: A Double-blind Randomized Controlled Clinical Trial. International journal of preventive medicine, 4(7), 777–785.

[35] Serban, M. C., Sahebkar, A., Zanchetti, A., Mikhailidis, D. P., Howard, G., Antal, D., Andrica, F., Ahmed, A., Aronow, W. S., Muntner, P., Lip, G. Y., Graham, I., Wong, N., Rysz, J., Banach, M., & Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group (2016). Effects of Quercetin on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Journal of the American Heart Association, 5(7), e002713. https://doi.org/10.1161/JAHA.115.002713

[36] Zhu Y., Xia M., Yang Y., Liu F., Li Z., Hao Y., Mi M., Jin T., Ling W. Purified anthocyanin supplementation improves endothelial function via NO-cGMP activation in hypercholesterolemic individuals. Clinical Chemistry, 57(11), 1524–1533, https://doi.org/10.1373/clinchem.2011.167361

[37] Rodriguez-Mateos A., Rendeiro C., Bergillos-Meca T., Tabatabaee S., George T., Heiss C., Spencer J.P. Intake and time dependence of blueberry flavonoid-induced improvements in vascular function: a randomized, controlled, double-blind, crossover intervention study with mechanistic insights into biological activity. The American Journal of Clinical Nutrition, 98(5), 1179-1191, https://doi.org/10.3945/ajcn.113.066639

[38] Garcia, C., & Blesso, C. N. (2021). Antioxidant properties of anthocyanins and their mechanism of action in atherosclerosis. Free radical biology & medicine, 172, 152–166. https://doi.org/10.1016/j.freeradbiomed.2021.05.040

[39] Ference, B. A., Ginsberg, H. N., Graham, I., Ray, K. K., Packard, C. J., Bruckert, E., ... & Catapano, A. L. (2017). Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. European heart journal, 38(32), 2459-2472.

[40] Pan, B., Yu, B., Ren, H., Willard, B., Pan, L., Zu, L., ... & Zheng, L. (2013). High-density lipoprotein nitration and chlorination catalyzed by myeloperoxidase impair its effect of promoting endothelial repair. Free Radical Biology and Medicine, 60, 272-281.

[41] Qin, Y., Xia, M., Ma, J., Hao, Y., Liu, J., Mou, H., ... & Ling, W. (2009). Anthocyanin supplementation improves serum LDL-and HDL-cholesterol concentrations associated with the inhibition of cholesteryl ester transfer protein in dyslipidemic subjects. The American journal of clinical nutrition, 90(3), 485-492.

[42] Zhu, Y., Huang, X., Zhang, Y., Wang, Y., Liu, Y., Sun, R., & Xia, M. (2014). Anthocyanin supplementation improves HDL-associated paraoxonase 1 activity and enhances cholesterol efflux capacity in subjects with hypercholesterolemia. The Journal of Clinical Endocrinology & Metabolism, 99(2), 561-569.

[43] Sahebkar, A., Serban, M. C., Ursoniu, S., & Banach, M. (2015). Effect of curcuminoids on oxidative stress: A systematic review and meta-analysis of randomized controlled trials. Journal of functional foods, 18, 898-909.

[44] Huang, F., Zheng, X., Ma, X., Jiang, R., Zhou, W., Zhou, S., Zhang, Y., Lei, S., Wang, S., Kuang, J., Han, X., Wei, M., You, Y., Li, M., Li, Y., Liang, D., Liu, J., Chen, T., Yan, C., Wei, R., … Jia, W. (2019). Theabrownin from Pu-erh tea attenuates hypercholesterolemia via modulation of gut microbiota and bile acid metabolism. Nature communications, 10(1), 4971. https://doi.org/10.1038/s41467-019-12896-x.