WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

The role of nutraceuticals in the prevention of cardiovascular disease

Atul Yadav (B. Pharm)[1],Mr. Mark Masih (Assistant professor)[2],Rudra Kumar Chaubey (B.Pharm)[3]

College - S.N College of pharmacy

ABSTRACT :

Heart disease (CVD) is one of the biggest health and financial problems in the world. What we eat plays a major role in either increasing or lowering the risk of heart problems. Diet affects heart health both directly and by influencing other risk factors like high blood pressure, high cholesterol, and diabetes.

Nutraceuticals are natural food-based products that can help prevent or treat diseases. Research shows that certain foods and supplements can help protect the heart and reduce the chances of developing CVD.

Keywords: Nutraceuticals, cardiovascular disease (CVD), polyphenols

Introduction

Cardiovascular Disease (CVD)

Heart disease (CVD) is very common—most people over 60 years old will experience some form of it. Based on data from 2012–2013, CVD causes about **17.3 million deaths each year worldwide**. In Europe, it costs around **200 billion Euros** in healthcare spending each year.
CVD risk factors are divided into two groups:

- **Non-modifiable** (cannot be changed): age, gender, and genetics.
- **Modifiable** (can be changed): obesity, high blood pressure, high cholesterol, diabetes, metabolic syndrome, poor diet, smoking, and lack of exercise.

Diet plays a key role—it can directly affect heart health or influence other risks like high blood pressure, cholesterol, and diabetes. Lowering these risk factors, especially blood pressure and cholesterol, can greatly reduce deaths from CVD.
Studies show that certain foods and supplements can protect against heart disease. For example, in the **PREDIMED study**, people who ate the most polyphenols (plant-based compounds) had **about half the risk** of developing heart disease compared to those who ate the least.
This review looks at recent research on how **nutraceuticals**—natural food-based compounds—can help prevent and treat CVD. However, few studies have directly measured how these substances affect death rates, and large clinical trials are rare. Therefore, most research focuses on how nutraceuticals affect risk factors like cholesterol and blood pressure.

What Are Nutraceuticals?

The word **"nutraceutical"** was first used in 1989 by Dr. Stephen DeFelice. It means **"a food or part of a food that provides health or medical benefits, including preventing or treating disease."**
Nutraceuticals are made from natural ingredients and can include certain foods, extracts, or supplements. Several types have shown possible benefits for heart health. The main ones discussed here are:

1. Sterols and Stanols

- **What they are:** Natural substances found in plants like fruits, vegetables, nuts, seeds, and grains.
- **How they work:** Their structure is similar to cholesterol, so they help block cholesterol absorption in the intestine.
- **Effects:**
  - Lower total cholesterol (TC) and LDL ("bad") cholesterol by up to **10%**.
  - Have little or no effect on HDL ("good") cholesterol or triglycerides.
- **Combination with statins:** When taken with statin drugs, they can further reduce cholesterol levels compared to statins alone.
- **In food or supplements:** They work equally well whether eaten naturally in foods or taken as supplements.
- **Possible downside:** They may reduce absorption of some vitamins (like carotenoids and fat-soluble vitamins), though more research is needed to confirm this.

2. Polyphenols

- **What they are:** Plant compounds found in fruits, vegetables, cereals, legumes, tea, coffee, wine, and cocoa.
- **Types:** Flavonoids, phenolic acids, stilbenes, and lignans—over 8,000 different kinds are known.
- **Examples:**
  - **Grapes and red wine:** Contain compounds like resveratrol, which may protect the heart.
  - **Cocoa and chocolate:** Rich in catechins and flavonoids, offering more antioxidants per serving than tea or wine.
  - **Tea:** Green tea has more catechins (such as EGCG), while black tea (more fermented) contains other compounds like theaflavins and thearubigins.
- **Benefits:** Regular intake of polyphenol-rich foods is linked with lower risk of heart disease.

3. Spirulina

- **What it is:** A blue-green algae that's been eaten safely for centuries.
- **Nutrients:** High in protein, vitamins, minerals, carotenoids, and antioxidants (like phycocyanins).
- **Potential benefits:** May support heart health and reduce cholesterol, though more research is still needed.

Dyslipidemia (Abnormal Blood Lipids)

Dyslipidemia refers to having unhealthy levels of fats (lipids) in the blood—especially high total cholesterol or LDL ("bad") cholesterol. Lowering LDL levels is known to reduce the risk of heart attacks and other heart problems.
Because of this, **nutraceuticals that improve lipid levels** may help reduce CVD risk.

Plant Sterols/Stanols and Cholesterol

- Studies show that consuming plant sterols/stanols can **lower total and LDL cholesterol levels** in humans.
- Their cholesterol-lowering effect is strongest for LDL and works by:
  1. Reducing cholesterol absorption in the intestine.
  2. Increasing the liver's uptake of cholesterol from the blood.
  3. Reducing the body's own cholesterol production.
- The more sterols you consume (within safe limits), the greater the LDL reduction.
- Some evidence suggests they may help prevent heart attacks, especially in men, though other studies found that cholesterol improvements don't always lead to fewer CVD events.

In summary, **nutraceuticals like plant sterols, polyphenols, and spirulina** can positively affect risk factors for heart disease—mainly by improving cholesterol levels and reducing oxidative stress. However, more large-scale studies are needed to confirm their long-term effects on preventing heart attacks and reducing mortality.

Polyphenols

Effects of Nutraceuticals on Heart Disease, Blood Pressure, and Diabetes (Simplified Summary)

1. Effects on Blood Lipids (Cholesterol and Fats)

Grape Polyphenols

- Some studies show that **grape products** (like grape juice or grape extract) can help raise "good" cholesterol (HDL-C) and lower "bad" cholesterol (LDL-C) and total cholesterol (TC).
- However, other research, including large reviews (meta-analyses), found **no clear effect** on LDL-C.
- In one study, grape powder reduced large LDL particles (which are less harmful), but not the small, more dangerous LDL particles.
- **Resveratrol**, a compound found in grapes and red wine, showed **no significant improvement** in cholesterol or blood sugar, though it slightly lowered HDL-C in some studies.
- More large, high-quality studies are needed.

Cocoa and Chocolate

- Several studies show that **cocoa** (especially rich in flavanols) can **reduce LDL-C** by about 6 mg/dL and slightly lower total cholesterol.
- These effects are stronger in people with high heart disease risk and weaker in healthy people.
- **Dark chocolate** didn't show much benefit in people with diabetes or high blood pressure.
- A review of 19 studies (over 1,100 people) found that cocoa **lowered triglycerides** and **raised HDL-C** slightly.
- The **Flaviola Health Study** found that 450 mg cocoa flavanols taken twice daily for a month lowered total cholesterol and LDL-C and raised HDL-C, predicting a lower 10-year heart disease risk.
- Overall, cocoa flavanols seem beneficial, but only consistent, well-controlled studies can confirm this.

Tea Polyphenols

- Drinking **green or black tea** has been linked with **lower total cholesterol and LDL-C**, but little or no change in HDL-C.
- Studies show that green tea tends to have stronger effects than black tea.
- Differences in how tea is processed and prepared may explain why results vary between studies.

- Tea seems especially helpful for people with high cholesterol.
- One long-term study in postmenopausal women found that **green tea extract** reduced LDL-C and non-HDL-C after 12 months.

Armolipid Plus

- A supplement called **Armolipid Plus** (made from red yeast rice, policosanol, berberine, folic acid, astaxanthin, and coenzyme Q10) has shown strong cholesterol-lowering effects.
- It reduced total cholesterol by about **11–21%**, LDL-C by **15–31%**, and triglycerides by **16%**.
- It is generally safe and well tolerated.

Spirulina

- **Spirulina**, a blue-green algae, may help improve cholesterol.
- Taking 1–4.5 g daily for 6–12 weeks reduced **total cholesterol, LDL-C, and triglycerides**, though it did **not affect HDL-C**.
- A review of several studies confirmed these benefits, but more research is needed to understand how it works.

2. Effects on Blood Pressure (Hypertension)

High blood pressure is a major risk factor for heart attacks, strokes, and heart failure. Lowering blood pressure can reduce these risks by 20–50%.

Sterols/Stanols

- These compounds are known for lowering cholesterol, but **they do not affect blood pressure**.
- Studies lasting up to a year found no change in blood pressure.

Polyphenols

- **Polyphenol-rich foods** like grapes, berries, cocoa, tea, and pomegranate may help lower blood pressure, but results are mixed.
- Grape seed extract can **reduce systolic blood pressure (SBP)** by about 5–6% and diastolic blood pressure (DBP) by about 4–5%, especially in people with higher starting blood pressure.
- **Resveratrol** may lower SBP only at high doses (≥150 mg/day), but findings are inconsistent.
- **Cocoa flavanols** are the most studied and often show **blood pressure–lowering effects**, especially in people with diabetes, high blood pressure, or older adults.
    - Some studies show no benefit, likely due to dose or population differences.
    - The Flaviola Health Study found cocoa flavanols lowered SBP by 4.4 mmHg and DBP by 3.9 mmHg and improved blood vessel function.
- **Tea polyphenols** (green and black tea) also modestly lower blood pressure.
    - A review of 10 trials showed small but significant reductions in both SBP and DBP.
    - Green tea may also reduce the risk of heart attacks and strokes.
- **Pomegranate juice** has been found to lower both SBP and DBP and improve cholesterol and antioxidant levels.
- **Armolipid Plus** may also reduce blood pressure slightly in people with high cholesterol and mild hypertension.
- **Spirulina** might lower blood pressure, but results are inconsistent—some studies show improvement, others do not.
    - Higher doses (2 g/day) seem more effective, but more research is needed.

3. Effects on Diabetes and Blood Sugar Control

Type 2 diabetes greatly increases the risk of heart disease. People with both diabetes and high blood pressure have roughly **double the risk** of heart problems.
By 2030, over **550 million people** are expected to have diabetes.
A healthy diet, especially one high in **polyphenols**, can help reduce diabetes risk and inflammation.

Polyphenols

- **Grapes and red wine**: Some studies show regular red wine drinkers have a **30% lower risk** of developing type 2 diabetes.
    - Grape seed extract and grape flour also reduced blood sugar in some studies, though not all.
- **Resveratrol**:
    - Improves blood sugar control (lower fasting glucose, insulin, HbA1c, and insulin resistance) **in people with diabetes**, but not in healthy people.
    - Works by improving insulin sensitivity, reducing oxidative stress, and helping cells take in glucose more effectively.
- **Cocoa and chocolate**:
    - May reduce insulin levels and improve insulin resistance but **don't change fasting glucose or HbA1c**.
    - High-polyphenol chocolate might also improve liver enzymes and lower insulin resistance.
- **Green tea**:
    - Some studies show lower fasting glucose and HbA1c, but others show no effect.
    - Benefits may appear only after **8+ weeks** of use.
    - Overall, the evidence is mixed and not strong enough to recommend green tea as a diabetes treatment.

Polyphenols may help control blood sugar by:

- Slowing down carbohydrate digestion and glucose absorption.

- Protecting insulin-producing cells in the pancreas.
- Reducing glucose release from the liver.
- Making the body more sensitive to insulin.

Spirulina

- Some studies show that **2 g/day of Spirulina for 2 months** reduces fasting blood sugar, post-meal blood sugar, and HbA1c in people with type 2 diabetes.
- Other studies found no effect.
- More research is needed to confirm these results.

In Summary

Nutraceutical	Cholesterol	Blood Pressure	Blood Sugar	Notes
Plant Sterols/Stanols	↓ LDL-C	No effect	–	Safe, works well with statins
Grape Polyphenols / Resveratrol	Mixed results	↓ BP in some studies	May improve in diabetes	Need larger studies
Cocoa / Chocolate	↓ LDL-C, ↑ HDL-C slightly	↓ BP (esp. in high-risk people)	May improve insulin resistance	Effects depend on dose and form
Tea (Green/Black)	↓ LDL-C, ↓ TC	Slight ↓ BP	Mixed effects	Widely available and safe
Pomegranate Juice	↓ Cholesterol	↓ BP	Antioxidant benefits	Promising but limited data
Armolipid Plus	Strong ↓ in LDL-C and TG	Slight ↓ BP	–	Safe, effective supplement
Spirulina	↓ LDL-C, ↓ TC	Mixed results	May lower glucose	More studies needed

Conclusions

Summary in Simple Words

Main Message

High cholesterol (dyslipidemia), high blood pressure (hypertension), and diabetes are the **main modifiable risk factors** for heart disease (CVD). Although medicines are available to control these conditions, some high-risk patients don't get enough benefit from drugs alone.

This is where **nutraceuticals**—natural food-based supplements—might help. They can **support medical treatment**, improve results, and possibly **reduce leftover (residual) cardiovascular risk**.

Most nutraceuticals studied for heart disease are **well tolerated and safe**, but there's still not enough information about their **long-term effects** or how well they prevent serious outcomes like heart attacks or death.

Therefore, **more clinical studies** are needed to find which nutraceuticals work best and are cost-effective for preventing and treating heart disease.

Summary of Key Studies (Simplified Table)

Nutraceutical	Type of Study	Participants	What Was Done	Main Idea
Sterols / Stanols	Many meta-analyses and clinical trials	Hundreds of adults with high cholesterol	Doses 1–9 g/day for 4–85 weeks	Shown to **lower LDL ("bad") cholesterol**, but no effect on blood pressure.
	Observational and case-control studies	100–35,000 people	Daily intake of sterol-rich foods	May help reduce cholesterol and possibly heart attack risk.
Grape Polyphenols (including Resveratrol)	Many randomized controlled trials (RCTs) and reviews	Dozens to hundreds of people (healthy, hypertensive, diabetic, or metabolic syndrome)	Grape juice, grape seed extract, or resveratrol supplements	Mixed results: can **improve cholesterol and blood pressure** in some people, but not all. **Resveratrol** may help control blood sugar in diabetes.
Cocoa Polyphenols (Chocolate, Cocoa Drinks)	Meta-analyses and clinical studies	20–1,300 participants	Doses 80–2,000 mg/day for 2–52 weeks	Cocoa flavanols can **reduce LDL and blood pressure**, slightly improve HDL, and may improve insulin sensitivity. Effects depend on dose and population.
Tea Polyphenols (Green/Black Tea)	Over 10 meta-analyses and clinical trials	Hundreds to thousands of participants	Green/black tea or extracts for 2–48 weeks	Both green and black tea **lower total and LDL cholesterol**, may **slightly reduce blood pressure**, and could lower diabetes risk. Results vary with type and amount of tea.

Nutraceutical	Type of Study	Participants	What Was Done	Main Idea
Armolipid Plus	Controlled studies and meta-analyses	Patients with high cholesterol or mild hypertension	Supplement with red yeast rice, berberine, CoQ10, etc.	Shown to **lower total cholesterol, LDL, and triglycerides**, and slightly **lower blood pressure**. Safe and well tolerated.
Spirulina (Blue-green Algae)	RCTs and meta-analyses	People with diabetes, high cholesterol, or hypertension	1–10 g/day for 2–48 weeks	Can **lower total cholesterol, LDL, triglycerides, and blood sugar**. Effects on blood pressure are mixed. Generally safe.

Overall Conclusions (Simplified)

- **Nutraceuticals** can support conventional therapy for heart disease, diabetes, and hypertension.
- They are **natural, generally safe**, and may improve cholesterol, blood pressure, and blood sugar control.
- However, **long-term studies** are still needed to confirm whether they actually reduce heart attacks and deaths.
- Future research should focus on finding the most **effective and affordable** nutraceuticals for real-world heart disease prevention.

REFERENCES

1. 1.Roth GA, Huffman MD, Moran AE, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. Circulation 2015;132:1667-78. 10.1161/CIRCULATIONAHA.114.008720 [DOI] [PubMed] [Google Scholar]
2. 2.Voelter-Mahlknecht S. Epigenetic associations in relation to cardiovascular prevention and therapeutics. Clin Epigenetics 2016;8:4. 10.1186/s13148-016-0170-0 [DOI] [PMC free article] [PubMed] [Google Scholar]
3. 3.Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2016;37: 2315-81. 10.1093/eurheartj/ehw106 [DOI] [PMC free article] [PubMed] [Google Scholar]
4. 4.O'Keeffe C, Kabir Z, O'Flaherty M, et al. Modelling the impact of specific food policy options on coronary heart disease and stroke deaths in Ireland. BMJ Open 2013;3: e002837. 10.1136/bmjopen-2013-002837 [DOI] [PMC free article] [PubMed] [Google Scholar]
5. 5.Alissa EM, Ferns GA. Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases. J Nutr Metab 2012;2012:569486. 10.1155/2012/569486 [DOI] [PMC free article] [PubMed] [Google Scholar]
6. 6.Tresserra-Rimbau A, Rimm EB, Medina-Remón A, et al. Inverse association between habitual polyphenol intake and incidence of cardiovascular events in the PREDIMED study. Nutr Metab Cardiovasc Dis 2014; 24:639-47. 10.1016/j.numecd.2013.12.014 [DOI] [PubMed] [Google Scholar]
7. 7.DeFelice SL. The nutraceutical revolution: its impact on food industry R&D. Trends in Food Science and Technology 1995;2:59-61. 10.1016/S0924-2244(00)88944-X [DOI] [Google Scholar]
8. 8.Moreau RA, Whitaker BD, Hicks KB. Phytosterols, Phytostanols, and Their Conjugates in Foods: Structural Diversity, Quantitative Analysis, and Health-Promoting Uses. Prog Lipid Res 2002;41:457-500. 10.1016/S0163-7827(02)00006-1 [DOI] [PubMed] [Google Scholar]
9. 9.Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev 2009;2:270-8. 10.4161/oxim.2.5.9498 [DOI] [PMC free article] [PubMed] [Google Scholar]
10. 10.Spácil Z, Novakova L, Solich P. Analysis of phenolic compounds by high performance liquid chromatography and ultra-performance liquid chromatography. Talanta 2008;76:189-99. 10.1016/j.talanta.2008.02.021 [DOI] [PubMed] [Google Scholar]
11. 11.Burns J, Yokota T, Ashihara H, et al. Plant foods and herbal sources of resveratrol. J Agric Food Chem 2002;50: 3337-40. 10.1021/jf0112973 [DOI] [PubMed] [Google Scholar]
12. 12.Andres-Lacueva C, Monagas M, Khan N, et al. Flavanol and flavonol contents of cocoa powder products: Influence of the manufacturing process. J Agric Food Chem 2008;56:3111-7. 10.1021/jf0728754 [DOI] [PubMed] [Google Scholar]
13. 13.Hammerstone JF, Lazarus SA, Mitchell AE, et al. Identification of procyanidins in cocoa (Theobroma cacao) and chocolate using high-performance liquid chromatography/mass spectrometry. J Agric Food Chem 1999;47:490-6. 10.1021/jf980760h [DOI] [PubMed] [Google Scholar]
14. 14.Lee KW, Kim YJ, Lee HJ, et al. Cocoa has more phenolic phytochemicals and a higher antioxidant capacity than teas and red wine. J Agric Food Chem 2003;51:7292-5. 10.1021/jf0344385 [DOI] [PubMed] [Google Scholar]
15. 15.Khan N, Mukhtar H. Tea polyphenols for health promotion. Life Sci 2007;81:519-33. 10.1016/j.lfs.2007.06.011 [DOI] [PMC free article] [PubMed] [Google Scholar]
16. 16.Balentine DA, Wiseman SA, Bouwens LC. The chemistry of tea flavonoids. Crit Rev Food Sci Nutr 1997;37: 693-704. 10.1080/10408399709527797 [DOI] [PubMed] [Google Scholar]
17. 17.Khan Z, Bhadouria P, Bisen P. Nutritional and therapeutic potential of Spirulina. Curr Pharm Biotechnol 2005; 6:373-9. 10.2174/138920105774370607 [DOI] [PubMed] [Google Scholar]
18. 18.Sarubin-Fragakis A. The health professional's guide to popular dietary supplements. Am J Clin Nutr 2003;78:808 [Google Scholar]
19. 19.Amir Shaghaghi M, Abumweis SS, Jones PJ. Cholesterol-lowering efficacy of plant sterols/stanols provided in capsule and tablet formats: results of a systematic review and meta-analysis. J Acad Nutr Diet 2013;113:1494-503. 10.1016/j.jand.2013.07.006 [DOI] [PubMed] [Google Scholar]

20. 20.Ras RT, Geleijnse JM, Trautwein EA. LDL cholesterol-lowering effect of plant sterols and stanols across different dose ranges: A meta-analysis of randomised controlled studies. Br J Nutr 2014;112:214-9. 10.1017/S0007114514000750 [DOI] [PMC free article] [PubMed] [Google Scholar]

21. 21.Han S, Jiao J, Xu J, et al. Effects of plant stanol or sterol-enriched diets on lipid profiles in patients treated with statins: systematic review and meta-analysis. Sci Rep 2016;6:31337. 10.1038/srep31337 [DOI] [PMC free article] [PubMed] [Google Scholar]

22. 22.Klingberg S, Ellegard L, Johansson I, et al. Dietary intake of naturally occurring plant sterols is related to a lower risk of a first myocardial infarction in men but not in women in northern Sweden. J Nutr 2013;143:1630-5. 10.3945/jn.113.178707 [DOI] [PubMed] [Google Scholar]

23. 23.Ras RT, van der Schouw YT, Trautwein EA, et al. Intake of phytosterols from natural sources and risk of cardiovascular disease in the European prospective investigation into cancer and nutrition- the Netherlands (EPIC-NL) population. Eur J Prev Cardiol 2015;22:1067-75. 10.1177/2047487314554864 [DOI] [PubMed] [Google Scholar]

24. 24.Gylling H, Hallikainen M, Raitakari OT, et al. Long-term consumption of plant stanol and sterol esters, vascular function and genetic regulation. Br J Nutr 2009;101:1688-95. 10.1017/S0007114508116300 [DOI] [PubMed] [Google Scholar]

25. 25.Raitakari OT, Salo P, Ahotupa M. Carotid artery compliance in users of plant stanol ester margarine. Eur J Clin Nutr 2008;62:218-24. 10.1038/sj.ejcn.1602705 [DOI] [PubMed] [Google Scholar]

26. 26.Gylling H, Halonen J, Lindholm H, et al. The effects of plant stanol ester consumption on arterial stiffness and endothelial function in adults: a randomised controlled clinical trial. BMC Cardiovasc Disord 2013;13:50. 10.1186/1471-2261-13-50 [DOI] [PMC free article] [PubMed] [Google Scholar]

27. 27.Khadem-Ansari MH, Rasmi Y, Ramezani F. Effects of red grape juice consumption on high density lipoprotein-cholesterol, apolipoprotein AI, apolipoprotein B and homocysteine in healthy human volunteers. Open Biochem J 2010;4:96-9. 10.2174/1874091X01004010096 [DOI] [PMC free article] [PubMed] [Google Scholar]

28. 28.Yubero N, Sanz-Buenhombre M, Guadarrama A, et al. LDL cholesterol-lowering effects of grape extract used as a dietary supplement on healthy volunteers. Int J Food Sci Nutr 2013;64:400-6. 10.3109/09637486.2012.753040 [DOI] [PubMed] [Google Scholar]

29. 29.Feringa HH, Laskey DA, Dickson JE, et al. The effect of grape seed extract on cardiovascular risk markers: a meta-analysis of randomized controlled trials. J Am Diet Assoc 2011;111:1173-81. 10.1016/j.jada.2011.05.015 [DOI] [PubMed] [Google Scholar]

30. 30.Zunino SJ, Peerson JM, Freytag TL, et al. Dietary grape powder increases IL-1β and IL-6 production by lipopolysaccharide-activated monocytes and reduces plasma concentrations of large LDL and large LDL-cholesterol particles in obese humans. Br J Nutr 2014;112:369-80. 10.1017/S0007114514000890 [DOI] [PubMed] [Google Scholar]

31. 31.Barona J, Aristizabal JC, Blesso CN, et al. Grape polyphenols reduce blood pressure and increase flow-mediated vasodilation in men with metabolic syndrome. J Nutr 2012;142:1626-32. 10.3945/jn.112.162743 [DOI] [PubMed] [Google Scholar]

32. 32.Draijer R, de Graaf Y, Slettenaar M, et al. Consumption of a polyphenol-rich grape-wine extract lowers ambulatory blood pressure in mildly hypertensive subjects. Nutrients 2015;7:3138-53. 10.3390/nu7053138 [DOI] [PMC free article] [PubMed] [Google Scholar]

33. 33.Vaisman N, Niv E. Daily consumption of red grape cell powder in a dietary dose improves cardiovascular parameters: a double blind, placebo-controlled, randomized study. Int J Food Sci Nutr 2015;66:342-9. 10.3109/09637486.2014.1000840 [DOI] [PubMed] [Google Scholar]

34. 34.Hodgson JM, Croft KD, Woodman RJ, et al. Effects of vitamin E, vitamin C and polyphenols on the rate of blood pressure variation: results of two randomized controlled trials. Br J Nutr 2014;112:1551-61. 10.1017/S0007114514002542 [DOI] [PubMed] [Google Scholar]

35. 35.Díaz-Rubio ME, Perez-Jimenez J, Martinez-Bartolome MA, et al. Regular consumption of an antioxidant-rich juice improves oxidative status and causes metabolome changes in healthy adults. Plant Foods Hum Nutr 2015;70:9-14. 10.1007/s11130-014-0455-4 [DOI] [PubMed] [Google Scholar]

36. 36.Park E, Edirisinghe I, Choy YY, et al. Effects of grape seed extract beverage on blood pressure and metabolic indices in individuals with pre-hypertension: a randomized, double-blinded, two-arm, parallel, placebo-controlled trial. Br J Nutr 2016;115:226-38. 10.1017/S0007114515004328 [DOI] [PubMed] [Google Scholar]

37. 37.Urquiaga I, D'Acuña S, Pérez D, et al. Wine grape pomace flour improves blood pressure, fasting glucose and protein damage in humans: a randomized controlled trial. Biol Res 2015;48:49. 10.1186/s40659-015-0040-9 [DOI] [PMC free article] [PubMed] [Google Scholar]

38. 38.Toaldo IM, Cruz FA, da Silva EL, et al. Acute consumption of organic and conventional tropical grape juices (Vitis labrusca L.) increases antioxidants in plasma and erythrocytes, but not glucose and uric acid levels, in healthy individuals. Nutr Res 2016;36:808-17. 10.1016/j.nutres.2016.04.010 [DOI] [PubMed] [Google Scholar]

39. 39.Bhatt JK, Thomas S, Nanjan MJ. Resveratrol supplementation improves glycemic control in type 2 diabetes mellitus. Nutr Res 2012;32:537-41. 10.1016/j.nutres.2012.06.003 [DOI] [PubMed] [Google Scholar]

40. 40.Liu K, Zhou R, Wang B, et al. Effect of resveratrol on glucose control and insulin sensitivity: a meta-analysis of 11 randomized controlled trials. Am J Clin Nutr 2014;99:1510-9. 10.3945/ajcn.113.082024 [DOI] [PubMed] [Google Scholar]

41. 41.Sahebkar A, Serban C, Ursoniu S, et al. Lipid and Blood Pressure Meta-analysis Collaboration Group Lack of efficacy of resveratrol on C-reactive protein and selected cardiovascular risk factors--Results from a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol 2015;189:47-55. 10.1016/j.ijcard.2015.04.008 [DOI] [PubMed] [Google Scholar]

42. 42.Liu Y, Ma W, Zhang P, et al. Effect of resveratrol on blood pressure: a meta-analysis of randomized controlled trials. Clin Nutr 2015;34:27-34. 10.1016/j.clnu.2014.03.009 [DOI] [PubMed] [Google Scholar]

43. 43.Jia L, Liu X, Bai YY, et al. Short-term effect of cocoa product consumption on lipid profile: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2010;92:218-25. 10.3945/ajcn.2009.28202 [DOI] [PubMed] [Google Scholar]

44. 44.Rostami A, Khalili M, Haghighat N, et al. High-cocoa polyphenol-rich chocolate improves blood pressure in patients with diabetes and hypertension. ARYA Atheroscler 2015;11:21-9. [PMC free article] [PubMed] [Google Scholar]

45. 45.Nogueira Lde P, Knibel MP, Torres MR, et al. Consumption of High-Polyphenol Dark Chocolate Improves Endothelial Function in Individuals with Stage 1 Hypertension and Excess Body Weight. Int J Hypertens 2012;2012:147321. [DOI] [PMC free article] [PubMed] [Google Scholar]

46. 46.West SG, McIntyre MD, Piotrowski MJ, et al. Effects of dark chocolate and cocoa consumption on endothelial function and arterial stiffness in overweight adults. Br J Nutr 2014;111:653-61. 10.1017/S0007114513002912 [DOI] [PubMed] [Google Scholar]

47. 47.Flammer AJ, Sudano I, Wolfrum M, et al. Cardiovascular effects of flavanol-rich chocolate in patients with heart failure. Eur. Heart J 2012;33:2172-80. 10.1093/eurheartj/ehr448 [DOI] [PubMed] [Google Scholar]

48. 48.Lin X, Zhang I, Li A, et al. Cocoa Flavanol Intake and Biomarkers for Cardiometabolic Health: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Nutr 2016;146:2325-33. 10.3945/jn.116.237644 [DOI] [PMC free article] [PubMed] [Google Scholar]

49. 49.Sansone R, Rodriguez-Mateos A, Heuel J, et al. Cocoa flavanol intake improves endothelial function and Framingham Risk Score in healthy men and women: a randomized, controlled, double-masked trial: the Flaviola Health Study. Br J Nutr 2015;114:1246-55. 10.1017/S0007114515002822 [DOI] [PMC free article] [PubMed] [Google Scholar]

50. 50.Ried K, Sullivan TR, Fakler P, et al. Effect of cocoa on blood pressure. Cochrane Database Syst Rev 2012;15:CD008893. [DOI] [PubMed] [Google Scholar]

51. 51.Hooper L, Kay C, Abdelhamid A, et al. Effects of chocolate, cocoa, and flavan-3-ols on cardiovascular health: A systematic review and meta-analysis of randomized trials. Am J Clin Nutr 2012;95:740-51. 10.3945/ajcn.111.023457 [DOI] [PubMed] [Google Scholar]

52. 52.Mastroiacovo D, Kwik-Uribe C, Grassi D, et al. Cocoa flavanol consumption improves cognitive function, blood pressure control, and metabolic profile in elderly subjects: the Cocoa, Cognition, and Aging (CoCoA) Study—a randomized controlled trial. Am J Clin Nutr 2015;101:538-48. 10.3945/ajcn.114.092189 [DOI] [PMC free article] [PubMed] [Google Scholar]

53. 53.Grassi D, Desideri G, Necozione S, et al. Cocoa consumption dose-dependently improves flow-mediated dilation and arterial stiffness decreasing blood pressure in healthy individuals. J Hypertens 2015;33:294-303. 10.1097/HJH.0000000000000412 [DOI] [PubMed] [Google Scholar]

54. 54.Koli R, Köhler K, Tonteri E, et al. Dark chocolate and reduced snack consumption in mildly hypertensive adults: an intervention study. Nutr J 2015;14:84. 10.1186/s12937-015-0075-3 [DOI] [PMC free article] [PubMed] [Google Scholar]

55. 55.Alkerwi A, Sauvageot N, Crichton GE, et al. Daily chocolate consumption is inversely associated with insulin resistance and liver enzymes in the Observation of Cardiovascular Risk Factors in Luxembourg study. Br J Nutr 2016;115:1661-8. 10.1017/S0007114516000702 [DOI] [PubMed] [Google Scholar]

56. 56.Zheng XX, Xu YL, Li SH, et al. Green tea intake lowers fasting serum total and LDL cholesterol in adults: a meta-analysis of 14 randomized controlled trials. Am J Clin Nutr 2011;94:601-10. 10.3945/ajcn.110.010926 [DOI] [PubMed] [Google Scholar]

57. 57.Kim A, Chiu A, Barone MK, et al. Green tea catechins decrease total and low-density lipoprotein cholesterol: a systematic review and meta-analysis. J Am Diet Assoc 2011;111:1720-9. 10.1016/j.jada.2011.08.009 [DOI] [PubMed] [Google Scholar]

58. 58.Hartley L, Flowers N, Holmes J, et al. Green and black tea for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev 2013;18:CD009934. [DOI] [PMC free article] [PubMed] [Google Scholar]

59. 59.Zhao Y, Asimi S, Wu K, et al. Black tea consumption and serum cholesterol concentration: Systematic review and meta-analysis of randomized controlled trials. Clin Nutr 2015;34:612-9. 10.1016/j.clnu.2014.06.003 [DOI] [PubMed] [Google Scholar]

60. 60.Samavat H, Newman AR, Wang R, et al. Effects of green tea catechin extract on serum lipids in postmenopausal women: a randomized, placebo-controlled clinical trial. Am J Clin Nutr 2016;104:1671-82. 10.3945/ajcn.116.137075 [DOI] [PMC free article] [PubMed] [Google Scholar]

61. 61.Khalesi S, Sun J, Buys N, et al. Green tea catechins and blood pressure: a systematic review and meta-analysis of randomised controlled trials. Eur J Nutr 2014;53:1299-311. 10.1007/s00394-014-0720-1 [DOI] [PubMed] [Google Scholar]

62. 62.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. 10.1093/nutrit/nuv001 [DOI] [PubMed] [Google Scholar]

63. 63.Pang J, Zhang Z, Zheng T, et al. Green tea consumption and risk of cardiovascular and ischemic related diseases: A meta-analysis. Int J Cardiol 2016;202:967-74. 10.1016/j.ijcard.2014.12.176 [DOI] [PubMed] [Google Scholar]

64. 64.Liu K, Zhou R, Wang B, et al. Effect of green tea on glucose control and insulin sensitivity: a meta-analysis of 17 randomized controlled trials. Am J Clin Nutr 2013;98:340-8. 10.3945/ajcn.112.052746 [DOI] [PubMed] [Google Scholar]

65. 65.Zheng XX, Xu YL, Li SH, et al. Effects of green tea catechins with or without caffeine on glycemic control in adults: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2013;97:750-62. 10.3945/ajcn.111.032573 [DOI] [PubMed] [Google Scholar]

66. 66.Wang X, Tian J, Jiang J, et al. 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 randomized controlled trials. J Hum Nutr Diet 2014;27:501-12. 10.1111/jhn.12181 [DOI] [PubMed] [Google Scholar]

67. 67.Li Y, Wang C, Huai Q, et al. Effects of tea or tea extract on metabolic profiles in patients with type 2 diabetes mellitus: a meta-analysis of ten randomized controlled trials. Diabetes Metab Res Rev 2016;32:2-10. 10.1002/dmrr.2641 [DOI] [PubMed] [Google Scholar]

68. 68.Mazza A, Lenti S, Schiavon L, et al. Nutraceuticals for Serum Lipid and Blood Pressure Control in Hypertensive and Hypercholesterolemic Subjects at Low Cardiovascular Risk. Adv Ther 2015;32:680-90. 10.1007/s12325-015-0229-x [DOI] [PubMed] [Google Scholar]

69. 69.Barrios V, Escobar C, Cicero AF, et al. A nutraceutical approach (Armolipid Plus) to reduce total and LDL cholesterol in individuals with mild to moderate dyslipidemia: Review of the clinical evidence. Atheroscler Suppl 2017;24:1-15. 10.1016/j.atherosclerosissup.2016.10.003 [DOI] [PubMed] [Google Scholar]

70. 70.Parikh P, Mani U, Iyer U. Role of Spirulina in the Control of Glycemia and Lipidemia in Type 2 Diabetes Mellitus. J Med Food 2001;4:193-9. 10.1089/10966200152744463 [DOI] [PubMed] [Google Scholar]

71. 71.Lee EH, Park JE, Choi YJ, et al. A randomized study to establish the effects of spirulina in type 2 diabetes mellitus patients. Nutr Res Pract 2008;2:295-300. 10.4162/nrp.2008.2.4.295 [DOI] [PMC free article] [PubMed] [Google Scholar]

72. 72.Torres-Duran PV, Ferreira-Hermosillo A, Juarez-Oropeza MA. Antihyperlipemic and antihypertensive effects of Spirulina maxima in an open sample of Mexican population: a preliminary report. Lipids Health Dis 2007;6:33. 10.1186/1476-511X-6-33 [DOI] [PMC free article] [PubMed] [Google Scholar]

73. 73.Mazokopakis EE, Starakis IK, Papadomanolaki MG, et al. The hypolipidaemic effects of Spirulina (Arthrospira platensis) supplementation in a Cretan population: a prospective study. J Sci Food Agric 2014;94:432-7. 10.1002/jsfa.6261 [DOI] [PubMed] [Google Scholar]

74. 74.Serban MC, Sahebkar A, Dragan S, et al. A systematic review and meta-analysis of the impact of Spirulina supplementation on plasma lipid concentrations. Clin Nutr 2016;35:842-51. 10.1016/j.clnu.2015.09.007 [DOI] [PubMed] [Google Scholar]

75. 75.Miczke A, Szulińska M, Hansdorfer-Korzon R, et al. Effects of spirulina consumption on body weight, blood pressure, and endothelial function in overweight hypertensive Caucasians: a double-blind, placebo-controlled, randomized trial. Eur Rev Med Pharmacol Sci 2016;20:150-6. [PubMed] [Google Scholar]

76. 76.Reiner Z, Catapano AL, De Backer G, et al. ESC/EAS Guidelines for the Management of Dyslipidaemias. The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Europ Heart J 2011;32:1769-818. 10.1093/eurheartj/ehr158 [DOI] [PubMed] [Google Scholar]

77. 77.Silverman MG, Ference BA, Im K, et al. Association Between Lowering LDL-C and Cardiovascular Risk Reduction Among Different Therapeutic Interventions: A Systematic Review and Meta-analysis. JAMA 2016;316: 1289-97. 10.1001/jama.2016.13985 [DOI] [PubMed] [Google Scholar]

78. 78.Sahebkar A, Serban MC, Gluba-Brzózka A, et al. Lipid-modifying effects of nutraceuticals: An evidence-based approach. Nutrition 2016;32:1179-92. 10.1016/j.nut.2016.04.007 [DOI] [PubMed] [Google Scholar]

79. 79.Andersson SW, Skinner J, Ellegard L, et al. Intake of dietary plant sterols is inversely related to serum cholesterol concentration in men and women in the EPIC Norfolk population: A cross-sectional study. Eur J Clin Nutr 2004;58:1378-85. 10.1038/sj.ejcn.1601980 [DOI] [PubMed] [Google Scholar]

80. 80.Wang P, Chen YM, He LP, et al. Association of natural intake of dietary plant sterols with carotid intima-media thickness and blood lipids in Chinese adults: A cross-section study. PLoS One 2012;7:e32736. 10.1371/journal.pone.0032736 [DOI] [PMC free article] [PubMed] [Google Scholar]

81. 81.Gylling H, Plat J, Turley S, et al. for the European atherosclerosis society consensus panel on phytosterols. Plant sterols and plant stanols in the management of dyslipidaemia and prevention of cardiovascular disease. Atherosclerosis 2014;232:346-60. 10.1016/j.atherosclerosis.2013.11.043 [DOI] [PubMed] [Google Scholar]

82. 82.de Jong A, Plat J, Mensink RP. Metabolic effects of plant sterols and stanols. J Nutr Biochem 2003;14;362-9. 10.1016/S0955-2863(03)00002-0 [DOI] [PubMed] [Google Scholar]

83. 83.Gylling H, Hallikainen M, Nissinen MJ, et al. The effect of a very high daily plant stanol ester intake on serum lipids, carotenoids, and fat soluble vitamins. Clin Nutr 2010;29:112-8. 10.1016/j.clnu.2009.08.005 [DOI] [PubMed] [Google Scholar]

84. 84.Voutilainen S, Nurmi T, Mursu J, et al. Carotenoids and cardiovascular health. Am J Clin Nutr 2006;83:1265-71. [DOI] [PubMed] [Google Scholar]

85. 85.Koba S, Yokota Y, Hirano T, et al. Small LDL-cholesterol is superior to LDL-cholesterol for determining severe coronary atherosclerosis. J Atheroscler Thromb 2008;15:250-60. 10.5551/jat.E572 [DOI] [PubMed] [Google Scholar]

86. 86.Papadogiannis DE, Protogerou AD. Blood pressure variability: A confounder and a cardiovascular risk factor. Hypertens Res 2011;34:162-3. 10.1038/hr.2010.223 [DOI] [PubMed] [Google Scholar]

87. 87.Antonakoudis G, Poulimenos L, Kifnidis K, et al. Blood pressure control and cardiovascular risk reduction. Hippokratia 2007;11:114-9. [PMC free article] [PubMed] [Google Scholar]

88. 88.Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. BMJ 2014;349:g4490. 10.1136/bmj.g4490 [DOI] [PMC free article] [PubMed] [Google Scholar]

89. 89.Sahebkar A, Ferri C, Giorgini 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. 10.1016/j.phrs.2016.11.018 [DOI] [PubMed] [Google Scholar]

90. 90.Asgary S, Keshvari M, Sahebkar A, et al. Pomegranate consumption and blood pressure: A review. Curr Pharm Des 2016. [Epub ahead of print]. [DOI] [PubMed] [Google Scholar]

91. 91.Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. JAMA 1999;281:1291-7. 10.1001/jama.281.14.1291 [DOI] [PubMed] [Google Scholar]

92. 92.Arauz-Pacheco C, Parrott MA, Raskin P. The treatment of hypertension in adult patients with diabetes. Diabetes Care 2002;25:134-47. 10.2337/diacare.25.1.134 [DOI] [PubMed] [Google Scholar]

93. 93.Whiting DR, Guariguata L, Weil C, et al. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011;94:311-21. 10.1016/j.diabres.2011.10.029 [DOI] [PubMed] [Google Scholar]

94. 94.Bosch J, Yusuf S, Gerstein HC, et al. Effect of ramipril on the incidence of diabetes. N Engl J Med 2006;355:1551-62. 10.1056/NEJMoa065061 [DOI] [PubMed] [Google Scholar]

95. 95.Vitale M, Vaccaro O, Masulli M, et al. Polyphenol intake and cardiovascular risk factors in a population with type 2 diabetes: The TOSCA.IT study. Clin Nut 2016. [Epub ahead of print]. [DOI] [PubMed] [Google Scholar]

96. 96.Guilford JM, Pezzuto JM. Wine and health: A review. Am J Enol Vitic 2011;62:471-86. 10.5344/ajev.2011.11013 [DOI] [Google Scholar]

97. 97.Akaberi M, Hosseinzadeh H. Grapes (Vitis vinifera) as a Potential Candidate for the Therapy of the Metabolic Syndrome. Phytother Res 2016;30:540-56. 10.1002/ptr.5570 [DOI] [PubMed] [Google Scholar]

98. 98.Yao L, Wan J, Li H, et al. Resveratrol relieves gestational diabetes mellitus in mice through activating AMPK. Reprod Biol Endocrinol 2015;13:118. 10.1186/s12958-015-0114-0 [DOI] [PMC free article] [PubMed] [Google Scholar]

99. 99.Gencoglu H, Tuzcu M, Hayirli A, et al. Protective effects of resveratrol against streptozotocin-induced diabetes in rats by modulation of visfatin/sirtuin-1 pathway and glucose transporters. Int J Food Sci Nutr 2015;66:314-20. 10.3109/09637486.2014.1003534 [DOI] [PubMed] [Google Scholar]

100. 100.Goh KP, Lee HY, Lau DP, et al. Effects of resveratrol in patients with type 2 diabetes mellitus on skeletal muscle SIRT1 expression and energy expenditure. Int J Sport Nutr Exerc Metab 2014;24:2-13. 10.1123/ijsnem.2013-0045 [DOI] [PubMed] [Google Scholar]

101. 101.Hanhineva K, Torronen R, Bondia-Pons I, et al. Impact of dietary polyphenols on carbohydrate metabolism. Int J Mol Sci 2010;11:1365-402. 10.3390/ijms11041365 [DOI] [PMC free article] [PubMed] [Google Scholar]

102. 102.Sahebkar A, Serban C, Ursoniu S, et al. Effect of garlic on plasma lipoprotein(a) concentrations: A systematic review and meta-analysis of randomized controlled clinical trials. Nutrition 2016;32:33-40. 10.1016/j.nut.2015.06.009 [DOI] [PubMed] [Google Scholar]

103. 103.Serban C, Sahebkar A, Antal D, et al. Effects of supplementation with green tea catechins on plasma C-reactive protein concentrations: A systematic review and meta-analysis of randomized controlled trials. Nutrition 2015;31:1061-71. 10.1016/j.nut.2015.02.004 [DOI] [PubMed] [Google Scholar]

104. 104.Banach M, Aronow WS, Serban C, et al. Lipids, blood pressure and kidney update 2014. Pharmacol Res 2015;95-96:111-25. 10.1016/j.phrs.2015.03.009 [DOI] [PubMed] [Google Scholar]

105. 105.Ursoniu S, Sahebkar A, Serban MC, et al. Lipid profile and glucose changes after supplementation with astaxanthin: a systematic review and meta-analysis of randomized controlled trials. Arch Med Sci 2015;11:253-66. 10.5114/aoms.2015.50960 [DOI] [PMC free article] [PubMed] [Google Scholar]