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The Effect of Flavonoid Consumption on Blood Pressure: A Systematic Review

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A B S T R A C T

Hypertension is a common condition in which the long-term force of blood against artery walls is high enough to cause health problems, such as heart disease eventually. High blood pressure is known as the "silent killer". Most people with high blood pressure are unaware of the problem because it may not have any warning signs or symptoms. For this reason, it is essential to measure blood pressure regularly. A new study has shown that consuming foods rich in flavonoids can help patients with high blood pressure. This advantage of these compounds is due to their vasodilator properties. Flavonoids are a diverse group of biologically active polyphenol compounds found in plants and herbs. Regular consumption of flavonoids has cardioprotective effects and may reduce the onset or progression of many cardiovascular diseases, especially hypertension. The article search was done in PubMed, ScienceDirect, and Google Scholar databases. The current body of evidence supports the ingestion of flavonoids for their beneficial effect on blood pressure. However, more significant research should further investigate the vascular moderating effects and the safety and acceptability of almond consumption.

1. Introduction

Hypertension is one of the leading causes of death worldwide.[1] Its popularity is increasing dramatically; The rate of death from high blood pressure in the United States increased by 10.5% between 2005 and 2015.[2] Worldwide, 1.3 billion people with hypertension were diagnosed in 2010. According to WHO, the number one cause of death in 2016 was ischemic heart disease and stroke, the main complication of the killer disease. In the United States, 11% of children and adolescents were susceptible to this NCD in 2012, according to the American Heart Association.[1] Flavonoids are a diverse group of biologically active polyphenol compounds found in plants and herbs. Regular consumption of flavonoids has cardioprotective effects and may reduce the onset or progression of many cardiovascular diseases, especially hypertension. Observational studies show an inverse association between any of these three combinations: a) anthocyanin intake and risk of myocardial infarction (MI), b) flavanone intake and risk of stroke caused by ischemia, and c) flavonol intake and risk of type 2 diabetes. Randomized controlled trials (RCTs) in humans have shown that catechins and quercetin significantly affect lowering blood pressure. Mechanistically, flavonoids mediate their hypotensive effects by increasing nitric oxide (NO) bioavailability, reducing oxidative stress in endothelial cells, or modulating vascular ion channel activity.

Several studies have demonstrated that consuming foods rich in flavonoids can help patients with high blood pressure.[3,4]

2. Methods

Data collection

The articles were searched online by December 2021 on PubMed, ScienceDirect, and Google Scholar databases using keywords related to "hypertension," "flavonoid,". The term "flavonoid" was used in the search for all databases. The relevant papers then get selected based on inclusion and exclusion criteria. This study reviews research articles published between 2000 and 2021 to examine the effect of flavonoids on lowering blood pressure. The flowchart presents the data acquisition process to select the concordant studies as illustrated in figure 1.

The inclusion and exclusion of this study were already decided before the search. This study included all research articles using naringin with or without control groups. In the studies that have already been collected and then filtered, duplicates are removed. The articles are then studied, and the irrelevant studies get removed.

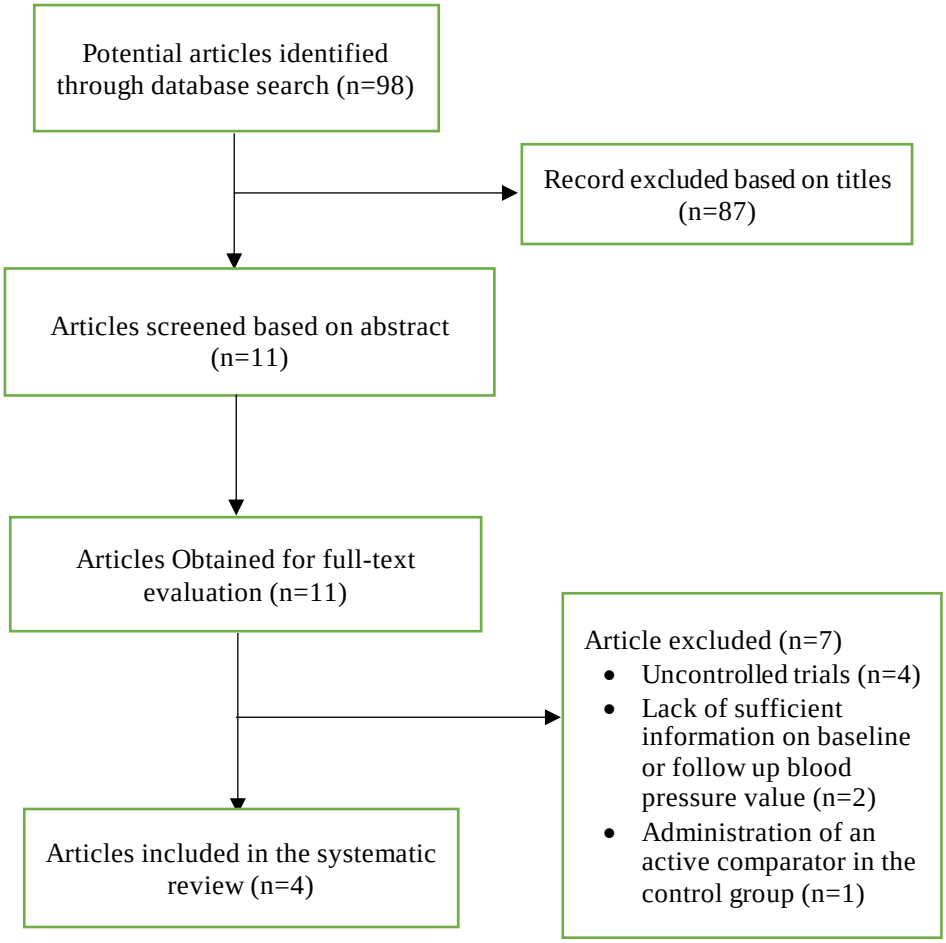

Figure 1. The flow chart in the selection of the article.

This study was written as a systematic review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[6] The search tool for this systematic review is PICO or population, intervention, comparison, and outcome.[7] The PICO is population: hypertension model; intervention: the use of flavonoid; comparison: with or without antihypertension or statin groups and;

outcome: decrease blood pressure.

Statistical analysis

The relevant information from selected articles and then extracted, such as the subject characteristics, interventions, duration, results from the intervention, and methods in data analysis. The main result expected from the selected articles were the potential of flavonoid to decrease blood pressure because of hypertension subject compared to the available control or standard available.

3. Results and Discussion

Based on online searching in several sites resulted in 98 articles from the initial search; however, only 11 articles are regarded as relevant from 4 sources which six articles from PubMed, three articles from Science Direct, and two from Google Scholar, while 89 articles are excluded because of irrelevant titles. Another four articles are removed from the selection because of the uncontrolled trial; two articles lack sufficient information on baseline or follow-up blood pressure values, and 1 article was administered by an active comparator in the control group.

The final seven articles selected are from Iran (2014, 2013)[5,6] Korea (2011)[7], and Germany (2013).[8] In total, 299 participants were randomized, of whom 152 were allocated to quercetin supplementation and 140 to the control group in the seven selected studies with nine treatment arms. The number of participants in these trials ranged from 13 to 93. Included studies were published between 2011 and 2014 and were conducted in the Iran, Korea, and Germany Ranges of doses from 100 to 1000 mg/day of quercetin were administered in the included trials. The duration of supplementation with quercetin ranged between 8 and 10 weeks.

Table 1. Summary of data description from the included studies

Study	Subject criteria	Flavonoid dose	Length of follow up	Outcome
Zahedi et al. 2013 (Iran)				
	Women with a history T2DM for at least 3y, lack of severe heart disease, stroke, severe liver Design: Randomized double-blind placebo-controlled clinical trial	500 mg/day	8 weeks, sacrificed at the end	flavonoids decrease hypertension 95% CI: 2.44, 0.49, P=0.191)
Javadi et al. 2014 (Iran)				
	Women unchanged type and dose of medications form previous month Design: Randomized double-blind placebo-controlled clinical trial	500 mg/day	8 weeks, sacrificed at the end	flavonoids decrease hypertension 95% CI: 2.00, 1.52, P=0.788)
Lee et al. 2011 (Korea)				
	Healthy male smokers Design: Randomized double-blind placebo-controlled clinical trial	100 mg/day	10 weeks, sacrificed at the end	flavonoids decrease hypertension 95% CI: 3.23, 1.47, P=0.464)
Pfeuffer et al. 2013 (Germany)				
	Healthy man patients with apolipoprotein E genotype Design: Randomized double-blind placebo-controlled crossover trial	150 mg/day	8 weeks, sacrificed at the end	flavonoids decrease high blood 95% CI: 3.72, 0.02, P=0.053

In this systematic review, we reviewed existing studies on dietary polyphenols and blood pressure in epidemiological studies and investigated the association between total or individual subclasses of flavonoid intake and the risk of hypertension in prospective cohort studies. The epidemiological studies evaluating the association between total dietary polyphenols and cardio-metabolic risk factors, including hypertension, generally showed contrasting results. Among articles with a cross-sectional design, while no study but one[9] reported an inverse association between total polyphenol or flavonoid intake and occurrence of hypertension, few studies reported significant results for phenolic acids.[10,11] The findings on the relation between dietary phytoestrogens intake and blood pressure are more univocal, with a general significant inverse association between intake of either isoflavones or lignans and blood pressure levels, despite the heterogeneity of results between sexes and the cross-sectional design of most of the studies reviewed limiting the level of evidence. Among subclasses of flavonoids, the meta-analysis showed that dietary intake of anthocyanins was significantly associated with a reduced risk of hypertension: a comparison of the highest vs. lowest anthocyanins exposure showed an 8% reduction in risk of hypertension. Moreover, after the exclusion of data from one cohort, also the analyses for total flavonoids and flavones demonstrated significant results. Significant heterogeneity between studies observed for total flavonoids should be considered a major limitation of these findings. Nevertheless, heterogeneity was mainly related to the strength of the association rather than to the direction of risk estimates, suggesting overall promising perspectives for future studies.

Existing literature on studies aiming to explore the relation between flavonoid-rich foods, dietary flavonoids and hypertension is generally consistent but not univocal. Two meta-analyses of dietary interventions characterized by isocaloric diets with pulses or fruits and vegetables (including one portion of berries/day and 50 g of dark chocolate) showed significant reduction in systolic/diastolic blood pressure[12] and of markers of endothelial function[13], respectively. Among major food sources of anthocyanins, potential blood pressure lowering effects have been demonstrated for pomegranate juice[14] and berries[15,16], whereas a lack of effects has been reported for blueberry supplementation.[17] Among food sources of isoflavones, a meta-analysis exploring the effects of soybeans on blood pressure in postmenopausal women showed that ingestion of ≥25 g soy protein per day had blood pressure-lowering effects, and the improvements in blood pressure may be due to the isoflavones component of soy protein.[18] Other sources of phytoestrogens are seeds, which are rich in lignans: meta-analyses on clinical trials evaluating the effects of flaxseeds and sesame consumption on blood pressure concluded that they both may exert blood pressure-lowering effects.[19,20] Among the major sources of phenolic acids, the most comprehensive meta-analysis of cohort studies on coffee consumption and incidence of new-onset hypertension reported a modest decrease in risk of hypertension[21], while several meta-analyses investigating the effects of tea on blood pressure, showing potential benefits for long-term (>12 weeks) intake[22,23] and significant effects also for secondary prevention of cardiovascular disease among overweight and obese adults[24] and in individuals within pre-hypertensive and hypertensive ranges[25]. However, a meta-analysis of clinical trials on polyphenol supplementation showed contrasting results. A previous meta-analysis of randomized controlled trials on the effects of anthocyanins on blood pressure showed overall null results.[26] Other meta-analyses on soy isoflavones supplementation reported that soy isoflavone extracts significantly decreased systolic but not diastolic blood pressure in adult humans, and no dose-response relationship was observed[27], while another meta-analysis suggested that the effects were more evident in hypertensive, but not in normotensive individuals.[27] Similarly, the beneficial potential of flaxseed to reduce blood pressure may be greater when it is consumed as a

whole seed rather than as a lignan extract.[28] Possible reasons for such scarce findings may depend on limitations in the study design of the trials included in the analysis, or on the short-term consumption to which the trials refer, which may be indicative of potential acute effects, but not equivalent to long-term consumption. Moreover, supplementation using pharmaceutical formulas (i.e., pills or capsules) of pure extracts may not be equivalent to dietary intake. Finally, it has been suggested that flavonoid bioactivity may not follow a classical linear dose-response association, and attention should be paid when designing and pooling together results from randomized controlled trials.[29]

4. Conclusion

Flavonoid intake resulted in significantly decreased hypertension in humans. Moreover, participants who consumed quercetin for 8 weeks or more showed significantly changed levels of high-density lipoprotein cholesterol and triglycerides in trials with a parallel design.

5. References

1. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, et al. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. Circulation. 2016; 134(6):441–50.
2. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. Circulation. 2018; 137(12).
3. Ibrahim MA, Asuka E, Jialal I. Hypercholesterolemia. [Updated 2021 Sep 28]. In: StatPearls [Online]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available: https://www.ncbi.nlm.nih.gov/books/NBK459188/. [Accessed 10 December 2021].
4. Tripoli E, Guardia ML, Giammanco S, Majo DD, Giammanco M. Citrus flavonoids: molecular structure, biological activity and nutritional properties: a review. Food Chem 2007; 104:466-79.
5. Zahedi M, Ghiasvand R, Feizi A, Asgari G, Darvish L. Does quercetin improve cardiovascular risk factors and inflammatory biomarkers in women with type 2 diabetes: a double-blind randomized controlled clinical trial. Int J Prev Med. 2013; 4:777
6. Javadi F, Eghtesadi S, Ahmadzadeh A, Aryaeian N, Zabihiyeganeh M, et al. The effect of quercetin on plasma oxidative status, C-reactive protein and blood pressure in women with rheumatoid arthritis. Int J Prev Med. 2014; 5:293.
7. Lee K-H, Park E, Lee H-J, Kim M-O, Cha Y-J, et al. Effects of daily quercetin-rich supplementation on cardiometabolic risks in male smokers. Nutr Res Pract. 2011; 5:28–33.
8. Pfeuffer M, Auinger A, Bley U, Kraus-Stojanowic I, Laue C, et al. Effect of quercetin on traits of the metabolic syndrome, endothelial function and inflammation in men with different APOE isoforms. Nutr Metab Cardiovasc Dis. 2013; 23:403–9.
9. Sohrab G, Hosseinpour-Niazi S, Hijazi J, Yuzbashian E, Mirmiran P, et al. Dietary polyphenols and the metabolic syndrome among Iranian adults.int. J. Food Science. Nutrition. 2013; 64:661–7.
10. Miranda AM, Steluti J, Fisberg RM, Marchioni DM. Association between coffee consumption and its polyphenols and cardiovascular risk factors: A population-based study.Nutrition. 2017; 9:276.
11. Godos J, Sinatra D, Blanco I, Mule S, La Verde M, Marranzano M. Association between dietary phenolic acids and hypertension in a Mediterranean cohort. Nutritients. 2017; 9.
12. Jayalath VH, de Souza RJ, Sievenpiper JL, Ha V, Chiavaroli L, et al. Effect of dietary pulse on blood pressure: A systematic review and meta-

analysis of controlled eating trials.NS. J. hypertension. 2014; 27:56–64.

13. Noad RL, Rooney C, McCall D, Young IS, McCance D, et al. Beneficial effects of a polyphenol-rich diet on cardiovascular risk: A randomized control trial.Heart 2016; 102:1371–9.
14. Sahebkar A, Feri C, Giorgini P, Bo S, Nachtigal P, et al. Effects of pomegranate juice on blood pressure: A systematic review and meta-analysis of randomized controlled trials. Pharmacol Res. 2017; 115:149-61.
15. Huang H, Chen G, Liao D, Zhu Y, Xue X. Effect of berry consumption on cardiovascular risk factors: A meta-analysis with sequential analysis of randomized controlled trials. Sci Rep. 2016; 6:23625.
16. Kent K, Charlton KE, Jenner A, Roodenrys S. Acute reduction in blood pressure after consumption of anthocyanin-rich cherry juice may be dependent on dose intervals: A pilot cross-over study. int. J. Food. science. nutrition. 2016; 67:47–52.
17. Zhu Y, Sun J, Lu W, Wang X, Wang X, et al. Effects of blueberry supplementation on blood pressure: A systematic review and meta-analysis of randomized clinical trials.J. Hum. Hypertension. 2017; 31: 165-171. [CrossRef]
18. Kou T, Wang T, Cai J, Song J, Du B, et al. Effect of soy protein on blood pressure in postmenopausal women: A meta-analysis of randomized controlled trials. Food Function. 2017; 8:2663–71.
19. Khosravi-Boroujeni H, Nikbakht E, Nathanelov E, Khalesi, S. Can consumption of sesame increase blood pressure? Systematic review and meta-analysis of controlled trials.J.Sci. food agriculture. 2017: 97:3087–94.
20. Ursonu S, Sahebkar A, Andrika F, Serbia C, Banach M. Lipid and blood pressure meta-analysis collaboration. Effects of flaxseed supplementation on blood pressure: A systematic review and meta-analysis of controlled clinical trials. Clin Nutr. 2016; 35:615–25.
21. Grosso G, Micek A, Godos J, Pajak A, Sciacca S, et al. Long-term coffee consumption is associated with a reduced incidence of new-onset hypertension: A dose-response meta-analysis. Nutrition. 2017; 9:890.
22. Liu G, I XN, Zheng XX, Xu YL, Lu J, et al. Effects of tea intake on blood pressure: A meta-analysis of randomized controlled trials.Mr. J. Nutr. 2014, 112:1043–54.
23. Turban C, Sahebkar A, Ursonu S, Andrika F, Banach M. Effect of sour tea (*Hibiscus sabdariffA* L.) on arterial hypertension: a systematic review and meta-analysis of randomized controlled trials. J. Hypertension. 2015; 33(6):1119-27.
24. Liu J, Tang W, Sang L, Dai X, Wei D, Luo Y, Zhang J. Milk, yogurt, and lactose intake and ovarian cancer risk: A meta-analysis. Nutr Cancer. 2015: 67:68–72.
25. Yarmolinsky J, Gon G, Edwards P. Effect of tea on blood pressure for secondary prevention of cardiovascular disease: A systematic review and meta-analysis of randomized controlled trials. Nutr Rev. 2015; 73:236–46.
26. Zhu Y; Bo Y, Wang X, Lu W, Wang X, et al. Effect of anthocyanins on blood pressure: A prism-compliant meta-analysis of randomized clinical trials. Medicines 2016; 95:e3380.
27. Taku K, Lin N, Cai D, Hu J, Zhao X, et al. Effects of soy isoflavone extract supplements on blood pressure in adult humans: A systematic review and meta-analysis of randomized placebo-controlled trials. J. Hypertension. 2010; 28:1971-82.
28. Liu XX, Li SH, Chen JZ, Sun K, Wang XJ, et al. Effect of soy isoflavones on blood pressure: A meta-analysis of randomized controlled trials.Meta Cardiovascular nutrition. Dec. 2012; 22:463–70.

29. Khalesi S, Irwin C, Schubert M. Consumption of flaxseed may reduce blood pressure: A systematic review and meta-analysis of controlled trials.J. Nutr. 2015; 145:758–65.