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|----|---|------|--|---|--|---------------------|--|---|--|---|--|-----|
| 14 | Cinnamon, chromium- and magnesium-formulated honey | 2016 | The effect of a cinnamon, chromium- and magnesium-formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over randomised controlled trial | An open-label cross-over randomised controlled trial | Twelve individuals with type 2 diabetes received 53.5 g of a formulated honey and a control (non-formulated) kanuka honey in a random order for 40 days, using cross-over design. Fasting glucose, insulin, HbA1c, lipids and anthropometric measures were measured at baseline and end of treatment. A meal tolerance test was performed at baseline to assess acute metabolic response. | Control | There was a statistically significant reduction in total cholesterol by -0.29 mmol/L (95% CI -0.57 to -0.23), LDL cholesterol by -0.29 mmol/L (95% CI -0.57 to -0.23) and weight by -2.2 kg (95% CI -4.2 to -0.1). There was a trend towards increased HDL, and reduced systolic blood pressure in the intervention treatment. | The addition of cinnamon, chromium and magnesium supplementation to kanuka honey was not associated with a significant improvement in glucose metabolism or glycaemic control in individuals with type 2 diabetes. | Use of the formulated honey was associated with a reduction in weight and improvements in lipid parameters, and should be investigated further. | https://pubmed.ncbi.nlm.nih.gov/25986159/ | Whitefield, P., Parry-Strong, A., Walsh, E., Weatherall, M., & Krebs, J. D. (2016). The effect of a cinnamon, chromium- and magnesium-formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over randomised controlled trial. <i>European Journal of Nutrition</i> , 55(3), 1122-1131. https://doi.org/10.1007/s00394-015-0926-x | No |
| 15 | NutraforChol [®] , a nutraceutical product containing red yeast rice extract, guggulipid extract and chromium picolinate | 2020 | Efficacy and tolerability of a nutraceutical combination of red yeast rice, guggulipid, and chromium picolinate evaluated in a randomized, placebo-controlled, double-blind study | Randomized, double-blind study | NutraforChol [®] , a nutraceutical product containing red yeast rice extract, guggulipid extract and chromium picolinate, was evaluated on subjects who had total cholesterol level 200-239 mg/dL and LDL cholesterol level 100-159 mg/dL. In this study, a randomized, placebo-controlled, double-blind study which consisted of 4 weeks run-in period and 8 weeks treatment period was performed. | Placebo | NutraforChol [®] effectively decreased total cholesterol (-15.8%) and LDL level (-19.9%) after two weeks consumption. The total cholesterol and LDL reduction were maintained during 8 weeks study period. At study termination (week 8), there was a significant difference between total cholesterol level of NutraforChol [®] treated group (173.5 ± 21.7 mg/dL) and placebo-treated group (204.5 ± 22.8 mg/dL) (p < 0.05). | Thus, NutraforChol [®] may be considered as a complementary or alternative safe nutraceuticals for the treatment of mild dyslipidemic subjects. | In addition, there was a significant difference between LDL level at week 8 in NutraforChol [®] group (115.5 ± 22.2 mg/dL) and placebo-treated group (145.1 ± 23.7 mg/dL) (p < 0.05). | https://pubmed.ncbi.nlm.nih.gov/31987238/ | Iskandar, I., Harahap, Y., Wijayanti, T. R., Sandra, M., Prasaja, B., & Cahyaningsih, P. (2020). Efficacy and tolerability of a nutraceutical combination of red yeast rice, guggulipid, and chromium picolinate evaluated in a randomized, placebo-controlled, double-blind study. <i>Complementary Therapies in Medicine</i> , 48. https://doi.org/10.1016/j.ctim.2019.102282 | Yes |
| 16 | probiotic Bifidobacterium longum B8536 and red yeast rice extract | 2019 | Nutraceutical approach for the management of cardiovascular risk - a combination containing the probiotic Bifidobacterium longum B8536 and red yeast rice extract: results from a randomized, double-blind, placebo-controlled study | Randomized, double-blind, placebo-controlled study | A 12-week randomized, parallel, double-blind, placebo-controlled study. Thirty-three subjects (18-70 years) in primary CV prevention and low CV risk (SCORE: 0-1% in 24 and 2-4% in 9 subjects; LDL-C: 130-200 mg/dL) were randomly allocated to either nutraceutical (N = 16) or placebo (N = 17). | Placebo | Twelve-week treatment with the nutraceutical combination, compared to placebo, significantly reduced TC (-16.7%), LDL-C (-25.7%), non-HDL-C (-24%) (all p < 0.0001), apoB (-17%, p = 0.003). | A 12-week treatment with a nutraceutical combination containing the probiotic Bifidobacterium longum B8536 and RYR extract significantly improved the atherogenic lipid profile and was well tolerated by low CV risk subjects. | No adverse effects and a 97% compliance were observed. | https://pubmed.ncbi.nlm.nih.gov/30795775/ | Bascico, M., Pavanello, C., Gandini, S., Macchi, C., Botta, M., Dall'Orto, D., Del Puppo, M., Bertolotti, M., Bossio, R., Mombelli, G., Sirtori, C. R., Calabrese, L., & Magni, P. (2019). Nutraceutical approach for the management of cardiovascular risk - a combination containing the probiotic Bifidobacterium longum B8536 and red yeast rice extract: results from a randomized, double-blind, placebo-controlled study. <i>Nutrition Journal</i> , 18(1). https://doi.org/10.1186/s12937-019-0438-2 | Yes |
| 17 | Armolipid Plus (AP) (berberine 500 mg, red yeast rice, monacolin K 3 mg and policosanol 10 mg) | 2019 | Efficacy of a nutraceutical combination on lipid metabolism in patients with metabolic syndrome: a multicenter, double blind, randomized, placebo controlled trial | A multicenter, double blind, randomized, placebo controlled trial | One hundred and fifty eight patients, aged between 28 and 76 years old, were enrolled and randomized to receive either one tablet of AP or placebo (P) once daily for 24 weeks. | Placebo | After 24 weeks of treatment, the analysis performed on 141 subjects (71 in AP arm and 70 in PL arm), showed a significant improvement of lipid profile in the AP group, with reduction in tot-C (-13.2 mg/dL), LDL-C (-13.9 mg/dL) and NHDL-C (-15.3 mg/dL) and increase in HDL-C (+2.0 mg/dL). These changes were equally significant compared with placebo | The results of this study, applicable to a specific local population show that, in a population of subjects affected by MetS, treatment with AP improves the lipid profile and the most atherogenic factors, thus suggesting a reduction in the risk of development and progression of atherosclerosis, particularly in subjects with high atherogenic risk, due to the presence of sLDL-C. | Although no significant difference was observed between the two arms in the reduction of HDL-C nevertheless it increased significantly in the AP group (AP + 2 mg/dL p < 0.05, PL 0.13 mg/dL). | https://pubmed.ncbi.nlm.nih.gov/30685221/ | Galletti, F., Fazio, V., Gentile, M., Schillaci, G., Pucci, G., Battista, L., Mercurio, V., Bossio, G., Bonaduce, D., Brambilla, N., Vitalini, C., P'Anna, M., & Giacovelli, G. (2019). Nutraceutical combination on lipid metabolism in patients with metabolic syndrome: a multicenter, double blind, randomized, placebo controlled trial. <i>Lipids in Health and Disease</i> , 18(1). https://doi.org/10.1186/s12944-019-1002-Y | Yes |
| 18 | inulin and phytosterols | 2015 | Effect of phytosterols and inulin-enriched soy milk on LDL-cholesterol in Thai subjects: a double-blinded randomized controlled trial | Double-blinded randomized controlled trial | Two hundred and forty subjects who were 18 years old or older and had a baseline LDL-C of 130 mg/dl or higher were enrolled into the double-blinded randomized controlled trial. Subjects were randomly assigned into the study group that received 2 g/day of phytosterols and 10 g/day of inulin-enriched soy milk or into the control group that received standard soy milk. The lipid profile was measured every 2 weeks for 8 weeks. | Control | At the end of the study, the median LDL-C levels decreased significantly from 165 (132, 254) mg/dl to 150 (105, 263) mg/dl in the study group (p < 0.001) and from 165 (130, 243) mg/dl to 159 (89, 277) mg/dl in the control group (p = 0.034). The LDL-C reduction was significantly better in the study group (1.0 (0.0%, 1.37), 36.00) vs -1.31% (-53.40, 89.73), p < 0.001). TC also reduced significantly by 6.60% in the study group while it reduced only by 1.76% in the control group (p < 0.001). | Daily consumption of soy milk containing 2 g of phytosterols and 10 g of inulin reduced TC and LDL-C better than standard soy milk. | It had no effect on TG and HDL-C levels compared to standard soy milk. | https://pubmed.ncbi.nlm.nih.gov/26553065/ | Kesiriroje, N., Kwankaw, J., Kitpakornchai, S., & Leelawatana, R. (2015). Effect of phytosterols and inulin-enriched soy milk on LDL-cholesterol in Thai subjects: a double-blinded randomized controlled trial. <i>Lipids in Health and Disease</i> , 14(1). https://doi.org/10.1186/s12944-015-049-4 | No |
| 19 | Inulin, Pomegranate extract | 2017 | Cholesterol-lowering effects of dietary pomegranate extract and inulin in mice fed an obesogenic diet | Animal study | Male C57BL/6J mice were fed high-fat/high-sucrose (HF/HIS) (32% energy from fat, 25% energy from sucrose) diets supplemented with PomX (0.25%) and inulin (9%) alone or in combination for 4 weeks. | Control | Feeding the HF/HIS diet supplemented with PomX and inulin individually resulted in a significant decrease in serum TC compared HF/HIS control. | Inulin mainly targeted hepatic cholesterol de novo synthesis and fecal cholesterol and bile acid excretion involving changes in the metabolism of the intestinal microbiome. | Supplementation with PomX and inulin together resulted in lower hepatic and serum total cholesterol compared to individual treatments. PomX showed a trend to decrease liver triglyceride (TG) levels, while inulin or PomX-inulin combination had no effect on either serum or liver TG levels. | https://www.sciencedirect.com/science/article/pii/S095526316308294 | Yang, J., Zhang, S., Henning, S. M., Lee, R., Hsu, M., Grogan, E., Pisagna, R., Ly, A., Heber, D., & Li, Z. (2018). Cholesterol-lowering effects of dietary pomegranate extract and inulin in mice fed an obesogenic diet. <i>Journal of Nutritional Biochemistry</i> , 52, 62-69. https://doi.org/10.1016/j.jnutbio.2017.10.003 | No |
| 20 | Artichoke and Bergamot | 2021 | Artichoke and Bergamot Phytosome Alliance: A Randomized Double Blind Clinical Trial in Mild Hypercholesterolemia | Randomized placebo-controlled trial. | 600 mg of bergamot phytosome [®] (from Citrus bergamia Risso) and 100 mg of artichoke leaf standardized dry extract (from Cynara cardunculus L.). Sixty overweight adults were randomized into two groups: 30 were supplemented and 30 received a placebo. The metabolic parameters and DXA body composition were evaluated at the start, after 30 and 60 days. | Placebo | Between the two groups, total and LDL cholesterol in the supplemented group (compared to placebo) showed significant decreases overtime. | In conclusion, the synergism between Citrus bergamia polyphenols and Cynara cardunculus extracts may be an effective option and may potentially broaden the therapeutic role of botanicals in dyslipidemic patients. | A significant reduction of waist circumference and visceral adipose tissue (VAT) was recorded in the supplemented group (compared to placebo), even in subjects who did not follow a low-calorie diet. | https://pubmed.ncbi.nlm.nih.gov/35010984/ | Riva, A., Petrangolini, G., Allegrini, P., Perna, S., Giacosa, A., Perani, G., Fallo, M. A., Nasso, M., & Rondelli, M. (2021). Artichoke and Bergamot Phytosome Alliance: A Randomized, Double Blind Clinical Trial in Mild Hypercholesterolemia. <i>Nutrients</i> , 14(1). https://doi.org/10.3390/nu14010108 | Yes |
| 21 | Artichoke and bergamot | 2022 | Artichoke and bergamot extracts: a new opportunity for the management of dyslipidemia and related risk factors. | Review | This review aimed to describe the effects of artichoke and bergamot in modifying the lipid and inflammatory parameters described in vitro, in vivo and clinical studies. | Not Applicable - NA | Significant presence of polyphenols in their extracts, can exert this action associated with a number of other complementary inflammation and oxidation benefits. | The available data support the use of standardized compositions of artichoke and bergamot extracts, alone or in combination, in the treatment of mild to moderate dyslipidemia | Significant presence of polyphenols in their extracts, can exert this action associated with a number of other complementary inflammation and oxidation benefits. | https://europpgmc.org/article/med/35313442 | Arababidi, L., Corsini, A., & Bellotti, S. (2022). Artichoke and bergamot extracts: a new opportunity for the management of dyslipidemia and related risk factors. <i>Minerva Medica</i> , 113(1), 141-157. https://doi.org/10.23736/s0026-4806-21-07950-7 | No |
| 22 | lysine, vitamin B(6), and carnitine | | Effect of lysine, vitamin B(6), and carnitine supplementation on the lipid profile of male patients with hypertriglyceridemia: a 12-week, open-label, randomized, placebo-controlled trial | Randomized, placebo-controlled clinical trial | This 12-week, randomized, placebo-controlled clinical trial. A total of 85 hypertriglyceridemic (TG > 150 mg/dL) male patients were randomized to 1 of 5 groups and given supplements of lysine (1 g/d), vitamin B(6) (50 mg/d), lysine (1 g/d) + vitamin B(6) (50 mg/d), carnitine (1 g/d), or placebo for 12 weeks. The lipid profile (TG, total cholesterol, LDL-C, and HDL-C) and fasting plasma glucose levels were assessed at baseline and at 6 and 12 weeks. | Placebo | Vitamin B(6) supplementation was associated with a significant reduction in total cholesterol and HDL-C of -10%. In addition, plasma TG was reduced by 36.6 mg/dL at 6 weeks, whereas levels in the placebo group increased by 18 mg/dL. | Vitamin B(6) supplementation in these male patients with hypertriglyceridemia reduced plasma total cholesterol and HDL-C concentrations. | No major changes in the lipid profile were observed in the lysine and carnitine groups or when lysine was added to vitamin B(6). | https://pubmed.ncbi.nlm.nih.gov/32281869/ | Hlais, S., Reslan, D. R. A., Sarienedine, H. K., Nasredine, L., Taab, G., Azar, S., & Obied, O. A. (2021). Effect of lysine, vitamin B(6), and carnitine supplementation on the lipid profile of male patients with hypertriglyceridemia: a 12-week, open-label, randomized, placebo-controlled trial. <i>Clinical Therapeutics</i> , 43(9), 1672-1682. https://doi.org/10.1016/j.clinthera.2021.06.019 | No |
| 23 | omega-3 fatty acids and vitamin E | 2015 | A randomized-controlled clinical trial investigating the effect of omega-3 fatty acids and vitamin E co-supplementation on markers of insulin metabolism and lipid profiles in gestational diabetes | Randomized, double-blind, placebo-controlled clinical trial | 60 patients with GDM. Patients were randomly allocated to take either 1000-mg omega-3 fatty acids from flaxseed oil plus 400-IU vitamin E supplements (n = 30) or placebo (n = 30) for 6 weeks. Fasting blood samples were obtained from at the beginning of the study and after 6-week intervention to quantify related variables. | Placebo | After 6 weeks of intervention, changes in serum triglycerides (+10.8 ± 41.5 vs +34.2 ± 35.5 mg/dL, P = .02), VLDL-cholesterol (+2.1 ± 8.3 vs +6.8 ± 7.1 mg/dL, P = .02), low-density lipoprotein (LDL)-cholesterol (+11.5 ± 18.8 vs +1.7 ± 15.9 mg/dL, P = .03) and HDL-cholesterol concentrations (+1.9 ± 8.7 vs -2.4 ± 7.7 mg/dL, P = .04) were significantly different between the supplemented women and placebo group. | Overall, we demonstrated that omega-3 fatty acids and vitamin E co-supplementation in GDM women had beneficial effects on glucose homeostasis parameters, serum triglycerides, VLDL-cholesterol, and HDL-cholesterol concentrations, but it did not influence total-cholesterol and LDL-cholesterol levels. | However, after controlling for baseline total cholesterol levels, maternal age, and BMI at baseline, the changes in serum LDL-cholesterol concentrations were not significantly different between the 2 groups. We did not find any significant effect of joint omega-3 fatty acids and vitamin E supplementation on total cholesterol concentrations. | https://pubmed.ncbi.nlm.nih.gov/27055970/ | Tajhadeh, M., Jamilian, M., Masloumi, M., Sanani, M., & Asemi, Z. (2016). A randomized-controlled clinical trial investigating the effect of omega-3 fatty acids and vitamin E co-supplementation on markers of insulin metabolism and lipid profiles in gestational diabetes. <i>Journal of Clinical Lipidology</i> , 10(2), 386-393. https://doi.org/10.1016/j.jacl.2015.12.017 | No |
| 24 | Magnesium and Vitamin E | 2018 | The effects of magnesium and vitamin E co-supplementation on parameters of glucose homeostasis and lipid profiles in patients with gestational diabetes | Randomized, double-blinded, placebo-controlled trial | 60 subjects diagnosed with gestational diabetes (GDM), aged 18-40 years. Subjects were randomly allocated into two groups to receive 250 mg/day magnesium oxide plus 400 IU/day vitamin E supplements or placebo (n = 30 each group) for 6 weeks. Participants' blood samples were taken to determine their metabolic profiles. | Placebo | magnesium plus vitamin E supplementation resulted in a significant reduction in serum triglycerides, VLDL, LDL and total-/HDL-cholesterol ratio compared with placebo. Magnesium and vitamin E co-supplementation did not affect HDL-cholesterol levels. | Overall, magnesium and vitamin E co-supplementation for 6 weeks in women with GDM significantly improved lipid profiles, except for HDL-cholesterol levels. | Magnesium and vitamin E co-supplementation did not affect HDL-cholesterol levels. | https://pubmed.ncbi.nlm.nih.gov/30025222/ | Maktabi, M., Jamilian, M., Amirani, E., Chamani, M., & Asemi, Z. (2018). The effects of magnesium and vitamin E co-supplementation on parameters of glucose homeostasis and lipid profiles in patients with gestational diabetes. <i>Lipids in Health and Disease</i> , 17(1). https://doi.org/10.1186/s12944-018-0814-5 | Yes |

Table S2: Summary of articles on Coenzyme Q10.

| Co enzyme Q10 | | | | | | | | | | | | |
|---------------|--|------|--|--|--|---------------------|---|--|--|--|---|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Co enzyme Q10 | 2018 | Coenzyme Q10 protects against hyperlipidemia-induced cardiac damage in apolipoprotein E-deficient mice | Animal study | Eight-week-old male mice were randomly divided into four groups: mice fed a normal diet; mice fed a normal diet + CoQ10; ApoE-deficient mice fed a high-fat diet; and ApoE-deficient mice fed a high-fat diet + CoQ10. All groups were fed the different diets for 16 weeks. | Control | The metabolic parameters such as total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), and triglycerides (TG) levels were lower in ApoE ^{-/-} HD + CoQ10 mice than in ApoE ^{-/-} HD mice. | These results indicate that CoQ10 is a potential therapeutic target for cardiac damage caused by hyperlipidemia | CoQ10 contributes to the mitigation of hyperlipidemia-induced cardiac damage, findings provide new insights into the role of CoQ10 in hyperlipidemia-induced cardiac damage and raise the possibility of a novel therapeutic intervention for treatment of CVDs. | https://link.springer.com/content/pdf/10.1186/s12944-018-0293-9.pdf | Zhang J, Liu H, Hao Y, Wu L, Zhang T, Liu Y, Guo J, Zhu L, & Ren Z. (2018). Coenzyme Q10 protects against hyperlipidemia-induced cardiac damage in apolipoprotein E-deficient mice. <i>Lipids in Health and Disease</i> , 17(1). https://doi.org/10.1186/s12944-018-0928-9 | No |
| 2 | Co enzyme Q10 | 2020 | The effects of coenzyme Q10 supplementation on lipid profiles among patients with coronary artery disease: a systematic review and meta-analysis of randomized controlled trials | Systematic review | A systematic review and meta-analysis of randomized controlled trials. A total of eight trials (267 participants in the intervention group and 259 in placebo group) were included in the current meta-analysis. | Not Applicable - NA | This meta-analysis demonstrated the promising effects of CoQ10 supplementation on lowering lipid levels among patients with CAD, though it did not affect triglycerides, LDL-cholesterol and lip(a) levels. | CoQ10 supplementation significantly improved some of the parameters of lipid profile including total cholesterol and HDL-cholesterol levels in patients with CAD | CoQ10 deficiency usually occurs with aging and may increase the risk of CVD. Meta-analysis conducted by Pirro et al. [18] showed that taking a nutraceutical combination of red yeast rice, berberine, policosanol, astaxanthin, CoQ10 and folic acid significantly reduced serum triglycerides, total-LDL and HDL-cholesterol levels. | https://onlinelibrary.wiley.com/doi/10.1111/1365-3113.12484 https://doi.org/10.1111/1365-3113.12484 | Jorali, M., V. Tabrizi, R. Mirhosseini, M. Lankarani, K. B. Akbari, M. Heydari, S. T. Mottaghi, R., & Asemi, Z. (2018). The effects of coenzyme Q10 supplementation on lipid profiles among patients with coronary artery disease: A systematic review and meta-analysis of randomized controlled trials. <i>Lipids in Health and Disease</i> (Vol. 17, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s12944-018-0876-4 | Yes |
| 3 | Co enzyme Q10, Vitamin C, monacolin K, and L-arginine. | 2018 | LDL-cholesterol lowering effect of a new dietary supplement: An open label, controlled, randomized, cross-over clinical trial in patients with mild-to-moderate hypercholesterolemia | Single center, controlled, randomized, open-label, cross-over clinical study | 30 Caucasian outpatients aged 18-75 years with serum LDL-C between 130 and 180 mg/dL. Patients assumed two different dietary supplements (A and N) both containing monacolin K 10 mg for 8 weeks each, separated by a 4-week wash-out period. | Control | LDL-C decreased by 23.3% during treatment with N and by 25.6% during treatment with A. Total-C decreased significantly within each treatment period. HDL-C increase was negligible during A whereas it was significant during N. TG diminished markedly during A and not significantly during N. The difference between treatments was not statistically significant for all variables. | Our results confirm the clinically meaningful LDL-C lowering properties of monacolin K. At variance with supplement already in the market (N), the novel association (A) of monacolin K with L-arginine, coenzyme Q10 and ascorbic acid also produces a significant reduction of triglycerides without significant effects on HDL. | Results confirm the clinically meaningful LDL-C lowering properties of monacolin K | https://pubmed.ncbi.nlm.nih.gov/29793488/ | Magno, S., Caccarini, G., Pedrini, C., Jaccheri, R., Vitelli, L., Fierabracci, P., Salvetti, G., Airolidi, G., Minale, M., Saponati, G., & Santini, F. (2018). LDL-cholesterol lowering effect of a new dietary supplement: An open label, controlled, randomized, cross-over clinical trial in patients with mild-to-moderate hypercholesterolemia. <i>Lipids in Health and Disease</i> , 17(1). https://doi.org/10.1186/s12944-018-0775-8 | Yes |
| 4 | Co enzyme Q10 | 2017 | Effects of coenzyme Q10 supplementation on inflammatory markers: A systematic review and meta-analysis of randomized controlled trials | Systematic review | A systematic review and meta-analysis of seventeen randomized controlled trials. The aims of this meta-analysis is to evaluate the effects of coenzyme Q10 (CoQ10) supplementation on inflammatory mediators including C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) by analyzing published randomized controlled trials (RCTs). | Not Applicable - NA | CoQ10 supplementation significantly reduced the levels of circulating CRP, IL-6 and TNF- α . | meta-analysis of RCTs suggests significant lowering effects of CoQ10 on CRP, IL-6 and TNF- α . | However, results should be interpreted with caution because of the evidence of heterogeneity and limited number of studies. | https://www.sciencedirect.com/science/article/abs/pii/S1048614314128429 | Sun, L., Feng, Y., Chen, S. C., Qin, J. D., Fu, C., Jing, & Chen, L. H. (2017). Effects of coenzyme Q10 supplementation on inflammatory markers: A systematic review and meta-analysis of randomized controlled trials. <i>Pharmacological Research</i> , 119, 328-336. https://doi.org/10.1016/j.phrs.2017.01.032 | Yes |
| 5 | Co enzyme Q10 | 2018 | Treatment of coenzyme Q10 for 24 weeks improves lipid and glycemic profile in dyslipidemic individuals | Randomized, double-blinded, placebo-controlled trial | 101 dyslipidemic subjects without taking any hypoglycemic or placebo daily for 24 weeks. Anthropometric parameters, lipid and glycemic profile, biomarkers of inflammation, and antioxidant capacity were evaluated before and after 12 and 24 weeks of intervention. | Placebo | Coenzyme Q10 treatment for 24 weeks reduced triglycerides to 12.6%, low-density lipoprotein cholesterol to 7.6% and increased ApoA-I to 7.7%. | The versatility and safety of CoQ10 makes it a potential candidate for the primary prevention of CVD. | Twenty-four-week treatment of CoQ10 ameliorates multiple CVD risk factors. | https://www.sciencedirect.com/science/article/abs/pii/S193326541730541X | Zhang P., Yang, C., Guo, H., Wang, J., Lin, S., Li, H., Yang, Y., & Ling, W. (2018). Treatment of coenzyme Q10 for 24 weeks improves lipid and glycemic profile in dyslipidemic individuals. <i>Journal of Clinical Lipidology</i> , 12(2), 417-427.e5. https://doi.org/10.1016/j.jacl.2017.12.006 | Yes |
| 6 | Co enzyme Q10 and Omega-3 | 2017 | Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia | Pilot randomized double-blind trial | 105 subjects who met the criteria of combined dyslipidemia and elevated TAG levels were randomly divided into three groups. In the control group, unaltered statin therapy was indicated. In the second and third groups, omega-3 PUFA 2.52 g/day (Zenklin Fa Pleuran) and omega-3 PUFA 2.52 g+CoQ10 200 mg/day (Pharma Nord Aps) were added, res/./ At the end of the 3-month period (13 weeks), all patients were evaluated. | Control | Significant reduction of hepatic enzymes activity, systolic blood pressure, total inflammatory markers and TAG levels were detected in both groups in comparison to the control group. | Coenzyme Q10 addition significantly reduced most of the abovementioned parameters (systolic blood pressure, total cholesterol, LDL, hsCRP, IL-6, SOD) in comparison with the statin+omega-3 PUFA group. | The results of this pilot study suggest the possible beneficial effects of triple combination on the lipid and non-lipid parameters related to atherogenesis and side effects of statin treatment. | https://pubmed.ncbi.nlm.nih.gov/28541926/ | Toth, S., Sajty, M., Pekárová, T., Mughées, A., Stefančík, P., Katz, M., Spiláková, K., Pella, J., & Pella, D. (2017). Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia. <i>Journal of Basic and Clinical Physiology and Pharmacology</i> , 28(4), 327-336. https://doi.org/10.1155/2016-2016-0149 | Yes |
| 7 | Co enzyme Q10 | 2017 | Treatment of coenzyme Q10 for 24 weeks improves lipid and glycemic profile in dyslipidemic individuals | Randomized, double-blinded, placebo-controlled trial | 101 dyslipidemic subjects without taking any hypoglycemic or placebo daily for 24 weeks. Anthropometric parameters, lipid and glycemic profile, biomarkers of inflammation, and antioxidant capacity were evaluated before and after 12 and 24 weeks of intervention. | Placebo | All 101 subjects were included in the analysis. On the 12th week, compared to placebo, CoQ10 supplementation decreased systolic (P = .010) and diastolic pressure (P = .003) and increased serum total antioxidant capacity (TAC, P = .003). On the 24th week, compared to placebo, CoQ10 supplementation further lowered blood pressure and TAC, reduced triglyceride (P = .003) and low-density lipoprotein cholesterol (P = .016). | Twenty-four-week treatment of CoQ10 ameliorates multiple CVD risk factors. The versatility and safety of CoQ10 makes it a potential candidate for the primary prevention of CVD. | led to significant decrease of non-high-density lipoprotein cholesterol in CoQ10 group compared to placebo (P = .031). | https://pubmed.ncbi.nlm.nih.gov/29454678/ | Zhang, P., Yang, C., Guo, H., Wang, J., Lin, S., Li, H., Yang, Y., & Ling, W. (2018). Treatment of coenzyme Q10 for 24 weeks improves lipid and glycemic profile in dyslipidemic individuals. <i>Journal of Clinical Lipidology</i> , 12(1), 417-427.e5. https://doi.org/10.1016/j.jacl.2017.12.006 | Yes |
| 8 | Co enzyme Q10 | 2020 | Ubiquinol Ameliorates Endothelial Dysfunction in Subjects with Mild-to-Moderate Dyslipidemia: A Randomized Clinical Trial | Randomized, double-blind, single-center trial | Fifty-one subjects with low-density lipoprotein (LDL) cholesterol levels of 130-200 mg/dL, not taking statins or other lipid lowering treatments, moderate (2.5%-6.0%) endothelial dysfunction as measured by flow-mediated dilation (FMD) of the brachial artery, and no clinical signs of cardiovascular disease were randomized to receive either ubiquinol (200 or 100 mg/day) or placebo for 8 weeks. | Placebo | 48 participants who completed the study demonstrated a significantly increased FMD in both treated groups compared with the placebo group (200 mg/day, +1.28% \pm 0.90%; 100 mg/day, +1.34% \pm 1.44%; p < 0.001) and a marked increase in plasma CoQ10, either total (p < 0.001) and reduced (p < 0.001). Serum NOx increased significantly and dose-dependently in all treated subjects (p = 0.016), while LDL oxidation lag time improved significantly in those receiving 200 mg/day (p = 0.017). Ubiquinol significantly ameliorated dyslipidemia-related endothelial dysfunction. | This effect was strongly related to increased nitric oxide bioavailability and was partly mediated by enhanced LDL antioxidant protection. | N/A | https://pubmed.ncbi.nlm.nih.gov/32326664/ | Sabbatelli, J., Orjando, P., Galazzi, R., Silvestri, S., Cavilli, L., Marchionni, F., D'Adda, P., Colucci, A., Bonfigli, A. L., Mazzanti, L., Olivero, F., Antonelli, B., & Triano, L. (2020). Ubiquinol Ameliorates Endothelial Dysfunction in Subjects with Mild-to-Moderate Dyslipidemia: A Randomized Clinical Trial. <i>Nutrients</i> , 12(4). https://doi.org/10.3390/nu12041098 | No |
| 9 | Co enzyme Q10 and fatty acid | 2017 | Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia | Pilot randomized double-blind trial | 105 subjects who met the criteria of combined dyslipidemia and elevated TAG levels were randomly divided into three groups. In the control group, unaltered statin therapy was indicated. In the second and third groups, omega-3 PUFA 2.52 g/day (Zenklin Fa Pleuran) and omega-3 PUFA 2.52 g+CoQ10 200 mg/day (Pharma Nord Aps) were added, res/./ At the end of the 3-month period (13 weeks), all patients were evaluated. | Control | Coenzyme Q10 addition significantly reduced most of the abovementioned parameters (systolic blood pressure, total cholesterol, LDL, hsCRP, IL-6, SOD) in comparison with the statin+omega-3 PUFA group. | The results of this pilot study suggest the possible beneficial effects of triple combination on the lipid and non-lipid parameters related to atherogenesis and side effects of statin treatment. | The intensity of statin adverse effects were significantly reduced in the group with the addition of CoQ10. | https://pubmed.ncbi.nlm.nih.gov/28541926/ | Toth, S., Sajty, M., Pekárová, T., Mughées, A., Stefančík, P., Katz, M., Spiláková, K., Pella, J., & Pella, D. (2017). Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia. <i>Journal of Basic and Clinical Physiology and Pharmacology</i> , 28(4), 327-336. https://doi.org/10.1155/2016-2016-0149 | No |
| 10 | Co enzyme Q10 | 2018 | Comparison of efficacy and safety of combination therapy with statins and omega-3 fatty acids versus statin monotherapy in patients with dyslipidemia: A systematic review and meta-analysis | Systematic review and meta-analysis | published data to compare the safety and efficacy of combination therapy with statins and omega-3 fatty acids versus statin monotherapy in patients with dyslipidemia. Six articles were assessed in the present meta-analysis (quantitative assessment) and qualitative assessment. | Not Applicable - NA | the combination treatment afforded a significantly greater reduction in total cholesterol/high-density lipoprotein (cholesterol) than statin alone did. However, there was no significant difference in low-density lipoprotein (LDL) cholesterol between the 2 groups. Combination therapy with statins and omega-3 fatty acids was generally more effective on lipid concentration than statin monotherapy. | We suggest that combination therapy with statins and omega-3 fatty acids enhances lipid profile, except LDL cholesterol, compared with statin monotherapy. | Nevertheless, statin and omega-3 fatty acid combination should be cautiously recommended, taking into account the clinical importance of LDL cholesterol and safety issues associated with their concomitant use. | https://pubmed.ncbi.nlm.nih.gov/30558030/ | cdif class="cs1-entry">Choi, H. D., & Cha, S. M. (2018). Comparison of efficacy and safety of combination therapy with statins and omega-3 fatty acids versus statin monotherapy in patients with dyslipidemia: A systematic review and meta-analysis. <i>ckMedline/10.5597/15300</i> . https://doi.org/10.1097/MD.00000000000013493/abstract | Yes |

Table S3: Summary of articles on vitamins.

| Vitamin | | | | | | | | | | | | |
|---------|---------------|------|---|---|---|-------------------|---|--|--|---|---|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Vitamin D | 2016 | Vitamin D Supplementation and High-Density Lipoprotein Cholesterol: A Study in Healthy School Children | Controlled clinical trial | 47 healthy children (23 boys) aged 10–14 years, students of Bijnor (I) elementary schools, were selected and randomly divided into two groups. The study group received a vitamin D supplement (1000 mg capsule) daily for one month, and placebo tablets were prescribed to the controls. Before and after the treatment course, the serum HDL-C and 25-hydroxy vitamin D levels of both groups were measured. | Placebo | Forty children completed the study. The mean serum levels of both HDL-C and vitamin D showed a significant rise following the treatment in the study group, whereas both variables decreased slightly in the control group. There was no statistically significant difference in the mean serum levels of HDL-C and vitamin D between the two groups after the intervention. | Vitamin D supplements seem to have a positive impact on serum HDL-C levels and may be effective in reducing the risk of cardiovascular diseases in the long term. | Despite the small sample size, the present study provides consistent support for a relationship between vitamin D and HDL-C, indicating that vitamin D supplementation results in increased blood levels of HDL and that it can be regarded as a protective factor to reduce the risk of cardiovascular disease. | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5046666/pdf/p-24-06-3111.pdf | Levashin, E., Namaliev, K., & Zardasi, M. (2016). Vitamin D supplementation and high-density lipoprotein cholesterol: A study in healthy school children. <i>Iranian Journal of Pediatrics, 26(4)</i> . https://doi.org/10.38172/ijp.3111 | No |
| 2 | Vitamin D | 2021 | Effects of Calcium and Vitamin D Co-supplementation on the Lipid Profile: A Systematic Review and Meta-analysis | Systematic Review and Meta-analysis | Controlled Trials, and clinical trial registry databases was conducted to identify placebo-controlled RCTs that were published through September 2020 and that evaluated the impact of calcium and vitamin D co-supplementation on total cholesterol (TC), triglycerides (TGs), low- and very-low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol (HDL-C). Standardized mean differences (SMDs) were pooled using random-effects meta-analysis models. | not applicable | Thirteen studies in a total of 2304 participants met the inclusion criteria. Calcium and vitamin D co-supplementation was associated with significant reductions in both TC and TGs, and with a significant increase in HDL-C. However, calcium and vitamin D co-supplementation were not found to be associated with significantly decreased low-density lipoprotein cholesterol. | The findings from the present systematic review and meta-analysis suggest that calcium and vitamin D co-supplementation has a beneficial effect on TC, TG, and HDL-C. | larger-scale, well-designed RCTs are needed to clarify the effect of calcium and vitamin D co-supplementation on all lipid profile components. | https://www.sciencedirect.com/science/article/abs/pii/S0149268821002605 | Morvaridzadeh, M., Agha, S., Alibakhshi, P., Heydari, H., Hosseini, A. S., Palmowski, A., Toupchian, O., Abdollahi, S., Rezaei, G., & Heshmati, J. (2021). Effects of Calcium and Vitamin D Co-supplementation on the Lipid Profile: A Systematic Review and Meta-analysis. <i>Clinical Therapeutics, 43(9)</i> , 278–296. https://doi.org/10.1016/j.clinthera.2021.07.018 | Yes |
| 3 | Vitamin D | 2018 | Vitamin D supplementation and lipoprotein metabolism: A randomized controlled trial | Post hoc analysis of the single-center, double-blind, randomized placebo-controlled Syrian Vitamin D Hypertension Trial | Vitamin D supplementation significantly increased total cholesterol, triglycerides, very-low-density lipoprotein (VLDL) triglycerides, low-density lipoprotein (LDL) triglycerides, high-density lipoprotein (HDL) triglycerides. There was a nonsignificant increase in LDL cholesterol. | Placebo | Vitamin D supplementation significantly increased total cholesterol, triglycerides, very-low-density lipoprotein (VLDL) triglycerides, low-density lipoprotein (LDL) triglycerides, high-density lipoprotein (HDL) triglycerides. There was a nonsignificant increase in LDL cholesterol. | The effects of vitamin D on lipid metabolism are potentially unfavorable. | They require further investigation in view of the wide use of vitamin D testing and treatment. | https://www.sciencedirect.com/science/article/abs/pii/S1933384418380772 | Schwartz, V., Schragal, H., Trummer, C., Stojakovic, T., Pandis, M., Gubler, M., R. Verheum, N., Galsch, M., Zittermann, A., Aberer, F., Lechbaum, F., Obermayr-Rietz, B., Fischer, T. R., März, W., Tomaschitz, A., & Pilz, S. (2018). Vitamin D supplementation and lipoprotein metabolism: A randomized controlled trial. <i>Journal of Clinical Lipidology, 12(3)</i> , 588–596.e4. https://doi.org/10.1016/j.jclm.2018.03.079 | Yes |
| 4 | Vitamin D | 2021 | Effect of vitamin D supplementation on markers of cardiometabolic risk in children and adolescents: A meta-analysis of randomized clinical trials | A meta-analysis of randomized clinical trials | Eligible randomized controlled trials (RCTs) were identified by searching PubMed, EMBASE and Web of Science. The results of this study are synthesized and reported in accordance with the PRISMA statement. GRADE system was used to assess the certainty of evidence. A total of 9 RCTs were identified and included in the meta-analysis. | not applicable | However, vitamin D supplementation showed a beneficial effect on fasting glucose (-1.54 mg/dL, 95% CI -2.98 to -0.10) and TG (-24.76 mg/dL, 95% CI -37.66 to -11.86) in the sub-group analysis of total vitamin D supplementation $\geq 200,000$ IU. | Vitamin D supplementation appeared to have a beneficial effect on reducing fasting glucose and TG level when total vitamin D supplementation $\geq 200,000$ IU but not HDL-C, LDL-C, TC, blood pressure and waist circumferences levels in children and adolescents. Further studies are needed to address this issue. | When total vitamin D supplementation $\geq 200,000$ IU, it reduces TG level. Vitamin D supplementation does not affect HDL-C, LDL-C or TC. Vitamin D supplementation does not affect BP and waist circumferences and BP. | https://www.sciencedirect.com/science/article/pii/S0939733210029268 | Chen, L., Wei, X., Zhang, P., Yuan, Y., Cai, X., & He, X. (2021). Effect of vitamin D supplementation on markers of cardiometabolic risk in children and adolescents: A meta-analysis of randomized clinical trials. <i>Nutrition, Metabolism and Cardiovascular Diseases, 31(10)</i> , 2800–2814. https://doi.org/10.1016/j.numecd.2021.06.013 | No |
| 5 | Vitamin D | 2021 | Vitamin D supplementation reduces serum lipids of children with hypertriglyceridemia: A randomized, triple-masked, placebo-controlled crossover trial | A randomized, triple-masked, placebo-controlled crossover trial | 44 Brazilian children with hypertriglyceridemia, age 4 to 11 y. The sample included eutrophic and overweight/obese children according to body mass index for age, with sufficient and insufficient vitamin D basal levels. The intervention lasted 34 wk, with two periods of 12 wk each separated by a 10-wk washout. The two groups, supplemented and placebo, received five drops of cholecalciferol (equivalent to 1000 international unit) and five drops of sunflower oil, respectively, daily for 12 wk. | Placebo | There was a reduction in serum total cholesterol ($P < 0.001$), low-density lipoprotein cholesterol ($P < 0.001$), non-high-density lipoprotein cholesterol ($P < 0.001$), total cholesterol/high-density lipoprotein cholesterol ($P = 0.001$), and low/high-density lipoprotein cholesterol ratios ($P < 0.001$) in the supplemented group compared with the placebo group. | Cholecalciferol supplementation improved the lipid profile of children with hypertriglyceridemia without altering body composition. | N/A | https://www.sciencedirect.com/science/article/abs/pii/S0899268821001581 | Alexis, A. G. P., Cruvinet, B. A. C., Schinaglia, R. M., Godoi, L. S., & Silva, M. S. (2021). Vitamin D supplementation reduces serum lipids of children with hypertriglyceridemia: A randomized, triple-masked, placebo-controlled crossover trial. <i>Nutrition, 89</i> , 111296. https://doi.org/10.1016/j.nut.2021.111296 | Yes |
| 6 | Vitamin D | 2022 | Vitamin D Supplementation Improves Fasting Insulin Levels and HDL Cholesterol in Infertile Men | A single-center, double-blind, randomized clinical trial | A total of 307 infertile men were randomly assigned (1:1) to a single dose of 300,000 IU cholecalciferol followed by 1400 IU cholecalciferol + 500 mg of calcium daily (n = 151) or placebo (n = 156) for 150 days. | Placebo | Men in the vitamin D group had higher high-density lipoprotein (HDL) cholesterol levels (1.36 ± 1.32 mmol/L, $P = .008$) compared with the placebo group. | High-dose vitamin D supplementation has beneficial effects on glucose homeostasis and HDL cholesterol levels in infertile men. | At the end of the trial, men receiving vitamin D supplementation had 13% lower fasting serum insulin concentrations compared with the placebo-treated group (65 vs 74 pmol/L, $P = .018$) and 19% lower HOMA-IR (2.2 vs 2.7, $P = .025$). | https://pubmed.ncbi.nlm.nih.gov/34508607/ | Holt, R., Petersen, J. H., Finsdåle, E., Knop, F. K., Juul, A., Bjerggaard, N., & Blomberg Jensen, M. (2022). Vitamin D Supplementation Improves Fasting Insulin Levels and HDL Cholesterol in Infertile Men. <i>The Journal of Clinical Endocrinology and Metabolism, 102(1)</i> , 98–108. https://doi.org/10.1210/clinem.2021.064667 | No |
| 7 | Vitamin D | 2015 | Vitamin D Protects Against Atherosclerosis via Regulation of Cholesterol Efflux and Macrophage Polarization in Hypercholesterolemic Swine | Animal study | Vitamin D-deficient (0 IU/d), VD-sufficient (1000 IU/d), or Vitamin D-supplemented (3000 IU/d) high-cholesterol diet for 48 weeks. Serum lipids and 25(OH)-cholecalciferol levels were measured biweekly | CONTROL | Vitamin D protects against atherosclerosis in hypercholesterolemic swine via controlling cholesterol efflux and macrophage polarization via increased CYP27A1 activation. | VD deficiency exacerbates the lipid accumulation and atherosclerosis in hypercholesterolemic swine. Clinical studies suggest that Vitamin D deficiency is related to a higher risk for cardiovascular disease. | the exact role of Vitamin D in the progression of cardiovascular diseases has not been well defined | https://www.ahajournals.org/doi/full/10.1161/ATVBAHA.115.306323 | Yin, R., You, Y., Swier, W., Tang, L., Radwan, M. M., Pandya, A. N., & Agrawal, D. K. (2015). Vitamin D Protects Against Atherosclerosis via Regulation of Cholesterol Efflux and Macrophage Polarization in Hypercholesterolemic Swine. <i>Atherosclerosis, Thrombosis, and Vascular Biology, 35(4)</i> , 1432–1442. https://doi.org/10.1161/ATVBAHA.115.306323 | No |
| 8 | Vitamin D | 2018 | Lower Vitamin D Intake is Associated with Low HDL Cholesterol and Vitamin D Insufficiency/Deficiency in Brazilian Children | A cross-sectional study carried out with a representative sample of Brazilian children | 378 children 8–9-year-old age group. Blood was collected after 12 h of fasting. Laboratory tests were performed to determine total cholesterol, HDL cholesterol (HDL-C), LDL cholesterol, TAG, apolipoprotein A1, 25-hydroxyvitamin D and parathyroid hormone. Dietary intake was evaluated by 24-h recall. | CONTROL | Study has found that Brazilian children have a high prevalence of inadequate vitamin D intake, dyslipidemia and 25(OH)D insufficiency/deficiency. | The inadequate vitamin D intake was associated with higher prevalence of low HDL-C and vitamin D insufficiency/deficiency | It is important to develop specific actions in food and nutritional education as well as programs that stimulate and facilitate access to vitamin D food sources. | https://www.cambridge.org/core/journals/public-health-nutrition/article/lower-vitamin-d-intake-is-associated-with-low-hdl-cholesterol-and-vitamin-d-insufficiency-deficiency-in-brazilian-children/9D7997310A44CE61D8E26A47926912320 | de Santos, F. M., Sobrinho, L. S., Sato, M. A., Rocha, N. P., & de Novaes, J. F. (2018). Lower Vitamin D Intake is Associated with Low HDL Cholesterol and Vitamin D Insufficiency/Deficiency in Brazilian Children. <i>Public Health Nutrition, 21(11)</i> , 2006–2012. https://doi.org/10.1017/S1368800818000204 | No |
| 9 | Vitamin C | 2021 | Red Dragon Fruit (Hylocereus Polyrhizus) to Reduce Cholesterol Level in People With Excessive Nutritional Status | Experimental approach with a pretest and post-test control group design | The sample consisted of 2 groups, namely the control group and the intervention group, with 50 respondents in each group. The sample was taken using purposive sampling. The intervention group got red dragon fruit juice for seven days. Blood cholesterol levels are measured by laboratory tested using intravenous blood. | CONTROL | The difference mean posttest-pretest control group and intervention groups were 13.56 mmHg and -13.06 mmHg. | The results showed that red dragon fruit effectively reduced total cholesterol levels in people | This study's results can further increase the intake of healthy nutrients from fruit to keep cholesterol levels regular. | https://www.researchgate.net/publication/354403954_Red_Dragon_Fruit_Hylocereus_Polyrhizus_to_Reduce_Cholesterol_Level_in_People_With_Excessive_Nutritional_Status | Fadhilah, N., Supriyo, A., Iudha, M., Dede, C., Nekada, Y., Amelshah, T., Hendriah, F., & Prayana, C. (2021). Red Dragon Fruit (Hylocereus Polyrhizus) to Reduce Cholesterol Level in People With Excessive Nutritional Status. <i>Herbal Therapies to Prevent Diabetes Mellitus: New aspects. Obesities, Glycology, View project Red Dragon Fruit (Hylocereus Polyrhizus) to Reduce Cholesterol Level in People With Excessive Nutritional Status. In: Article in Journal of Forensic Medicine and Toxicology Vol. 34, Issue 4</i> . https://www.researchgate.net/publication/354403954 | No |
| 10 | Vitamin C | 2008 | Vitamin C supplementation lowers serum low-density lipoprotein cholesterol and triglycerides: a meta-analysis of 13 randomized controlled trials | Meta-analysis used a random-effects model | Thirteen randomized controlled trials published between 1970 and June 2007 were identified. From the 13 trials, 14 separate group populations with hypercholesterolemia and who were supplemented with at least 500 mg/d of vitamin C for between 3 and 24 weeks were entered into the meta-analysis. | CONTROL | The pooled estimate of effect for vitamin C supplementation on LDL and HDL cholesterol was -7.9 mg/dL and 1.1 mg/dL, respectively. The pooled estimate of effect for vitamin C supplementation on triglycerides was -20.1 mg/dL. | Supplementation with at least 500 mg/d of vitamin C, for a minimum of 4 weeks, can result in a significant decrease in serum LDL cholesterol and triglyceride concentrations | In this current meta-analysis, vitamin C supplementation provided a significant reduction in both LDL cholesterol and triglycerides, but failed to provide significant increase in HDL cholesterol | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2682928/ | McRae, M. P. (2008). Vitamin C supplementation lowers serum low-density lipoprotein cholesterol and triglycerides: a meta-analysis of 13 randomized controlled trials. <i>Journal of Chiropractic Medicine, 7(2)</i> , 48–58. https://doi.org/10.1016/j.jcm.2008.01.002 | Yes |
| 11 | Vitamin C & E | 2016 | Vitamin E (α-Tocopherol) and Vitamin C (Ascorbic Acid) Supplementation on Cholesterol and Triglyceride Blood Profile of Male Native Muscovy | Animal study | Eighty four muscovy duck were rationed to seven (7) treatments | CONTROL | vitamin E and vitamin C supplementation decreased blood cholesterol level. | Result showed that treatments significantly affected blood cholesterol level but did not significantly affect HDL, LDL and Triglyceride levels of muscovy blood. | In male muscovy, HDL was increased with Vitamin C and E supplementation. | http://medpub.litbang.ortalain.go.id/index.php/proceedings/article/view/15027/1376 | Widiyanti, E., Supriatni, Z., & Busmanan, B. (2016). Vitamin E (α-Tocopherol) and Vitamin C (Ascorbic Acid) Supplementation on Cholesterol and Triglyceride Blood Profile of Male Native Muscovy. <i>370–377</i> . https://doi.org/10.14343/proc-intern.litbang.2016.370-377 | No |
| 12 | Vitamin C | 2015 | Beetroot Juice Supplementation Increases High-Density Lipoprotein Cholesterol and Reduces Oxidative Stress in Physically Active Individuals | Controlled clinical trial | A group of randomly selected 30 infantry soldiers participated in the study, participants were supplemented with 400ml beetroot juice (consumed twice daily) for 15 days. Body composition of participants, at baseline and after 15 days of supplementation, was analyzed . | CONTROL | Beetroot juice supplementation beneficially influenced the lipid profile by significantly increasing the level of high-density lipoprotein cholesterol (HDL-C) from 42.5 ± 8.3 mg/dL to 50.2 ± 9.8 mg/dL and decreasing low-density lipoprotein cholesterol (LDL-C) from 129.7 ± 42.3 mg/dL to 119.5 ± 79.2 mg/dL | Beetroot juice consumption improves plasma lipid profile. A significant increase in plasma total antioxidant capacity and vitamin C levels was observed after beetroot juice intake for 15 days. | Beetroot juice consumption improves plasma lipid profile and antioxidant status. Encouraging further evaluation on a population with higher cardiovascular disease risk. | https://web.archive.org/web/20200307024530id/https://www.lifescienceglobal.com/media/31_fileseller/FILES/PANVSNS3A2_Singh.pdf | Singh, A., Kumar Verma, S., Singh, V. K., Nanjappa, C., Rana, N., Raju, P. S., & Singh, S. N. (2015). Beetroot Juice Supplementation Increases High-Density Lipoprotein Cholesterol and Reduces Oxidative Stress in Physically Active Individuals. <i>Journal of Pharmacy and Nutrition Sciences, 5</i> , 178–185. https://web.archive.org/web/20200307024530id/https://www.lifescienceglobal.com/media/31_fileseller/FILES/PANVSNS3A2_Singh.pdf | No |

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|----|---|------|---|---|---|----------------------|--|---|--|---|---|-----|
| 13 | Vitamin E and Omega 3 | 2019 | Effect of Omega-3 and vitamin E co-supplementation on serum lipids concentrations in overweight patients with metabolic disorders: A systematic review and meta-analysis of randomized controlled trials | A systematic review and meta-analysis of randomized controlled trials | A systematic search was performed to find the related articles, up to April, 2019. There was no language and time limitation. Meta-analyses were carried out using both the random and fixed effects model where appropriate, and I ² index was used to evaluate the heterogeneity. | not applicable | Search yielded 1236 publications. Five RCTs with 254 patients were eligible. Results of the meta-analysis indicated that omega-3 and vitamin E co-supplementation significantly reduced the serum concentrations of TG and LDL, whereas, it had no significant effect on the serum levels of TC and HDL in overweight patients with MS. | Present systematic review and meta-analysis revealed that omega-3 and vitamin E co-supplementation has beneficial effects on lipid profile of overweight patients with MS. It significantly reduced the serum levels of TG and LDL in such patients. | N/A | https://www.sciencedirect.com/science/article/abs/pii/S187140119303844 | Abaghi, O., Choghakbari, B. & Abbaszadeh, A. (2019). Effect of Omega-3 and vitamin E co-supplementation on serum lipids concentrations in overweight patients with metabolic disorders: A systematic review and meta-analysis of randomized, controlled trials. <i>Diabetes & Metabolic Syndrome: Clinical Research & Reviews</i> , 33(4), 2525–2531. https://doi.org/10.1016/j.dsx.2019.07.001 | Yes |
| 14 | Vitamin E | 2016 | Dietary vitamin E supplementation on cholesterol, vitamin E content, and fatty acid profile in chicken muscles | Animal study | Chickens (420 cocks) were randomly divided into two feeding groups (210 birds each). The control group was fed with standard diet containing 44 mg kg ⁻¹ of vitamin E, whereas the experimental group was supplemented with extra 200 mg kg ⁻¹ of vitamin E. | CONTROL | The dietary addition of vitamin E caused a significant increase in its content in the muscles, with higher value noted in the leg muscles. | Meat of chickens fed with the higher dose of vitamin E was also characterized by a lower cholesterol level. | The addition of vitamin E as well as type of the muscles had a significant effect on the fatty acid profile. | https://rdmsciencenpub.com/doi/pdf/10.1139/cjcp-2014-0103 | https://rdmsciencenpub.com/doi/pdf/10.1139/cjcp-2014-0103 | No |
| 15 | bergamot extract (120-mg flavonoids), phytosterols, vitamin C, and cholegric acid | 2019 | Three-arm, placebo-controlled, randomized clinical trial evaluating the metabolic effect of a combined nutraceutical containing a bergamot standardized flavonoid extract in dyslipidemic overweight subjects | Double-blind, placebo-controlled, parallel-group, dose-escalation, clinical trial | 90 overweight dyslipidemic subjects. Participants were randomly allocated to treatment with two pills of either active treatment or placebo, or a combination of both (a pill per treatment). | Placebo | After 8 weeks, all active-treated groups experienced a significant improvement in triglycerides (TG) versus placebo and in low-density lipoprotein cholesterol (LDL-C) versus baseline and placebo treatments. In the high-dose treated group, also total cholesterol (TC), significantly decreased. | The tested nutraceutical showed to improve lipid and glucose metabolism, adipokines pattern, and systemic inflammation in dyslipidemic overweight subjects. | All patients allocated to either low-dose or high-dose active treatment experienced a significant decrease in TG, LDL-C, and homocysteinol model assessment of insulin resistance. | https://pubmed.ncbi.nlm.nih.gov/31225673/ | Cicero, A. F. G., Fogacci, F., Boce, M., Giovannini, M., & Borghi, C. (2019). Three-arm, placebo-controlled, randomized clinical trial evaluating the metabolic effect of a combined nutraceutical containing a bergamot standardized flavonoid extract in dyslipidemic overweight subjects. <i>Phytotherapy Research: PTR</i> , 33(8), 2054–2101. https://doi.org/10.1002/ptr.6402 | Yes |
| 16 | Coenzyme Q10, Vitamin C, monacolin K, and L-arginine. | 2018 | LDL-cholesterol lowering effect of a new dietary supplement: An open label, controlled, randomized, cross-over clinical trial in patients with mild-to-moderate hypercholesterolemia | This was a single center, controlled, randomized, open-label, cross-over clinical study | 20 Caucasian outpatients aged 18–75 years with serum LDL-C between 130 and 180 mg/dL. Patients assumed two different dietary supplements (A and N) both containing monacolin K 10 mg for 8 weeks each, separated by a 4-week wash-out period. | control | LDL-C decreased by 23.2% during treatment with N and by 25.6% during treatment with A. Total-C decreased significantly within each treatment period. HDL-C increase was negligible during A whereas it was significant during N. TG diminished markedly during A and not significantly during N. The difference between treatments was not statistically significant for all variables. | Our results confirm the clinically meaningful LDL-C lowering properties of monacolin K. At variance with supplement already in the market (N), the novel association (A) of monacolin K with L-arginine, coenzyme Q10 and ascorbic acid also produces a significant reduction of triglycerides without significant effects on HDL. | Dietary supplement containing monacolin K, L-arginine, coenzyme Q10 and ascorbic acid, named Argicolin (A), compared to a commercially available product containing monacolin K and coenzyme Q10, Normolip (N), results confirm the clinically meaningful LDL-C lowering properties of monacolin K. | https://pubmed.ncbi.nlm.nih.gov/32793488/ | Mugno, S., Caccarioli, G., Polonaci, C., Jancini, R., Vitti, J., Ferraracci, P., Salveti, G., Alrodi, G., Manno, M., Saponati, G., & Santini, F. (2018). LDL-cholesterol lowering effect of a new dietary supplement: An open label, controlled, randomized, cross-over clinical trial in patients with mild-to-moderate hypercholesterolemia. <i>Lipids in Health and Disease</i> , 17(1). https://doi.org/10.1186/s12944-018-0775-8 | Yes |
| 17 | FOUIC ACID | 2016 | Folic Acid Therapy Reduces the First Stroke Risk Associated With Hypercholesterolemia Among Hypertensive Patients | Double-blind, randomized controlled trial. | A total of 20 702 hypertensive adults without a history of major cardiovascular disease were randomly assigned to a double-blind daily treatment of an enalapril 10-mg and a folic acid 0.8-mg tablet or an enalapril 10-mg tablet alone. The primary outcome was first stroke. | control | Folic acid supplementation significantly reduced the risk of first stroke among participants with high total cholesterol (4.0% in the enalapril-only group versus 2.7% in the enalapril-folic acid group; hazard ratio, 0.69; 95% confidence interval, 0.56–0.84; P<0.001; number needed to treat, 78; 95% confidence interval, 52–158), independent of baseline folate levels and other important covariates. By contrast, among participants with low total cholesterol, the risk of stroke was 2.6% in the enalapril-only group versus 2.5% in the enalapril-folic acid group (hazard ratio, 1.00; 95% confidence interval, 0.75–1.30; P=0.982). The effect was greater among participants with elevated total cholesterol (P for interaction=0.024). | Elevated total cholesterol levels may modify the benefits of folic acid therapy on first stroke. Folic acid supplementation reduced the risk of first stroke associated with elevated total cholesterol by 31% among hypertensive adults without a history of major cardiovascular diseases. | N/A | https://pubmed.ncbi.nlm.nih.gov/2729579/ | Qin, X., Li, J., Spence, D., Zhang, Y., Li, Y., Wang, X., Wang, B., Sun, N., Chen, F., Guo, J., Yin, D., Sun, L., Tang, G., He, M., Fu, J., Cai, Y., Shi, X., Ye, P., Chen, H., ... Huo, Y. (2016). Folic Acid Therapy Reduces the First Stroke Risk Associated With Hypercholesterolemia Among Hypertensive Patients. <i>Stroke</i> , 47(11), 2805–2812. https://doi.org/10.1161/STROKEAHA.116.014578 | Yes |
| 18 | FOUIC ACID | 2016 | Folic Acid Therapy Reduces the First Stroke Risk Associated With Hypercholesterolemia Among Hypertensive Patients | A double-blind, randomized controlled trial. | A total of 20 702 hypertensive adults without a history of major cardiovascular disease were randomly assigned to a double-blind daily treatment of an enalapril 10-mg and a folic acid 0.8-mg tablet or an enalapril 10-mg tablet alone. Participants were scheduled for follow-up every 3 months. | control | The primary outcome was first stroke. The secondary outcomes included first ischemic stroke (fatal or nonfatal), first hemorrhagic stroke (fatal or nonfatal), and a composite of cardiovascular events consisting of cardiovascular death, myocardial infarction, and stroke. | The median treatment duration was 4.3 years. For participants not receiving folic acid treatment (enalapril-only group), high total cholesterol (>200 mg/dL) was an independent predictor of first stroke when compared with low total cholesterol. Folic acid supplementation significantly reduced the risk of first stroke among participants with high total cholesterol. | Folic acid supplementation reduced the risk of first stroke associated with elevated total cholesterol by 31% among hypertensive adults without a history of major cardiovascular diseases. | https://www.abajournals.org/doi/epub/10.1161/STROKEAHA.116.014578 | Qin, X., Li, J., Spence, D., Zhang, Y., Li, Y., Wang, X., Wang, B., Sun, N., Chen, F., Guo, J., Yin, D., Sun, L., Tang, G., He, M., Fu, J., Cai, Y., Shi, X., Ye, P., Chen, H., ... Huo, Y. (2016). Folic acid therapy reduces the first stroke risk associated with hypercholesterolemia among hypertensive patients. <i>Stroke</i> , 47(11), 2805–2812. https://doi.org/10.1161/STROKEAHA.116.014578 | Yes |
| 19 | lysine, vitamin B(6), and carnitine | | Effect of lysine, vitamin B(6), and carnitine supplementation on the lipid profile of male patients with hypertriglyceridemia: a 12-week, open-label, randomized, placebo-controlled trial | Randomized, placebo-controlled clinical trial | This 12-week, randomized, placebo-controlled clinical trial. A total of 85 hypertriglyceridemic (TG >150 mg/dL) male patients were randomized to 1 of 5 groups and given supplements of lysine (1 g/d), vitamin B(6) (50 mg/d), lysine (1 g/d) + vitamin B(6) (50 mg/d), carnitine (1 g/d), or placebo for 12 weeks. The lipid profile (TG, total cholesterol, LDL-C, and HDL-C) and fasting plasma glucose levels were assessed at baseline and at 6 and 12 weeks. | placebo | Vitamin B(6) supplementation was associated with a significant reduction in total cholesterol and HDL-C of ~10%. In addition, plasma TG was reduced by 36.6 mg/dL at 6 weeks, whereas levels in the placebo group increased by 18 mg/dL. | Vitamin B(6) supplementation in these male patients with hypertriglyceridemia reduced plasma total cholesterol and HDL-C concentrations. | No major changes in the lipid profile were observed in the lysine and carnitine groups or when lysine was added to vitamin B(6). | https://pubmed.ncbi.nlm.nih.gov/2318869/ | Hain, S., Anson, D. R. A., Sarrafzadeh, H. K., Nassreddin, L., Tahn, G., Azar, S., & Obied, O. A. (2012). Effect of lysine, vitamin B(6), and carnitine supplementation on the lipid profile of male patients with hypertriglyceridemia: a 12-week open-label, randomized, placebo-controlled trial. <i>Clinical Therapeutics</i> , 34(8), 1674–1682. https://doi.org/10.1016/j.clinther.2012.06.019 | No |
| 20 | omega-3 fatty acids | 2015 | A randomized-controlled clinical trial investigating the effect of Omega-3 Fatty acids and vitamin E co-supplementation on markers of insulin metabolism and lipid profiles in gestational diabetes | Randomized, double-blind, placebo-controlled clinical trial | 50 patients with GDM. Patients were randomly allocated to take either 1000-mg omega-3 Fatty acids from flaxseed oil plus 400 IU vitamin E supplements (n = 30) or placebo (n = 30) for 6 weeks. Fasting blood samples were obtained from at the beginning of the study and after 6-week intervention to quantify related variables. | placebo | After 6 weeks of intervention, changes in serum triglycerides (+10.8 ± 4.1 vs +34.2 ± 35.5 mg/dL, P = .02), VLDL-cholesterol (+2.1 ± 8.3 vs +6.8 ± 7.1 mg/dL, P = .02), low-density lipoprotein (LDL)-cholesterol (+11.6 ± 18.8 vs +1.7 ± 5.9 mg/dL, P = .03) and HDL-cholesterol concentrations (-1.9 ± 8.7 vs -2.4 ± 7.7 mg/dL, P = .04) were significantly different between the supplemented women and placebo group. | Overall, we demonstrated that omega-3 fatty acids and vitamin E co-supplementation in GDM women had beneficial effects on glucose homeostasis parameters, serum triglycerides, VLDL-cholesterol, and HDL-cholesterol concentrations, but it did not influence total-cholesterol and LDL-cholesterol levels. | However, after controlling for baseline total cholesterol levels, maternal age, and BMI at baseline, the changes in serum LDL-cholesterol concentrations were not significantly different between the 2 groups. We did not find any significant effect of joint omega-3 fatty acids and vitamin E supplementation on total cholesterol concentrations. | https://pubmed.ncbi.nlm.nih.gov/27055070/ | Hajizadeh, M., Jamilian, M., Moshkoo, M., Sarumi, M., & Azemi, Z. (2016). A randomized-controlled clinical trial investigating the effect of omega-3 fatty acids and vitamin E co-supplementation on markers of insulin metabolism and lipid profiles in gestational diabetes. <i>Journal of Clinical Lipidology</i> , 10(2), 386–393. https://doi.org/10.1016/j.jacl.2015.12.017 | No |
| 21 | Magnesium and Vitamin E | 2018 | The effects of magnesium and vitamin E co-supplementation on parameters of glucose homeostasis and lipid profiles in patients with gestational diabetes | Randomized, double-blinded, placebo-controlled trial | 60 subjects diagnosed with gestational diabetes (GDM), aged 18-40 years. Subjects were randomly allocated into two groups to receive 250 mg/day magnesium oxide plus 400 IU/day vitamin E supplements or placebo (n = 30 each group) for 6 weeks. Participants' blood samples were taken to determine their metabolic profiles. | placebo | magnesium plus vitamin E supplementation resulted in a significant reduction in serum triglycerides, VLDL, LDL, and total/HDL-cholesterol ratio compared with placebo. Magnesium and vitamin E co-supplementation did not affect HDL-cholesterol levels. | Overall, magnesium and vitamin E co-supplementation for 6 weeks in women with GDM significantly improved lipid profiles, except for HDL-cholesterol levels. | Magnesium and vitamin E co-supplementation did not affect HDL-cholesterol levels. | https://pubmed.ncbi.nlm.nih.gov/30025522/ | Maktabi, M., Jamilian, M., Amirani, F., Chamani, M., & Azemi, Z. (2018). The effects of magnesium and vitamin E co-supplementation on parameters of glucose homeostasis and lipid profile in patients with gestational diabetes. <i>Lipids in Health and Disease</i> , 17(1). https://doi.org/10.1186/s12944-018-0814-5 | Yes |
| 22 | vitamin B3 or niacin | 2013 | Effect of Nicotinic Acid (Vitamin B3 or Niacin) on the lipid profile of diabetic and non-diabetic rats | Animal study | A total of 50 rats were included in the study. Nicotinic acid was administered to a hypercholesterolemic group and a hypercholesterolemic + diabetic group of Albino rats for 42 days and response to therapy was recorded on day 21 and day 42 of the experiment. | control | Lipid profile of the hypercholesterolemic group as well as hypercholesterolemic + diabetic group as compared with the control groups showed highly significant improvement on the day 21 and day 42 of the experiment. The values of serum total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL) cholesterol and total lipids (TL) showed highly significant decrease whereas serum high density lipoprotein (HDL) cholesterol showed highly significant increase. | Nicotinic acid is the most effective agent available in increasing HDL cholesterol and lowering serum TC, triglycerides (TG), LDL cholesterol and TL in hypercholesterolemic Diabetic and hypercholesterolemic non-diabetic Albino rats. | Nicotinic acid decreased the levels of serum total cholesterol, serum triglycerides, serum low density lipoprotein cholesterol and serum total lipids and it increased the high density lipoprotein cholesterol in both the diabetic as well as non-diabetic rats. | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3858911/ | Shah, T. Z., Ali, A. B., Infi, S. A., & Gazi, M. H. (2013). Effect of nicotinic acid (vitamin B3 or niacin) on the lipid profile of diabetic and non-diabetic rats. <i>Pakistan Journal of Medical Sciences</i> , 29(5). https://doi.org/10.12658/pjms.295.1493 | No |
| 23 | vitamin B3 or niacin | 2015 | Niacin as antilipidemic drug | Review | review | No control indicated | Niacin was shown to have beneficial effects on cardiovascular end-points; but in recent years, two major studies performed in patients whose LDL cholesterol levels had been optimized by a statin therapy did not demonstrate an additional significant effect on these end-points in the groups where niacin was administered. Both studies have several drawbacks that suggest that they are not representative for other patients. Thus, niacin still plays a role either as an additive to a statin or as a substitute for a statin in statin intolerant patients. | patients with elevated triglyceride and low HDL cholesterol levels and patients with elevated lipoprotein(a) concentrations will possibly benefit from niacin, although currently the study evidence for these indications is rather poor. | Niacin may be useful for complementary patients, however possible side effects (flushing, liver damage) and contraindications should be taken into consideration. | https://rdmsciencenpub.com/doi/abs/10.1139/cjcp-2014-0478 | Jullus, U. (2015). Niacin as antilipidemic drug. <i>Canadian Journal of Physiology and Pharmacology</i> , 93(11), 1043–1054. https://doi.org/10.1139/cjcp-2014-0478 | No |

Table S4: Summary of articles on minerals.

| | | | | | | | | | | | Mineral | |
|----|---|------|---|---|---|---------------------|--|--|--|---|--|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Cinnamon, chromium and magnesium formulated honey | 2016 | The effect of a cinnamon-, chromium- and magnesium-formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over randomised controlled trial | An open-label cross-over randomised controlled trial | Twelve individuals with type 2 diabetes received 53.5 g of a formulated honey and a control (non-formulated) kanuka honey in a random order for 40 days, using cross-over design. Fasting glucose, insulin, HbA1c, lipids and anthropometric measures were measured at baseline and end of treatment. A meal tolerance test was performed at baseline to assess acute metabolic response. | Control | There was a statistically significant reduction in total cholesterol by -0.29 mmol/L, LDL cholesterol by -0.29 mmol/L and weight by -2.2 kg. There was a trend towards increased HDL and reduced systolic blood pressure in the intervention treatment. | The addition of cinnamon, chromium and magnesium supplementation to kanuka honey was not associated with a significant improvement in glucose metabolism or glycaemic control in individuals with type 2 diabetes. | Use of the formulated honey was associated with a reduction in weight and improvements in lipid parameters, and should be investigated further. | https://pubmed.ncbi.nlm.nih.gov/25986159/ | A Whitefield, P., Parry-Strong, A., Walsh, E., Weatherall, M., & Krebs, J. D. (2016). The effect of a cinnamon-, chromium- and magnesium-formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over randomised controlled trial. <i>European Journal of Nutrition</i> , 55(3), 1123–1131. https://doi.org/10.1007/s00394-015-0926-X | No |
| 2 | Chromium | 2021 | Effects of chromium supplementation on lipid profile in patients with type 2 diabetes: A systematic review and dose-response meta-analysis of randomized controlled trials | Dose-response meta-analysis of randomized controlled trials | A systematic search was performed in Scopus, Embase, Web of Science, the Cochrane library and PubMed databases to find randomized controlled trials (RCTs) related to the effect of chromium supplementation on lipid profile in patients with T2DM, up to June 2020. Meta-analyses were performed using the random-effects model, and I2 index was used to evaluate heterogeneity. | Not Applicable - NA | The primary search yielded 725 publications. 24 RCTs (with 28 effect sizes) were eligible. Our meta-analysis indicated that chromium supplementation resulted in a significant decrease in serum levels of triglyceride (TG) and total cholesterol (TC). Chromium significantly increases high-density lipoprotein (HDL) level. However, chromium supplementation did not have significant effects on low-density lipoprotein (LDL) level. | Chromium supplementation may significantly improve lipid profile in patients with T2DM by decreasing TG and TC and increasing HDL. | However, based on our analysis, chromium failed to affect LDL. It should be noted that the lipid-lowering properties of chromium supplementation were small and may not reach clinical importance. | https://www.sciencedirect.com/science/article/abs/pii/S093946672021000316 | Asghari, O., Naeini, F., Ashary-Larky, D., Moradi, S., Zakari, N., Esfampour, E., Khatibadi, M. P., & Naeini, A. A. (2021). Effects of chromium supplementation on lipid profile in patients with type 2 diabetes: A systematic review and dose-response meta-analysis of randomized controlled trials. <i>Journal of Trace Elements in Medicine and Biology</i> , 66, 126741. https://doi.org/https://doi.org/10.1016/j.jtemb.2021.126741 | Yes |
| 3 | Magnesium and Vitamin E | 2018 | The effects of magnesium and vitamin E co-supplementation on parameters of glucose homeostasis and lipid profiles in patients with gestational diabetes | Randomized, double-blinded, placebo-controlled trial | 60 subjects diagnosed with gestational diabetes (GDM), aged 18-40 years. Subjects were randomly allocated into two groups to receive 250 mg/day magnesium oxide plus 400 IU/day vitamin E supplements or placebo (n = 30 each group) for 6 weeks. Participants' blood samples were taken to determine their metabolic profiles. | Placebo | magnesium plus vitamin E supplementation resulted in a significant reduction in serum triglycerides, VLDL, LDL and total-/HDL-cholesterol ratio compared with placebo. Magnesium and vitamin E co-supplementation did not affect HDL-cholesterol levels. | Overall, magnesium and vitamin E co-supplementation for 6 weeks in women with GDM significantly improved lipid profiles, except for HDL-cholesterol levels. | Magnesium and vitamin E co-supplementation did not affect HDL-cholesterol levels. | https://pubmed.ncbi.nlm.nih.gov/30025527/ | Maktabi, M., Jamilian, M., Amirani, E., Chamani, M., & Asemi, Z. (2018). The effects of magnesium and vitamin E co-supplementation on parameters of glucose homeostasis and lipid profiles in patients with gestational diabetes. <i>Lipids in Health and Disease</i> , 17(1). https://doi.org/10.1186/s12944-018-0814-5 | Yes |
| 4 | Magnesium | 2020 | Oral Magnesium Supplementation Improved Lipid Profile but Increased Insulin Resistance in Patients with Diabetic Nephropathy: a Double-Blind Randomized Controlled Clinical Trial | Double-Blind Randomized Controlled Clinical Trial | A total of 80 hypomagnesemic patients diagnosed with type 2 diabetes and early-stage nephropathy were recruited. Subjects received either daily magnesium oxide or placebo for 12 weeks. | Placebo | No significant changes were observed in serum total cholesterol, triglycerides, HDL, LDL, and total cholesterol/HDL cholesterol ratio. | No significant changes were observed in serum total cholesterol, triglycerides, HDL, LDL, and total cholesterol/HDL cholesterol ratio. | Oral magnesium supplementation slightly improved microalbuminuria but resulted in increased insulin resistance in patients with diabetic nephropathy. | https://link.springer.com/article/10.1007/s12011-019-01687-6 | Sadeghian, M., Azadbakht, L., Khalili, N., Mortazavi, M., & Esmaillizadeh, A. (2020). Oral Magnesium Supplementation Improved Lipid Profile but Increased Insulin Resistance in Patients with Diabetic Nephropathy: a Double-Blind, Randomized Controlled Clinical Trial. <i>Biological Trace Element Research</i> , 193(1), 23–35. https://doi.org/10.1007/s12011-019-01687-6 | No |
| 5 | Magnesium | 2016 | Serum magnesium status among obese children and adolescents | A cross-sectional study | 50 obese subjects of ages 2–16 years and 50 healthy normal weight subjects of matched age and sex as controls were consecutively enrolled. Fasting total serum magnesium, total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides were measured. | Not Applicable - NA | Obese cases compared to normal weight controls showed significantly lower serum magnesium and HDL-cholesterol levels and significantly higher total cholesterol, LDL-cholesterol, triglycerides, systolic and diastolic blood pressures. | Serum magnesium showed a significant, strong inverse correlation with the degree of obesity ($r = -0.8, p < 0.001$); significant, moderate inverse correlation with total cholesterol and LDL-cholesterol; and non-significant correlation with triglycerides and HDL-cholesterol. | Serum magnesium levels are inversely correlated with the degree of obesity, and is related to an unfavorable serum lipid profile in obese children and adolescents, who also show a trend to higher systemic blood pressure. | https://www.sciencedirect.com/science/article/pii/S1110663815000632 | Zaakouk, A. M., Hassan, M. A., & Tolba, O. A. (2016). Serum magnesium status among obese children and adolescents. <i>Egyptian Pediatric Association Gazette</i> , 64(1), 32–37. https://doi.org/https://doi.org/10.1016/j.epag.2015.11.002 | No |
| 6 | Zinc | 2018 | Zinc supplementation in prediabetes: A randomized double-blind placebo-controlled clinical trial | A randomized double-blind placebo-controlled clinical trial | A randomized double-blind placebo-controlled Phase 2 clinical trial was conducted over a 12-month period in 200 subjects, randomly assigned to the treatment or control group. The treatment group received zinc (20 mg daily). Subjects were evaluated at baseline and at 1, 3, 6, and 12 months. The primary outcome was the change in glycemic control from baseline. | Placebo | During the 12-month follow-up, a significantly higher percentage of participants developed type 2 diabetes in the control compared with zinc-treated group. total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) were significantly lower in the treated group | supplementation reduced disease progression to diabetes and had beneficial effects on TC and LDL-C. | Zinc supplementation reduced blood glucose and insulin resistance while improving β -cell function. | https://pubmed.ncbi.nlm.nih.gov/29072815/ | Ranasinghe, P., Wathurapatha, W. S., Galappatthy, P., Katulanda, P., Jayawardena, R., & Constantinou, G. R. (2018). Zinc supplementation in prediabetes: A randomized double-blind, placebo-controlled clinical trial. <i>Journal of Diabetes</i> , 10(5), 386–397. https://doi.org/10.1111/1753-0407.12621 | Yes |

Table S5: Summary of articles on amino acids.

| Amino acid | | | | | | | | | | | | |
|------------|---|------|--|--|---|---------------------|--|--|---|---|--|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Coenzyme Q10, Vitamin C, monacolin K, and L-arginine. | 2018 | LDL-cholesterol lowering effect of a new dietary supplement: An open label, controlled, randomized, cross-over clinical trial in patients with mild-to-moderate hypercholesterolemia | Single center, controlled, randomized, open-label, cross-over clinical study | 20 Caucasian outpatients aged 18–75 years with serum LDL-C between 130 and 180 mg/dL. Patients assumed two different dietary supplements (A and B) both containing monacolin K 10 mg for 8 weeks each, separated by a 4-week wash-out period. | Control | LDL-C decreased by 23.3% during treatment with N and by 25.6% during treatment with A. Total-C decreased significantly within each treatment period. HDL-C increase was negligible during A whereas it was significant during N. TG diminished markedly during A and not significantly during N. The difference between treatments was not statistically significant for all variables. | Our results confirm the clinically meaningful LDL-C lowering properties of monacolin K. At variance with supplement already in the market (N), the novel association (A) of monacolin K with L-arginine, coenzyme Q10 and ascorbic acid also produces a significant reduction of triglycerides without significant effects on HDL. | Results confirm the clinically meaningful LDL-C lowering properties of monacolin K | https://pubmed.ncbi.nlm.nih.gov/29793488/ | Magno, S., Ceccarini, G., Pelosini, C., Jaccheri, R., Vitti, J., Fierabracci, P., Salvetti, G., Airolodi, G., Minale, M., Saponati, G., & Santini, F. (2018). LDL-cholesterol lowering effect of a new dietary supplement: An open label, controlled, randomized, cross-over clinical trial in patients with mild-to-moderate hypercholesterolemia. <i>Lipids in Health and Disease</i> , 17(1). https://doi.org/10.1186/s12944-018-0775-8 | Yes |
| 2 | L-Carnitine | 2015 | L-Carnitine supplementation improved clinical status without changing oxidative stress and lipid profile in women with knee osteoarthritis | Randomized double-blind, placebo-controlled trial | 72 overweight or obese women with mild to moderate knee OA were randomly allocated into 2 groups to receive 750 mg/d L-carnitine or placebo for 8 weeks. Dietary intake was evaluated using 24-hour recall for 3 days. Lipid profile were assessed before and after supplementation. | Placebo | L-Carnitine supplementation resulted in significant reductions in serum total cholesterol, and low-density lipoprotein cholesterol levels compared with baseline, whereas these parameters increased in the placebo group. Serum triglyceride, high-density lipoprotein cholesterol, and TAC levels did not change significantly in both groups | L-carnitine improved clinical status without changing oxidative stress and lipid profile significantly in women with knee OA. | There were significant intragroup and intergroup differences in pain intensity and patient global assessment of disease status after supplementation. | https://www.sciencedirect.com/science/article/abs/pii/S0271531715001372 | Malek Mahdavi, A., Mahdavi, R., Kolahi, S., Zemestani, M., & Vatankeh, A.-M. (2015). L-Carnitine supplementation improved clinical status without changing oxidative stress and lipid profile in women with knee osteoarthritis. <i>Nutrition Research</i> , 35(8), 707–715. https://doi.org/https://doi.org/10.1016/j.nutres.2015.06.003 | Yes |
| 3 | Lysine, vitamin B(6), and carnitine | | Effect of lysine, vitamin B(6), and carnitine supplementation on the lipid profile of male patients with hypertriglyceridemia: a 12-week, open-label, randomized, placebo-controlled trial | Randomized, placebo-controlled clinical trial | This 12-week, randomized, placebo-controlled clinical trial. A total of 85 hypertriglyceridemic (TG> 150 mg/dL) male patients were randomized to 1 of 5 groups and given supplements of lysine (1 g/d), vitamin B(6) (50 mg/d), lysine (1 g/d) + vitamin B(6) (50 mg/d), carnitine (1 g/d), or placebo for 12 weeks. The lipid profile (TG, total cholesterol, LDL-C, and HDL-C) and fasting plasma glucose levels were assessed at baseline and at 6 and 12 weeks. | Placebo | Vitamin B(6) supplementation was associated with a significant reduction in total cholesterol and HDL-C of ~10%. In addition, plasma TG was reduced by 36.6 mg/dL at 6 weeks, whereas levels in the placebo group increased by 18 mg/dL | Vitamin B(6) supplementation in these male patients with hypertriglyceridemia reduced plasma total cholesterol and HDL-C concentrations. | No major changes in the lipid profile were observed in the lysine and carnitine groups or when lysine was added to vitamin B(6). | https://pubmed.ncbi.nlm.nih.gov/23818869/ | Hlais, S., Reslan, D. R. A., Sarieddine, H. K., Nasreddine, L., Taan, G., Azar, S., & Qbeid, O. A. (2012). Effect of lysine, vitamin B(6), and carnitine supplementation on the lipid profile of male patients with hypertriglyceridemia: a 12-week, open-label, randomized, placebo-controlled trial. <i>Clinical Therapeutics</i> , 34(8), 1674–1682. https://doi.org/10.1016/j.clinthera.2012.06.019 | No |
| 4 | L-lysine | 2019 | Dietary supplementation with L-lysine affects body weight and blood hematological and biochemical parameters in rats | Animal study | Male Sprague–Dawley rats at 10 weeks of age were assigned to ten diet groups (eight rats/group) and fed diets containing either 7% or 20% casein and supplemented with either 0% (Control), 1.5%, 3%, 6% Lys, or 6% Lys + 3% arginine for 1 week. | Control | Rats fed 7% casein with ≥ 1.5% Lys supplementation had lower serum albumin and leptin and higher LDL cholesterol (LDL-C), ratios of total cholesterol (TC):HDL cholesterol (HDL-C) and LDL-C:HDL-C than those fed 7% casein Control diet. Addition of 6% Lys in 7% casein caused significant BW loss and altered additional parameters. No major changes in the lipid profile were observed in the lysine and carnitine groups or when lysine was added to vitamin B(6). | these results show that Lys supplementation affects BW, food intake and a number of hematological and biochemical parameters. These effects of Lys supplementation were confined primarily in diets with lower levels of dietary protein | In the context of a low protein diet (7% casein), levels of Lys supplementation ≥ 1.5% may exert adverse health effects in rats. | https://link.springer.com/article/10.1007/s11033-018-4492-1#citeas | Xiao, C.-W., Wood, C., & Bertinato, J. (2019). Dietary supplementation with L-lysine affects body weight and blood, hematological and biochemical parameters in rats. <i>Molecular Biology Reports</i> , 46(1), 433–442. https://doi.org/10.1007/s11033-018-4492-1 | No |
| 5 | L-arginine | 2019 | The effect of L-arginine supplementation on lipid profile: a systematic review and meta-analysis of randomised controlled trials | A systematic review and meta-analysis of randomised controlled trials | twelve studies were included in the systematic review. | Not Applicable - NA | The meta-analysis revealed that L-arginine supplementation did not significantly change the concentrations of total cholesterol, or HDL. A significant reduction was observed only in serum TAG levels | This meta-analysis concludes that L-arginine supplementation can significantly reduce blood TAG levels; however, there is insufficient evidence to support its hypocholesterolaemic effects. | There is a need for more well-controlled trials targeting exclusively patients with dyslipidaemia. | https://www.cambridge.org/core/journals/british-journal-of-nutrition/article/Effect-of-arginine-supplementation-on-lipid-profile-a-systematic-review-and-meta-analysis-of-randomised-controlled-trials/P9FE43886AD15C869CA4364F45978CC2 | Hadi, A., Arab, A., Moradi, S., Pantovic, A., Clark, C. C. T., & Ghaedi, E. (2019). The effect of L-arginine supplementation on lipid profile: a systematic review and meta-analysis of randomised controlled trials. <i>British Journal of Nutrition</i> , 122(9), 1021–1032. https://doi.org/10.1017/S0007114519001855 | Yes |

Table S6: Summary of articles on probiotics.

| Probiotic | | | | | | | | | | | | |
|------------------|---|------|--|--|---|---------------------|--|--|---|---|---|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Probiotic | 2019 | The effect of probiotic supplementation on glycemic control and lipid profile in patients with type 2 diabetes: A randomized placebo controlled trial | Randomized double blind controlled trial | This randomized double blind controlled trial was performed among 60 patients; individuals were randomly assigned into 2 groups of 30 participants in order to take either probiotic supplements or placebo for 6 weeks. The probiotic supplement consisted of 7 viable strains Lactobacillus, Bifidobacterium and Streptococcus. Nutrient intakes were estimated using a 3-day and 24 hour dietary recall at the beginning and end of study. Fasting blood samples were taken before and after intervention to measure the levels of FPG, plasma insulin and lipid profiles. | Placebo | Within group comparisons showed significant decrease and increase in the levels of FPG and HDL-C in probiotic groups, respectively. No significant alterations were observed for within and between group comparisons in the levels of insulin, triglycerides, total cholesterol, insulin resistance and anthropometric measurements, including weight, waist circumference and body mass index. | This study showed a significant decrease in FPG level by multi-strain probiotic supplements in within group comparison | further studies are needed to confirm results | https://pubmed.ncbi.nlm.nih.gov/30641692/ | Ramposh, E, Javadi, A, Elshah, H, S, Mirmiran, P, Javadi, M, & Yousefnejad, A. (2019). The effect of probiotic supplementation on glycemic control and lipid profile in patients with type 2 diabetes: A randomized placebo controlled trial. <i>Diabetes & Metabolic Syndrome</i> , 13(1), 175-182. https://doi.org/10.1016/j.dsx.2018.08.008 | Yes |
| 2 | Probiotic | 2016 | The use of probiotic L. fermentum ME-3 containing Reg/Active Cholesterol supplement for 4 weeks has a positive influence on blood lipoprotein profiles and inflammatory cytokines: an open-label preliminary study | An open-label preliminary study | Forty-five clinically asymptomatic participants consumed an RAC (Reg/Active Cholesterol (RAC)) containing an antioxidant and antiatherogenic probiotic Lactobacillus fermentum ME-3 (LFME-3) for 4 weeks. | Control | The reduction of total cholesterol (from 6.5 ± 1.0 to 5.7 ± 0.9 mmol/L) and HDL cholesterol level rose from 1.60 ± 0.31 to 1.67 ± 0.34 mmol/L. | The consumption of RAC capsules in asymptomatic volunteers with borderline values of risk factors for cardio-vascular disease (BMI, HbA1c, LDL cholesterol) for 4 weeks had a positive effect on blood lipoprotein, oxidative stress and inflammatory profile. | The level of total cholesterol and LDL decreased significantly in all participants and HDL cholesterol showed a tendency of improvement after 4 weeks of consumption of LFME3 containing food supplement RAC. | https://www.researchgate.net/publication/309727288_The_use_of_probiotic_L_fermentum_ME_3_containing_RegActive_Cholesterol_supplement_for_4_weeks_has_a_positive_influence_on_blood_lipoprotein_profiles_and_inflammatory_cytokines_an_open-label_preliminary_study/links/51c3ab46299b1f04c905e78/download | https://www.researchgate.net/publication/309727288_The_use_of_probiotic_L_fermentum_ME_3_containing_RegActive_Cholesterol_supplement_for_4_weeks_has_a_positive_influence_on_blood_lipoprotein_profiles_and_inflammatory_cytokines_an_open-label_preliminary_study/links/51c3ab46299b1f04c905e78/download | No |
| 3 | probiotic Bifidobacterium longum BBS36 and red yeast rice extract | 2019 | Nutraceutical approach for the management of cardiovascular risk - a combination containing the probiotic Bifidobacterium longum BBS36 and red yeast rice extract: results from a randomized, double-blind, placebo-controlled study | Randomized, double-blind, placebo-controlled study | A 12-week randomized, parallel, double-blind, placebo-controlled study. Thirty-three subjects (18-70 years) in primary CV prevention and low CV risk (SCORE-D 1% to 2.4% in 9 subjects; LDL-C: 130-200 mg/dL) were randomly allocated to either nutraceutical (N = 16) or placebo (N = 17). | Placebo | Twelve-week treatment with the nutraceutical combination, compared to placebo, significantly reduced TC (-16.7%), LDL-C (-25.7%), non-HDL-C (-24%) (all p < 0.0001), apoB (-17%, p = 0.003). | A 12-week treatment with a nutraceutical combination containing the probiotic Bifidobacterium longum BBS36 and RYR extract significantly improved the atherogenic lipid profile and was well tolerated by low CV risk subjects. | No adverse effects and a 97% compliance were observed. | https://pubmed.ncbi.nlm.nih.gov/30795775/ | Bussica, M, Pavanello, C, Gandini, S, Maschi, C, Botta, M., Dall'Orto, D., del Puogo, M., Bertolotti, M., Bossio, R., Mombelli, S., Sirtori, C. R., Calabrese, L., & Jofino, P. (2019). Nutraceutical approach for the management of cardiovascular risk - a combination containing the probiotic Bifidobacterium longum BBS36 and red yeast rice extract: results from a randomized, double-blind, placebo-controlled study. <i>Nutrition Journal</i> , 18(1). https://doi.org/10.1186/s12937-019-0438-2 | Yes |
| 4 | lactobacillus fermentum | 2015 | Regulation of plasma lipid profile by lactobacillus fermentum (probiotic strain ME-3 DSM14241) in a randomized controlled trial of clinically healthy adults | Randomised, double-blind, placebo-controlled, parallel design, two-armed study | One hundred sixty four participants meeting the inclusion criteria were included. Participants were randomised to receive 200 ml/day kefir, either with probiotic(PG) or without probiotic (CG). The probiotic contained fermentum ME-3. At 4 weeks and at 8 weeks, evaluation of anthropologic, blood biochemical indices, and the faecal temporal persistence of the probiotic strain was done by real-time PCR. | Placebo | After 4 weeks, the lipid profiles were mostly similar between groups: only the values of oxidised LDL (ox-LDL) and TG were significantly reduced. After 8 weeks, the PG group exhibited reductions in LDL-C, ox-LDL, TG. Next, the ratio of LDL-C to HDL-C was decreased only in the PG while in the CG it was significantly increased. | Eight weeks of consuming probiotic L. fermentum ME-3, reduced serum LDL-C, ox-LDL and TG values in clinically healthy volunteers with borderline-high lipid profile indices. | L. fermentum ME-3 has potential to lower the risk of CVD that is tightly associated with maintenance of plasma lipid profile. | https://link.springer.com/content/pdf/10.1186/140795-015-0020-z.pdf | Mikeassar, M., Sepp, F., Stenpetova, J., Hilt, P., Zilmer, K., Kullisaar, T., & Zilmer, M. (2015). Regulation of plasma lipid profile by lactobacillus fermentum (probiotic strain ME-3 DSM14241) in a randomized controlled trial of clinically healthy adults. <i>BMC Nutrition</i> , 1(1). https://doi.org/10.1186/140795-015-0020-z | Yes |
| 5 | Probiotic | 2018 | The effects of probiotics on total cholesterol A meta-analysis of randomized controlled trials | A meta-analysis of randomized controlled trials | Thirty-two RCTs including 1971 patients met the inclusion criteria. The curative effects of probiotics on the reduction of TC were assessed using mean difference (MD), as well as their 95% confidence interval (CI). RevMan software (version 5.3) was used to carry out this meta-analysis. | Not Applicable - NA | Results of this analysis showed that compared with the control group serum TC was significantly reduced in probiotics group. In addition, specific strains also significantly reduced serum TC, L acidophilus and B lactis. | Available evidence indicates that probiotics supplements can significantly reduce serum TC. Furthermore, higher baseline TC, longer intervention time, and probiotics in capsules form might contribute to a better curative effect. | Subgroup analysis indicated that the difference of baseline TC, probiotics forms and intervention duration might have a significant impact on the results. However, strains and doses of probiotics had no significant influence on curative effects. | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5805418/ | Wang, L., Guo, M. J., Gao, D., Yang, J. F., Yang, L., Pang, X. L., & Jiang, X. J. (2018). The effects of probiotics on total cholesterol: A meta-analysis of randomized controlled trials. <i>Medicine</i> , 97(5). https://doi.org/10.1097/MD.00000000000009679 | Yes |
| 6 | Probiotic and Prebiotic | 2010 | Cholesterol-Lowering Effects of Probiotics and Prebiotics: A Review of In Vivo and In Vitro Findings | A Review | A Review | Not Applicable - NA | In conclusion, the mechanisms proposed for mediating hypocholesterolemic effect by probiotics and/or prebiotics are numerous. Although those hypotheses were proved via in vitro studies, the mechanisms are not firmly established and demonstrated in in vivo studies. Therefore, more in vivo studies are needed to explore the underlying mechanism of cholesterol-lowering effects by probiotics and/or prebiotics in order to have a better understanding of the mechanisms and better formulations for human consumption. | Probiotic and/or prebiotics have been widely assessed for their effects on lipid profiles such as total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides. However, not all trials have yielded conclusive results. | | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2904929/ | Dai, L. G., & Liang, M. T. (2010). Cholesterol-Lowering Effects of Probiotics and Prebiotics: A Review of In Vivo and In Vitro Findings. <i>International Journal of Molecular Sciences</i> , 11(6), 2499. https://doi.org/10.3390/IJMS11062499 | No |

Table S7: Summary of articles on prebiotics.

| Prebiotic | | | | | | | | | | | | |
|-----------|-----------------------------------|------|--|--|--|-------------------|---|--|--|---|---|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Inulin and phytosterols | 2015 | Effect of phytosterols and inulin-enriched soymilk on LDL-cholesterol in Thai subjects: a double-blinded randomized controlled trial | Double-blinded randomized controlled trial | Two hundred and forty subjects who were 18 years old or older and had a baseline LDL-c of 130 mg/dl or higher were enrolled into the double-blinded randomized controlled trial study. Subjects were randomly assigned into the study group that received 2 g/day of phytosterols and 10 g/day of inulin-enriched soymilk or into the control group that received standard soymilk. The lipid profile was measured every 2 weeks for 8 weeks. | Control | At the end of the study, the median LDL-c levels decreased significantly from 165 mg/dl to 150 mg/dl in the study group and from 165 mg/dl to 159 mg/dl in the control group. The LDL-c reduction was significantly better in the study group. TC also reduced significantly by 6.60% in the study group while it reduced only by 1.76% in the control group. | Daily consumption of soymilk containing 2 g of phytosterols and 10 g of inulin reduced TC and LDL-c better than standard soymilk. | It had no effect on TG and HDL-c levels compared to standard soymilk. | https://pubmed.ncbi.nlm.nih.gov/26553006/ | Kietmirroie, N., Kwankaw, J., Kipakornsanit, S., & Leelawattana, R. (2015). Effect of phytosterols and inulin-enriched soymilk on LDL-cholesterol in Thai subjects: a double-blinded randomized controlled trial. <i>Lipids in Health and Disease</i> , 14(1). https://doi.org/10.1186/s12944-015-0149-4 | No |
| 2 | Inulin, Pomegranate extract | 2017 | Cholesterol-lowering effects of dietary pomegranate extract and inulin in mice fed an obesogenic diet | Animal study | Male C57BL/6 J mice were fed high-fat/high-sucrose (HF/H5 (32% energy from fat, 25% energy from sucrose)) diets supplemented with PomX (0.25%) and inulin (9%) alone or in combination for 4 weeks. | Control | Feeding the HF/H5 diet supplemented with PomX and inulin individually resulted in a significant decrease in serum TC compared HF/H5 control. | Inulin mainly targeted hepatic cholesterol de novo synthesis and fecal cholesterol and bile acid excretion involving changes in the metabolism of the intestinal microbiome. | Supplementation with PomX and inulin together resulted in lower hepatic and serum total cholesterol compared to individual treatments. PomX showed a trend to decrease liver triglyceride (TG) levels, while inulin or PomX-inulin combination had no effect on either serum or liver TG levels. | https://www.sciencedirect.com/science/article/pii/S09552863636308294 | Yang, J., Zhang, S., Henning, S. M., Lee, R., Hsu, M., Grojean, E., Pusuga, N., Lv, A., Heber, D., & Li, Z. (2018). Cholesterol-lowering effects of dietary pomegranate extract and inulin in mice fed an obesogenic diet. <i>Journal of Nutritional Biochemistry</i> , 52, 62-69. https://doi.org/10.1016/j.jnutbio.2017.10.003 | No |
| 3 | Inulin | 2022 | Physical activity enhances the improvement of body mass index and metabolism by inulin: a multicenter randomized placebo-controlled trial performed in obese individuals | Randomized, single-blinded, multicentric, placebo-controlled trial | (placebo: n = 31, prebiotic: n = 30). trial was conducted in obese participants who received 16 g/day native inulin versus maltodextrin, coupled to dietary advice to consume inulin-rich versus -poor vegetables for 3 months, respectively. | Placebo | Obese subjects who increased PA during a 3 months intervention with inulin-enriched diet exhibited several clinical improvements such as reduced BMI (-1.6 kg/m ²), decreased liver enzymes and plasma cholesterol, and improved glucose tolerance. | We conclude that PA level is an important determinant of the success of a dietary intervention targeting the gut microbiota. | N/A | https://pubmed.ncbi.nlm.nih.gov/35351444/ | Rodriguez, J., Neyrick, A. M., van Keirckhoven, M., Gianfrancesco, M. A., Banguet, F., Bertrand, I., Ciani, P. D., Lanthier, N., Croop, M., Pasquet, N., Thissen, J. P., Bindels, L. B., & Delzenne, N. M. (2022). Physical activity enhances the improvement of body mass index and metabolism by inulin: a multicenter randomized placebo-controlled trial performed in obese individuals. <i>BMC Medicine</i> , 20(1). https://doi.org/10.1186/s12916-022-02299-2 | No |
| 4 | Inulin , Lactobacillus sporogenes | 2013 | Synbiotic food consumption reduces levels of triacylglycerols and VLDL, but not cholesterol, LDL, or HDL in plasma from pregnant women | Randomized, double-blind, controlled clinical trial | 52 primigravida pregnant women, aged 18 to 35-year-old at their third trimester. After a 2-week run-in period, subjects were randomly assigned to consume either a synbiotic (n = 26) or control food (n = 26) for 9 weeks. The synbiotic food consisted of a probiotic viable and heat-resistant Lactobacillus sporogenes (1 × 10 ⁸ CFU) and 0.04 g inulin (HPX)/g as the prebiotic. Patients were asked to consume the synbiotic and control foods two times a day. | Placebo | Consumption of a synbiotic food for 9 weeks resulted in a significant reduction in serum TAG (P = 0.04), VLDL (P = 0.04) and a significant rise in plasma GSH levels (P = 0.004) compared to the control food. | No significant effects of the synbiotic food consumption on serum TC, LDL, HDL and plasma TAG levels (P > 0.05) were observed. | N/A | https://pubmed.ncbi.nlm.nih.gov/24271261/ | Tajhizadeh, M., Hashemi, T., Shakeri, H., Abedi, F., Sabihi, S. S., Alizadeh, S. A., & Asemi, Z. (2014). Synbiotic food consumption reduces levels of triacylglycerols and VLDL, but not cholesterol, LDL, or HDL in plasma from pregnant women. <i>Lipids</i> , 49(2), 155-161. https://doi.org/10.1007/s11745-013-2862-2 | Yes |
| 5 | Inulin | 2018 | Probiotic and synbiotic supplementation could improve metabolic syndrome in prediabetic adults: A randomized controlled trial | Double-blind, placebo-controlled randomized parallel-group clinical trial. | Participants were randomized to a multi-species probiotic or inulin-based synbiotic or placebo. Blood samples and anthropometric measures were collected at baseline, 12 and 24 weeks after treatment. | Placebo | A significant trend for a reduction in the prevalence of hyperglycemia in probiotic and synbiotic groups (p = 0.01 and 0.005 respectively), and hypertension in probiotic group (p = 0.04) was found. The decreases in metabolic syndrome prevalence were significant after taking probiotic and synbiotic supplementation as compared with placebo (p = 0.02). Also, the prevalence of low HDL-cholesterol level was decreased during the study in the probiotic group compared with placebo (p = 0.02). | The potential benefits of using probiotic and synbiotic for metabolic syndrome management in prediabetes have been supported by the results in the current study which might provide an important strategy to combat metabolic syndrome-associated diseases. | N/A | https://pubmed.ncbi.nlm.nih.gov/30076087/ | Kassabian, N., Feizi, A., Aminoroaya, A., & Amini, M. (2019). Probiotic and synbiotic supplementation could improve metabolic syndrome in prediabetic adults: A randomized controlled trial. <i>Diabetes & Metabolic Syndrome</i> , 13(5), 2991-2996. https://doi.org/10.1016/j.dsx.2018.07.016 | Yes |

Table S8: Summary of articles on fatty acids.

| Fatty Acid | | | | | | | | | | | | |
|------------|------------------------------|------|--|---|--|-------------------|--|---|---|---|---|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Fatty acid | 2018 | Assessment of omega-3 carboxylic acids in statin-treated patients with high levels of triglycerides and low levels of high-density lipoprotein cholesterol: Rationale and design of the STRENGTH trial | Randomized, double-blind, placebo-controlled trial | 13 086 patients were randomized to Epanova 4 g or placebo daily in addition to standard medical therapy. The trial will continue until 1600 patients reach the primary endpoint, with a median duration of therapy of 3 years. STRENGTH study will determine whether Epanova 4 g daily will reduce cardiovascular events in statin-treated high-risk patients with hypertriglyceridemia and low HDL-C levels. | Placebo | STRENGTH will permit the opportunity to determine the effects of administration of Epanova 4 g daily, a much higher dose than evaluated in many studies | While omega-3 fatty acids are of interest as a potential preventive therapy, most studies have used suboptimal doses and formulations with variable bioavailability for non-HDL-C reduction and failed to evaluate their impact in patients who are most likely to derive potential benefit | The trial will continue until 1600 patients reach the primary end point. The primary efficacy outcome is time to first event of cardiovascular death, myocardial infarction, stroke, coronary revascularization or hospitalization for unstable angina. | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6489732/pdf/1161-411281.pdf | Nicholls, S. J., Lincoff, A. M., Bash, D., Ballantyne, C. M., Barter, P. J., Davidson, M. H., Kastelein, J. J. P., Koskinen, W., McGuire, D. K., Moraflorjan, D., Pedersen, T. R., Polter, P. M., Ray, K., Watkins, B. W., Lundström, T., Wolski, K., & Nissen, S. E. (2018). Assessment of omega-3 carboxylic acids in statin-treated patients with high levels of triglycerides and low levels of high-density lipoprotein cholesterol: Rationale and design of the STRENGTH trial. <i>Clinical Cardiology</i> , 41(10), 1281–1288. https://doi.org/10.1002/cc.23055 | Yes |
| 2 | Fatty acid | 2013 | Omega 3 Fatty Acids Promote Macrophage Reverse Cholesterol Transport in Hamster Fed High Fat Diet | Animal study | Three groups of hamsters (n = 6/group) were studied for 20 weeks: 1) control diet; Control, 2) HFD group; HF and 3) HFD group supplemented with v3PUFA (EPA and DHA): HFv3. | Control | Liver TG content was higher in HF compared to Control group [18.2 +/- 2.1 mg/g vs. 8.5 +/- 1.1 mg/g] and lower in HFv3 [11.1 +/- 2.6 mg/g] compared to HF group. | In conclusion, EPA and DHA supplementation improved macrophage to feces reverse cholesterol transport in hamster fed HFD. | In the present study performed in hamster, we showed that v3PUFA prevented the increase of plasma TG and cholesterol by decreasing VLDL TG and HDL cholesterol concentrations respectively. These changes were related to increase of RCT efficiency as showed by a higher fecal bile acid and cholesterol elimination. | https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0066110&type=printable | Kashi Chadi, F., Nazih, H., Krempf, M., Nguyen, P., & Ougueram, K. (2013). Omega 3 Fatty Acids Promote Macrophage Reverse Cholesterol Transport in Hamster Fed High Fat Diet. <i>PLOS ONE</i> , 8(4). https://doi.org/10.1371/journal.pone.0066110 | No |
| 3 | Coenzyme Q10 and Omega-3 | 2017 | Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia | Pilot randomized double-blind trial | 105 subjects who met the criteria of combined dyslipidemia and elevated TAG levels were randomly divided into three groups. In the control group, unaltered statin therapy was indicated. In the second and third groups, omega-3 PUFA 2.52 g/day (Zenix fa Pleuran) and omega-3 PUFA 2.52 g+CoQ10 200 mg/day (Pharma Nord ApS) were added, res//. At the end of the 3-month period (±1 week), all patients were evaluated. | Control | Significant reduction of hepatic enzymes activity, systolic blood pressure, inflammatory markers and TAG levels were detected in both groups in comparison to the control group. | Coenzyme Q10 addition significantly reduced most of the above-mentioned parameters (systolic blood pressure, total cholesterol, LDL, hsCRP, IL-6, SOD) in comparison with the statin+omega-3 PUFA group. | The results of this pilot study suggest the possible beneficial effects of triple combination on the lipid and non-lipid parameters related to atherogenesis and side effects of statin treatment. | https://pubmed.ncbi.nlm.nih.gov/28541926/ | Edth, S., Sajty, M., Pekárová, T., Mughales, A., Štefanić, D., Katz, M., Špišáková, K., Pella, J., & Pella, D. (2017). Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia. <i>Journal of Basic and Clinical Physiology and Pharmacology</i> , 28(4), 327–336. https://doi.org/10.1515/jbcpp-2016-0149 | Yes |
| 4 | Fish oil EPA/DHA | 2012 | The effect of a 12-week course of omega-3 polyunsaturated fatty acids on lipid parameters in hypertriglyceridemic adult HIV-infected patients undergoing HAART: a randomized, placebo-controlled pilot trial | Randomized, placebo-controlled pilot trial | A double-blind, placebo-controlled, randomized, multicenter pilot study was undertaken in 48 evaluable HIV-infected patients undergoing HAART, with fasting triglyceride levels of 3.39 to 11.3 mmol/L. Patients were allowed fibrate or niacin but not statins and were randomized to polyunsaturated fatty acids (PUFA) 4 g daily versus placebo for 12 weeks. The primary end point was mean fasting triglyceride levels. | Placebo | PUFA reduced triglycerides by a median of 1.75 mmol/L versus a 0.41 mmol/L increase for the placebo group | PUFA therapy with DHA/EPA reduced triglyceride levels significantly compared with placebo in HIV-infected patients with HAART-associated hypertriglyceridemia. | N/A | https://pubmed.ncbi.nlm.nih.gov/22212377/ | Peters, B. S., Wierzbicki, A. S., Moyle, G., Nair, D., & Brockmeier, N. (2012). The effect of a 12-week course of omega-3 polyunsaturated fatty acids on lipid parameters in hypertriglyceridemic adult HIV-infected patients undergoing HAART: a randomized, placebo-controlled pilot trial. <i>Clinical Therapeutics</i> , 34(1), 67–76. https://doi.org/10.1016/j.clinthera.2011.12.001 | Yes |
| 5 | Fish oil EPA/DHA | 2013 | Effect of fish oil supplementation on serum triglycerides, LDL cholesterol and LDL subfractions in hypertriglyceridemic adults | Double-blind, parallel design, placebo controlled trial | This was a secondary analysis from a double-blind, parallel design, placebo controlled trial with 42 adults that experienced significant TG lowering and modest increases in total LDL-C concentrations | Placebo | 42 adults that experienced significant TG lowering and modest increases in total LDL-C concentrations after 12 weeks of 4 g/d EPA + DHA. | In this population of hypertriglyceridemic adults, dietary supplementation with fish oil resulted in an increase in total LDL-C concentration | N/A | https://pubmed.ncbi.nlm.nih.gov/24924882/ | Delrb, B., Dwekel, A., & Gardner, C. D. (2013). Effect of fish oil supplementation on serum triglycerides, LDL cholesterol and LDL subfractions in hypertriglyceridemic adults. <i>Nutrition, Metabolism, and Cardiovascular Diseases: NMCD</i> , 23(4), 350–357. https://doi.org/10.1016/j.numecd.2011.06.003 | No |
| 6 | Sterols and fish oil | 2018 | A low-fat spread with added plant sterols and fish omega-3 fatty acids lowers serum triglyceride and LDL-cholesterol concentrations in individuals with modest hypercholesterolaemia and hypertriglyceridaemia | Randomized, double-blind, placebo-controlled, parallel group design | Following a 2-week placebo run-in period, 260 healthy individuals with modestly elevated blood TG (≥ 1.4 mmol/L) and LDL-C (≥ 3.4 mmol/L) concentrations consumed either the placebo or intervention spread for 4 weeks. The intervention spread contained 2.0 g/day PS and 1.0 g/day eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) from fish oil. | Placebo | Four-week consumption of the intervention spread resulted in significantly lower TG and LDL-C concentrations as compared to placebo. Total cholesterol non-HDL-C concentrations were also significantly lower, as compared to placebo. | Four-week consumption of the intervention spread led to significant and clinically relevant decreases in serum TG, LDL-C and other blood lipid concentrations. | No significant treatment effects were found for HDL-cholesterol, ApoA1, ApoCII, Apo E or ApoB/ApoA. | https://pubmed.ncbi.nlm.nih.gov/29725824/ | Blom, W. A. M., Koppelman, W. P., Hiemstra, H., Stojačević, T., Schanagl, H., & Trautwein, E. A. (2019). A low-fat spread with added plant sterols and fish omega-3 fatty acids lowers serum triglyceride and LDL-cholesterol concentrations in individuals with modest hypercholesterolaemia and hypertriglyceridaemia. <i>European Journal of Nutrition</i> , 58(4), 1615–1624. https://doi.org/10.1007/s00394-018-1706-1 | Yes |
| 7 | Co enzyme Q10 and fatty acid | 2017 | Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia | Pilot randomized double-blind trial | 105 subjects who met the criteria of combined dyslipidemia and elevated TAG levels were randomly divided into three groups. In the control group, unaltered statin therapy was indicated. In the second and third groups, omega-3 PUFA 2.52 g/day (Zenix fa Pleuran) and omega-3 PUFA 2.52 g+CoQ10 200 mg/day (Pharma Nord ApS) were added, res//. At the end of the 3-month period (±1 week), all patients were evaluated. | Control | Coenzyme Q10 addition significantly reduced most of the above-mentioned parameters (systolic blood pressure, total cholesterol, LDL, hsCRP, IL-6, SOD) in comparison with the statin+omega-3 PUFA group. | The results of this pilot study suggest the possible beneficial effects of triple combination on the lipid and non-lipid parameters related to atherogenesis and side effects of statin treatment. | The intensity of statin adverse effects were significantly reduced in the group with the addition of CoQ10. | https://pubmed.ncbi.nlm.nih.gov/28541926/ | Edth, S., Sajty, M., Pekárová, T., Mughales, A., Štefanić, D., Katz, M., Špišáková, K., Pella, J., & Pella, D. (2017). Addition of omega-3 fatty acid and coenzyme Q10 to statin therapy in patients with combined dyslipidemia. <i>Journal of Basic and Clinical Physiology and Pharmacology</i> , 28(4), 327–336. https://doi.org/10.1515/jbcpp-2016-0149 | No |

Table S9: Summary of articles on phospholipids.

| Phospholipids | | | | | | | | | | | | |
|---------------|---------------|------|---|---------------|---|-------------------|--|--|---|---|---|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | Phospholipids | 2018 | Effect of dietary cholesterol and phospholipids on feed intake, growth performance and cholesterol metabolism in juvenile turbot (<i>Scophthalmus maximus</i> L.) | Animal study | examined the effect of dietary cholesterol and phospholipids on feed intake, growth performance and cholesterol metabolism in juvenile turbot (<i>Scophthalmus maximus</i> L.) (initial body weight 5.18 ± 0.01 g) during a 10-week period. Nine isonitrogenous and isolipidic diets were formulated to contain 0.0, 1.0 and 2.0% cholesterol (LC, MC and HC), and each with 0.0, 2.0 and 4.0% phospholipids (LP, MP and HPI), respectively. | Control | Cholesterol transport was significantly affected by the interaction between dietary cholesterol and phospholipids. Except for total cholesterol, free cholesterol and cholesterol ester, both high-density lipoprotein cholesterol (HDL-C) (P = 0.012) and low-density lipoprotein cholesterol (LDL-C) (P = 0.002) in serum were significantly affected by the interaction between dietary cholesterol and phospholipids. | In conclusion, there is a significant interaction between dietary cholesterol and phospholipids on the growth performance and the HDL-C and LDL-C involved in cholesterol transport, while no significant interaction was found on the feed intake in juvenile turbot. | interaction between dietary cholesterol and phospholipids on the growth performance was found in terms of weight gain rate. | https://www.sciencedirect.com/science/article/abs/pii/S0044848617325678 | Zhu, T., Mai, K., Xu, W., & Ai, Q. (2018). Effect of dietary cholesterol and phospholipids on feed intake, growth performance and cholesterol metabolism in juvenile turbot (<i>Scophthalmus maximus</i> L.). <i>Aquaculture</i> , 495, 443–451. https://doi.org/10.1016/j.aquaculture.2018.06.002 | No |
| 2 | Phospholipids | 2018 | Effect of dietary phospholipid levels on growth, lipid metabolism, and antioxidative status of juvenile hybrid snakehead (<i>Channa argus</i> × <i>Channa maculata</i>) | Animal study | The study was conducted to evaluate the effect of dietary phospholipids (PLs) on growth, lipid metabolism, and antioxidative status of hybrid snakehead (<i>Channa argus</i> × <i>Channa maculata</i>). Five isonitrogenous and isolipidic diets with graded levels of PLs (8.5, 19.3, 30.7, 41.5, and 50.8 g kg ⁻¹) were fed to triplicate groups of juveniles (initial body weight 12.6 ± 0.23 g) for 8 weeks. | Control | Results showed that dietary PL supplementation significantly improved growth of juveniles. The final body weight (FBW) and specific growth rate (SGR) significantly increased with dietary PLs increasing from 8.5 to 41.5 g kg ⁻¹ (P < 0.05). Fish fed with the diet containing 8.5 g kg ⁻¹ PLs showed higher feed conversion ratio (FCR) compared to the other treatments (P < 0.05). Liver lipid contents, serum triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) contents significantly decreased with the increasing levels of dietary PLs (P < 0.05). However, serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) contents and HDL-C/TC and HDL-C/LDL-C value significantly increased with increasing dietary PL levels (P < 0.05). | These results confirmed that dietary PL supplementation has beneficial effects on growth performance and antioxidant capacity of juvenile hybrid snakehead. Dietary PLs might reduce lipid deposition in the liver of juvenile hybrid snakehead. | N/A | https://pubmed.ncbi.nlm.nih.gov/29147969/ | Lin, S. M., Li, F. J., Yuan, B., & Doolindachaporn, S. (2018). Effect of dietary phospholipid levels on growth, lipid metabolism, and antioxidative status of juvenile hybrid snakehead (<i>Channa argus</i> × <i>Channa maculata</i>). <i>Fish Physiology and Biochemistry</i> , 44(1), 401–410. https://doi.org/10.1007/s10695-017-0443-3 | No |

Table S10: Summary of articles on sterols.

| Sterol | | | | | | | | | | | | |
|---------------|--|------|--|---|---|---------------------|---|---|---|---|--|---------------------|
| No | Ingredient s | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | bergamot extract (120-mg flavonoids), phytosterols, vitamin C, and chlorogenic acid | 2019 | Three-arm, placebo-controlled, randomized clinical trial evaluating the metabolic effect of a combined nutraceutical containing a bergamot standardized flavonoid extract in dyslipidemic overweight subjects | Double-blind, placebo-controlled, parallel-group, dose-escalation, clinical trial | 90 overweight dyslipidemic subjects. Participants were randomly allocated to treatment with two pills of either active treatment or placebo, or a combination of both (a pill per treatment). | Placebo | After 8 weeks, all active-treated groups experienced a significant improvement in triglycerides (TG) versus placebo and in low-density lipoprotein cholesterol (LDL-C) versus baseline and placebo treatments. In the high-dose-treated group, also total cholesterol (TC), significantly decreased. | The tested nutraceutical showed to improve lipid and glucose metabolism, adipokines pattern, and systemic inflammation in dyslipidemic overweight subjects. | All patients allocated to either low-dose or high-dose active treatment experienced a significant decrease in TG, LDL-C, and homeostasis model assessment of insulin resistance. | https://pubmed.ncbi.nlm.nih.gov/31225673/ | Cicero, A. F. G., Fogacci, F., Bove, M., Giovannini, M., & Borghi, C. (2019). Three-arm, placebo-controlled, randomized clinical trial evaluating the metabolic effect of a combined nutraceutical containing a bergamot standardized flavonoid extract in dyslipidemic overweight subjects. <i>Phytotherapy Research: PTR</i> , 33(8), 2094–2101. https://doi.org/10.1002/ptr.6402 | Yes |
| 2 | Sterols and fish oil | 2018 | A low-fat spread with added plant sterols and fish omega-3 fatty acids lowers serum triglyceride and LDL cholesterol concentrations in individuals with modest hypercholesterolemia and hypertriglyceridaemia | Randomized, double-blind, placebo-controlled, parallel group design | Following a 2-week placebo run-in period, 260 healthy individuals with modestly elevated blood TG (≥ 1.4 mmol/L) and LDL-C (≥ 3.4 mmol/L) concentrations consumed either the placebo or intervention spread for 4 weeks. The intervention spread contained 2.0 g/day PS and 1.0 g/day eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) from fish oil. | Placebo | Four-week consumption of the intervention spread resulted in significantly lower TG and LDL-C concentrations as compared to placebo. Total cholesterol non-HDL-C concentrations were also significantly lower, as compared to placebo. | Four-week consumption of the intervention spread led to significant and clinically relevant decreases in serum TG, LDL-C and other blood lipid concentrations. | No significant treatment effects were found for HDL-cholesterol, ApoA1, ApoC1, Apo E or ApoB/ApoA1. | https://pubmed.ncbi.nlm.nih.gov/29725824/ | Bloom, W. A. M., Koppelman, W. P., Hiemstra, H., Stojakovic, T., Schrnagl, H., & Trautwein, E. A. (2019). A low-fat spread with added plant sterols and fish omega-3 fatty acids lowers serum triglyceride and LDL-cholesterol concentrations in individuals with modest hypercholesterolemia and hypertriglyceridaemia. <i>European Journal of Nutrition</i> , 58(4), 1615–1624. https://doi.org/10.1007/s00394-018-1706-1 | Yes |
| 3 | Sterols | 2018 | Plant sterols lower LDL-cholesterol and triglycerides in dyslipidemic individuals with or at risk of developing type 2 diabetes; a randomized, double-blind, placebo-controlled study | Double-blind, randomized, placebo-controlled, parallel study | 161 individuals at increased risk of and with established T2DM, consumed low-fat spreads without or with added PS (2 g/d) for 6 weeks. Fasting serum/plasma total cholesterol (TC), LDL-C, TG, high-density lipoprotein cholesterol (HDL-C), glucose and insulin were measured at baseline and after 6 weeks. | Placebo | PS intake significantly lowered fasting LDL-C and TG with no significant changes in HDL-C, glucose or insulin. | In individuals at risk of and with established T2DM and with elevated TG and LDL-C, 2 g/d of PS results in dual LDL-C plus TG lowering. | ostprandial lipid or glycemic responses did not differ between PS and control treatment. | https://pubmed.ncbi.nlm.nih.gov/29795368/ | Trautwein, E. A., Koppelman, W. P., de Jong, A., Hiemstra, H., Vermeer, M. A., Noakes, M., & Luscombe-Marsh, N. D. (2018). Plant sterols lower LDL-cholesterol and triglycerides in dyslipidemic individuals with or at risk of developing type 2 diabetes; a randomized, double-blind, placebo-controlled study. <i>Nutrition & Diabetes</i> , 8(1). https://doi.org/10.1038/s41387-018-0039-8 | Yes |
| 4 | Sterols | 2017 | Interindividual variability in the cholesterol-lowering effect of supplementation with plant sterols or stanols | Review | This review focuses on the interindividual variability in response to dietary supplementation with plant sterols and stanols. | Not Applicable - NA | Dietary plant sterols and stanols have no significant effects on LDL-C in substantial numbers of individuals. Higher responses, in absolute value and percentage of LDL-C, are observed in individuals with higher cholesterol absorption and a lower rate of cholesterol synthesis. | Dietary plant sterols and stanols have no significant effects on LDL-C in substantial numbers of individuals. | Plant sterol/stanol supplements have no effect on cholesterol for absorption in the intestine and induce an average decrease in LDL-C by 5% to 15% in a dose-dependent manner, but not in all individuals. | https://doi.org/10.1093/nutr/nux059 | Furman, E., Bard, J.-M., & Lecfer, J.-M. (2017). Interindividual variability in the cholesterol-lowering effect of supplementation with plant sterols or stanols. <i>Nutrition Reviews</i> , 75(2), 133–145. https://doi.org/10.1093/nutr/nux059 | Yes |
| 5 | Sterols | 2017 | Plant sterol ester diet supplementation increases serum plant sterols and markers of cholesterol synthesis, but has no effect on total cholesterol levels | Double-blind, randomized, placebo-controlled, cross-over intervention-study | Sixteen volunteers, average age 34 years, with no or mild hypercholesterolemia were subjected to a 4 week period of daily intake of 3 g plant sterols per day supplied via a supplemented margarine on top of regular eating habits. To evaluate the effects of plant sterol ester supplemented margarine on cholesterol, non-cholesterol sterols and oxidative stress in serum and monocytes. | Placebo | consumption of plant sterol ester supplemented margarine results in increased concentrations of plant sterols and cholesterol synthesis markers without affecting total cholesterol in the serum, activation of circulating monocytes or redox state. | Cholesterol serum levels, however, were not changed significantly | in a population of healthy volunteers with no or mild hypercholesterolemia, consumption of plant sterol ester supplemented margarine results in increased concentrations of plant sterols and cholesterol synthesis markers without affecting total cholesterol in the serum. | https://pubmed.ncbi.nlm.nih.gov/27247356/ | Weingärtner, O., Bogeski, I., Kummerow, C., Schirmer, S. H., Husche, C., Vannier, T., Wagenspiel, S., Hoth, M., Böhm, M., Lijngohan, D., & Laufs, U. (2017). Plant sterol ester diet supplementation increases serum plant sterols and markers of cholesterol synthesis, but has no effect on total cholesterol levels. <i>The Journal of Steroid Biochemistry and Molecular Biology</i> , 168, 219–225. https://doi.org/10.1016/j.jsbmb.2016.07.016 | Yes |
| 6 | Sterols | 2018 | LDL-Cholesterol Lowering of Plant Sterols and Stanols—Which Factors Influence Their Efficacy? | Review | This review summarizes evidence for the impact of various factors potentially influencing the LDL-C-lowering efficacy of plant sterols/stanols (PSS). | Not Applicable - NA | Numerous clinical studies have shown that the intake of PSS lowers LDL-C concentrations by 7.5 to 12% with daily intakes of 1.5 to 3 g. | Compared to multiple daily intakes, once-a-day intake of PSS, especially in the morning with light breakfast, leads to a sub-optimal LDL-C lowering. | In conclusion, PSS are efficacious in all foods and food supplements; for optimal efficacy they should be consumed with a (main) meal and twice daily. | https://pubmed.ncbi.nlm.nih.gov/30205492/ | Trautwein, E. A., Vermeer, M. A., Hiemstra, H., & Ras, R. T. (2018). LDL-cholesterol lowering of plant sterols and stanols—Which factors influence their efficacy? <i>Nutrients</i> , 10(1), 1–10. https://doi.org/10.3390/nu10091262 | Yes |
| 7 | phytosterols (800 mg) and red yeast rice, standardized to contain 5 mg of monacolin K from Monascus purpureus, with added niacin (27 mg) and policosanols (10 mg) (LEVELIP DUO™) | 2020 | A Randomized, Double-Blinded, Placebo-Controlled, Clinical Study of the Effects of a Nutraceutical Combination (LEVELIP DUO™) on LDL Cholesterol Levels and Lipid Pattern in Subjects with Sub-Optimal Blood Cholesterol Levels (NATCOL Study) | A Randomized, Double-Blinded, Placebo-Controlled, Clinical Study | randomizing 88 moderately hypercholesterolemic subjects to treatment with a combined nutraceutical or placebo. | Placebo | The mean LDL-Cholesterol (LDL-C) change at Week 8 was -32.5 ± 30.2 mg/dL (-19.8%) in the combined nutraceutical group and 2.5 ± 19.4 mg/dL (2.3%) in the placebo group. Total Cholesterol (TC), non-HDL cholesterol (non-HDL-C), Apolipoprotein B, TC/HDL-C and LDL-C/HDL-C improved in a similar way in the combined nutraceutical group only. | In conclusion, the tested combined nutraceutical was well tolerated, while significantly reducing the plasma levels of LDL-C, TC, non-HDL-C, ApoB, TC/HDL-C and LDL-C/HDL-C ratios in mildly hypercholesterolemic patients. | N/A | https://pubmed.ncbi.nlm.nih.gov/33066344/ | Cicero, A. F. G., D'addato, S., & Borghi, C. (2020). A Randomized, Double-Blinded, Placebo-Controlled, Clinical Study of the Effects of a Nutraceutical Combination (LEVELIP DUO™) on LDL Cholesterol Levels and Lipid Pattern in Subjects with Sub-Optimal Blood Cholesterol Levels (NATCOL Study). <i>Nutrients</i> , 12(10), 1–10. https://doi.org/10.3390/nu12103127 | Yes |
| 8 | Phytosterols | 2010 | Dose effects of dietary phytosterols on cholesterol metabolism: a controlled feeding study | Placebo-controlled, crossover feeding trial | 18 adults received a phytosterol-deficient diet (50 mg phytosterols/2000 kcal) plus beverages supplemented with 0, 400, or 2000 mg phytosterols/d for 4wk each, in random order. | Placebo | Phytosterol intakes (diet plus supplements) averaged 59, 459, and 2059 mg/d during the 3 diet periods. Relative to the 59-mg diet, the 459- and 2059-mg phytosterol intakes significantly (P<0.01) increased total fecal cholesterol excretion (36 +/- 6% and 74 +/- 10%, respectively) and biliary cholesterol excretion (38 +/- 7% and 77 +/- 12%, respectively) and reduced percentage intestinal cholesterol absorption (-10 +/- 1% and -25 +/- 3%, respectively). Serum LDL cholesterol declined significantly only with the highest phytosterol dose (-8.9 +/- 2.3%). | Dietary phytosterols in moderate and high doses favorably alter whole-body cholesterol metabolism in a dose-dependent manner. | A moderate phytosterol intake (459 mg/d) can be obtained in a healthy diet without supplementation. | https://academic.oup.com/ajcn/article/91/1/32/4597163?rctj | Bacette, S. B., Liu, X., Lefevre, M., Spearie, C. A., Mossi, M. M., Ma, L., & Ostlund, R. E. (2010). Dose effects of dietary phytosterols on cholesterol metabolism: A controlled feeding study. <i>American Journal of Clinical Nutrition</i> , 91(1), 32–38. https://doi.org/10.3945/ajcn.2009.28070 | No |
| 9 | Inulin and phytosterols | 2015 | Effect of phytosterols and inulin-enriched soy milk on LDL-cholesterol in Thai subjects: a double-blinded randomized controlled trial | Double-blinded randomized controlled trial | Two hundred and forty subjects who were 18 years old or older and had a baseline LDL-C of 130 mg/dl or higher were enrolled into the double-blinded randomized controlled trial study. Subjects were randomly assigned into the study group that received 2 g/day of phytosterols and 10 g/day of inulin-enriched soy milk or into the control group that received standard soy milk. The lipid profile was measured every 2 weeks for 8 weeks. | Control | At the end of the study, the median LDL-C levels decreased significantly from 165 (132, 254) mg/dl to 150 (105, 263) mg/dl in the study group (p < 0.001) and from 165 (130, 243) mg/dl to 159 (89, 277) mg/dl in the control group (p = 0.014). The LDL-C reduction was significantly better in the study group (-10.03%, (-37.07, 36.00) v -1.31% (-53.40, 89.73), p < 0.001). TC also reduced significantly by 6.60% in the study group while it reduced only by 1.76% in the control group (p < 0.001). | Daily consumption of soy milk containing 2 g of phytosterols and 10 g of inulin reduced TC and LDL-C better than standard soy milk. | It had no effect on TG and HDL-C levels compared to standard soy milk. | https://pubmed.ncbi.nlm.nih.gov/26553006/ | Kietisiriroje, N., Kwakkaew, J., Khatkhatrasanti, S., & Leksawatana, R. (2015). Effect of phytosterols and inulin-enriched soy milk on LDL-cholesterol in Thai subjects: a double-blinded randomized controlled trial. <i>Lipids in Health and Disease</i> , 14(1). https://doi.org/10.1186/s12944-015-0149-z | No |

Table S11: Summary of articles on plant compounds.

| Plant compound | | | | | | | | | | | | |
|----------------|--|------|--|--|--|-------------------|---|--|--|---|---|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | red yeast rice (RYR), policosanol and artichoke leaf extracts | 2013 | A combined natural supplement lowers LDL cholesterol in subjects with moderate untreated hypercholesterolemia: a randomized placebo-controlled trial | Randomized, double-blind, placebo-controlled trial. | natural cholesterol-lowering supplement (NCLS) containing red yeast rice, policosanol and artichoke leaf extracts on blood lipid concentrations as well as safety parameters when given over 16 weeks in 100 volunteers with untreated moderate hypercholesterolemia | Placebo | Reduction of primary outcome low-density lipoprotein cholesterol as well as total cholesterol were observed after 16 weeks of supplementation with NCLS. | The NCLS was effective in reducing low-density lipoprotein cholesterol in subjects with moderate hypercholesterolemia, without modifying safety parameters. | No significant changes were observed in high-density lipoprotein, triacylglycerol, creatine kinase, lactate dehydrogenase and coenzyme Q10 levels, as well as in markers of liver and renal function. | https://pubmed.ncbi.nlm.nih.gov/23815518/ | https://doi.org/10.1009/09637486.2013.809405 | Yes |
| 2 | Extract - Red yeast rice (RYR), sugar cane-derived policosanol (SCoP) and artichoke leaf extracts (ALEs) | 2013 | LDL-cholesterol-lowering effect of a dietary supplement with plant extracts in subjects with moderate hypercholesterolemia | Double-blind, randomized, parallel controlled study | 39 subjects from 21 to 55 years with moderate hypercholesterolemia without drug treatment were assigned to groups and then consumed either a DS containing RYR, SCoP and ALEs or a placebo over a 16-week period. | Placebo | LDL-cholesterol and TC were reduced by, respectively, 21.4% (95% CI, -13.3 to -24.9%, p < 0.001) and 14.1% (95% CI, -10.1 to -18.0%, p < 0.001) at week 16 in the DS group compared with baseline. | Daily consumption of this new DS decreased LDL-cholesterol and TC and is therefore an interesting, convenient aid in managing mild to moderate hypercholesterolemia. | N/A | https://link.springer.com/article/10.1007/s00394-012-0357-x | https://doi.org/10.1009/09637486.2013.809405 | Yes |
| 3 | Extract - red yeast rice extract, policosanol and artichoke leaf extract | 2013 | Effect on LDL-cholesterol of a large dose of a dietary supplement with plant extracts in subjects with untreated moderate hypercholesterolemia: a randomized, double-blind, placebo-controlled study | Randomised, double-blind, placebo-controlled clinical trial. | Forty-five healthy subjects (15 per group), with untreated hypercholesterolemia, were included for this trial for 4 weeks of supplementation. | Placebo | After 4 weeks of supplementation, LDL-C was significantly lower in 6-TAB (-0.21 g/l; 95% CI -0.38 to -0.03 g/l; p = 0.0037) and 3-TAB (-0.25 g/l; 95% CI -0.42 to -0.07 g/l; p = 0.0071) compared to Placebo, although no difference in LDL-cholesterol was observed between the two groups, while no effect was seen on triglycerol and HDL-cholesterol. | After 4 weeks of supplementation, LDL-C was significantly lower in TWICE DAILY DOSE (6 TABLET INSTEAD OF 3) | Supplementation with twice the recommended dose of the DS was effective in reducing LDL-cholesterol and appeared safe, but according to the present results, no additional benefit could be achieved compared to the recommended dose. | https://link.springer.com/article/10.1007/s00394-012-0486-2 | https://doi.org/10.1009/09637486.2013.809405 | Yes |
| 4 | Berberine | 2022 | Combined berberine and probiotic treatment as an effective regimen for improving postprandial hyperlipidemia in type 2 diabetes patients: a double blinded placebo controlled randomized study | Double blinded placebo controlled randomized study | Blood PL (120 min after taking 100 g standard carbohydrate meal) was examined in 365 participants with T2D from the Probiotics and BBR on the Efficacy and Change of Gut Microbiota in Patients with Newly Diagnosed Type 2 Diabetes | Placebo | study proved the therapeutic effect of a combined treatment of oral administration of probiotics with berberine on improving PL in patients newly diagnosed with T2D and proposed a new gut microbiome related remedy for managing dyslipidemia, covering both PL and FL in patients with T2D. | Prob+BBR was superior to BBR or Prob alone in improving postprandial total cholesterol (pTC) and low-density lipoprotein cholesterol (pLDL) levels | N/A | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8376665/ | https://doi.org/10.1089/19490976.2021.2003176 | Yes |
| 5 | Berberine | 2013 | The effects of berberine on blood lipids: a systemic review and meta-analysis of randomized controlled trials | Systemic review | eleven randomized controlled trials (including a total of 874 participants) were included in this study. | Not Applicable NA | The final analysis showed that administration of berberine produced a significant reduction in total cholesterol, triglycerides, and low-density lipoprotein cholesterol | berberine may have beneficial effects in the control of blood lipid levels. However, the efficacy of berberine in treating hyperlipidemia should be further evaluated by more randomized controlled trials in a larger population of patients. | No serious adverse effects of berberine have been reported. | https://pubmed.ncbi.nlm.nih.gov/23212497/ | https://doi.org/10.1055/S-0032-1328321 | No |
| 6 | Berberine | 2021 | Effect of Berberine on Cardiovascular Disease Risk Factors: A Mechanistic Randomized Controlled Trial | Randomized, double-blind, placebo-controlled, parallel trial | In total, 84 eligible Chinese men with hyperlipidemia were randomized to berberine (500 mg orally, twice a day) or placebo for 12 weeks. CVD risk factors (lipids, thromboxane A2, blood pressure, body mass index, and waist-hip ratio) and testosterone were assessed at baseline, and 8 and 12 weeks after intervention. | Placebo | Men randomized to berberine had larger reductions in total cholesterol and high-density lipoprotein cholesterol after 12 weeks. Considering changes after 8 and 12 weeks together, berberine lowered total cholesterol and possibly low-density lipoprotein-cholesterol. | Changes in triglycerides, thromboxane A2, blood pressure, body mass index and waist-hip ratio after the intervention did not differ between the berberine and placebo groups. | Berberine is a promising treatment for lowering cholesterol. Berberine did not lower testosterone but instead may increase testosterone in men, suggesting sex-specific effects of berberine. | https://pubmed.ncbi.nlm.nih.gov/34444731/ | https://doi.org/10.3390/nu13082550 | Yes |
| 7 | Berberine | 2019 | Efficacy and Safety of Berberine Alone or Combined with Statins for the Treatment of Hyperlipidemia: A Systematic Review and Meta-Analysis of Randomized Controlled Clinical Trials | Systematic Review and Meta-Analysis of Randomized Controlled Clinical Trials | A total of 11 RCTs involving 1386 patients were finally included. | Not Applicable NA | The results of meta-analysis showed that compared with the placebo group, berberine could significantly reduce the total cholesterol and low-density lipoprotein levels and elevate the high-density lipoprotein level. Compared with the simvastatin group, berberine was effective only in reducing the level of triglyceride | Compared with the simvastatin group, berberine plus simvastatin was more effective in reducing the level of triglyceride and total cholesterol. This study suggests that berberine is effective for hyperlipidemia. | In terms of adverse reactions, the incidence of adverse reactions including transaminase elevation and muscle aches was lower in the berberine alone or combined with simvastatin group than that in the control group. | https://pubmed.ncbi.nlm.nih.gov/31094214/ | https://doi.org/10.1142/S0192415419500393 | No |
| 8 | Berberine | 2014 | Berberine (BBR) decreases cholesterol levels in rats through multiple mechanisms, including inhibition of cholesterol absorption | Animal study | Male Sprague-Dawley rats were fed the AIN-93G diet (normal control) or modified AIN-93G diet containing 28% fat, 2% cholesterol and 0.5% cholic acid with treatment of 0 (atherogenic control), 50, 100, and 150 mg/kg of BBR, respectively by gavaging in water for 8 weeks. | Control | Treatment with BBR in rats on the atherogenic diet reduced plasma total cholesterol and nonHDL cholesterol levels by 29%-33% and 31%-41%, respectively, with no significant differences being observed among the three doses. The fractional dietary cholesterol absorption rate was decreased by 40%-51%. Rats fed the atherogenic diet showed lower plasma triacylglycerol levels, and no changes were observed after the BBR treatment. | In conclusion, BBR lowered blood cholesterol levels in diet-induced hypercholesterolemic rats at least in part through inhibiting intestinal cholesterol absorption. | due to the differences in diet composition and cholesterol metabolism between humans and rats, it is not possible to conclude that the NC diet is a better approach than the AC plus BBR in humans. Generally, the NC diet does not apply in humans, as people, even vegetarians, eat diets containing cholesterol and have high cholesterol absorption rates. | https://www.sciencedirect.com/science/article/pii/S05200904140001620 | https://doi.org/10.1016/j.metabol.2014.05.013 | No |
| 9 | Berberine | 2012 | Lipid-lowering effect of berberine in human subjects and rats | Clinical trial | In this pilot study, obese human subjects (Caucasian) were given 500 mg berberine orally three times a day for twelve weeks. The efficacy and safety of berberine treatment was determined by measurements of body weight, comprehensive metabolic panel, blood lipid and hormone levels, expression levels of inflammatory factors, complete blood count, and electrocardiograph. A Sprague-Dawley rat experiment was also performed to identify the anti-obesity effects of berberine treatment. | Not Applicable NA | The results demonstrate that berberine treatment produced a mild weight loss (average 5 lb/subject) in obese human subjects. But more interestingly, the treatment significantly reduced blood lipid levels (23% decrease of triglyceride and 12.2% decrease of cholesterol levels) in human subjects. The lipid-lowering effect of berberine treatment has also been replicated in the rat experiment (34.7% decrease of triglyceride and 9% decrease of cholesterol level). | this study demonstrates that berberine is a potent lipid-lowering compound with a moderate weight loss effect. | Tests of hematological, cardiovascular, liver, and kidney function following berberine treatment showed no detrimental side effects to this natural compound. | https://pubmed.ncbi.nlm.nih.gov/22739450/ | https://doi.org/10.1016/j.phytomed.2012.05.009 | No |
| 10 | Berberine | 2010 | Berberine and plant stanols synergistically inhibit cholesterol absorption in hamsters | Animal study | Male Golden Syrian hamsters were randomly divided into 4 groups (n=15/group) and fed a cornstarch-casein-sucrose-based diet containing 0.15% cholesterol and 5% fat. Three treatment groups were supplemented with 0.17% (equivalent to 100mg/kg-1d-1) BBR, 1% PS, or a combination of both (BBRPS) for 4wk | Control | Berberine (BBR), plant stanols (PS), and BBRPS supplementations significantly decreased (p<0.0001) plasma T.C and nonHDL-C levels as compared with the control group. These three treatments lowered plasma T.C by 22%, 30%, and 43% and nonHDL-C by 28%, 45%, and 63%, respectively. | BBR lowered plasma cholesterol and nonHDL-cholesterol levels possibly through a combination of inhibition of cholesterol absorption and stimulation of bile acid synthesis. | Moreover, we have observed that BBR and PS act synergistically to inhibit fractional cholesterol absorption when they were administered in combination. The significant correlation between fractional cholesterol absorption rates and plasmatotal cholesterol or nonHDL-cholesterol concentrations provides additional support to the important role of cholesterol absorption in reducing plasma cholesterol levels after the BBR, PS and BBRPS treatments, respectively. | https://reader.elsevier.com/reader/sd/pii/S0021915009007126?token=183814418997412256751885D19C4D773C621E20123502727A5491D28376C16426245801808408ACE1A55974D2646&e1=1&e2=1&e3=1&e4=1&e5=1&e6=1&e7=1&e8=1&e9=1&e10=1&e11=1&e12=1&e13=1&e14=1&e15=1&e16=1&e17=1&e18=1&e19=1&e20=1&e21=1&e22=1&e23=1&e24=1&e25=1&e26=1&e27=1&e28=1&e29=1&e30=1&e31=1&e32=1&e33=1&e34=1&e35=1&e36=1&e37=1&e38=1&e39=1&e40=1&e41=1&e42=1&e43=1&e44=1&e45=1&e46=1&e47=1&e48=1&e49=1&e50=1&e51=1&e52=1&e53=1&e54=1&e55=1&e56=1&e57=1&e58=1&e59=1&e60=1&e61=1&e62=1&e63=1&e64=1&e65=1&e66=1&e67=1&e68=1&e69=1&e70=1&e71=1&e72=1&e73=1&e74=1&e75=1&e76=1&e77=1&e78=1&e79=1&e80=1&e81=1&e82=1&e83=1&e84=1&e85=1&e86=1&e87=1&e88=1&e89=1&e90=1&e91=1&e92=1&e93=1&e94=1&e95=1&e96=1&e97=1&e98=1&e99=1&e100=1 | https://doi.org/10.1016/j.atherosclerosis.2009.08.050 | No |

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|----|--|------|---|---|---|----------------|--|--|--|---|---|-----|
| 11 | Berberine, Red Yeast Rice and Chitosan | 2017 | Effects of a New Nutraceutical Formulation (Berberine, Red Yeast Rice and Chitosan) on Non-HDL Cholesterol Levels in Individuals with Dyslipidemia: Results from a Randomized, Double-Blind, Placebo-Controlled Study | Randomized, Double-Blind, Placebo-Controlled Study | The aim of the study is to test the efficacy of the nutraceutical formulation (one daily) in lowering non-HDL cholesterol vs. placebo at 12 weeks in individuals with non-HDL cholesterol levels ≥ 160 mg/dL. 39 subjects (age 52±11 years; 54% females; body mass index 27±4 kg/m ²) were randomized (3:1) in a double blind phase II placebo-controlled study. | Placebo | The intervention significantly decreased non-HDL cholesterol (-30 ± 20 mg/dL), LDL cholesterol (-31 ± 18 mg/dL) and apolipoprotein (Apo B) (-14 ± 12 mg/dL) levels compared to the placebo. | In conclusion, the tested nutraceutical formulation was effective in the reduction of non-HDL/LDL-C levels at 4 and 12 weeks thus representing a possible therapeutic strategy in dyslipidemic individuals in primary prevention. | new combination of nutraceuticals (berberine 200 mg, monacolin K 3 mg, chitosan 10 mg and coenzyme Q ₁₀ 10 mg) | https://www.mdpi.com/1422-0067/18/7/1498 | Soigoni V., Aldigeri R., Antonini M., Mitchell M. M., Fantuzzi F., Frattar A., Pellizzato M., Delindati E., Zavorini L., Bonadonna B. C., & Del Cas A. (2017). Effects of a new nutraceutical formulation (Berberine, red yeast rice and chitosan) on non-HDL cholesterol levels in individuals with dyslipidemia: Results from a randomized, double-blind, placebo-controlled study. <i>International Journal of Molecular Sciences</i> , 18(7). https://doi.org/10.3390/ijms18071498 | Yes |
| 12 | Berberine, red yeast rice, plant sterols, fibers | 2018 | Cholesterol-Lowering Nutraceuticals Affecting Vascular Function and Cardiovascular Disease Risk | Review | The aim of this review is to provide an update on the effects of the dietary supplementation with cholesterol-lowering nutraceuticals and nutraceutical combinations affecting vascular function and CV risk in clinical interventional studies. | Not Applicable | Current evidence supports the mild-to-moderate cholesterol-lowering efficacy of red yeast rice, berberine, plant sterols, fibers, and some nutraceutical combinations whereas the data on the individual cholesterol-lowering action of other nutraceuticals are either less striking or even inconclusive. | There is also promising evidence on the vascular protective effects of some of the aforementioned nutraceuticals. | However, except for red yeast rice, clinical interventional studies have not investigated their impact on CV outcomes. | https://link.springer.com/article/10.1007/s11886-018-0994-7#Abstract | Bianconi V., Mamanfo, M. R., Sahabdar, A., Cosentino, T., & Pirro, M. (2018). Cholesterol-Lowering Nutraceuticals Affecting Vascular Function and Cardiovascular Disease Risk. <i>Current Cardiology Reports</i> , 20(7), 53. https://doi.org/10.1007/s11886-018-0994-7 | Yes |
| 13 | Betaine | 2018 | Metabolic Effects of Betaine: A Randomized Clinical Trial of Betaine Supplementation in Prediabetes | Randomized, double-masked, placebo-controlled trial | Persons with obesity and prediabetes (N = 27) were randomly assigned to receive betaine 3300 mg orally twice daily for 10 days, then 4950 mg twice daily for 12 weeks, or placebo. | Placebo | Betaine tended to reduce fasting glucose levels but had no other effect on glycemia. Serum total cholesterol levels increased after betaine treatment compared with placebo. | Betaine had little metabolic effect. Additional studies may elucidate mechanisms contributing to differences between preclinical and human responses to betaine. | N/A | https://pubmed.ncbi.nlm.nih.gov/29860335/ | Grizales, A. M., Patti, M. E., Lin, A. P., Beckman, J. A., Sahni, V. A., Cloutier, E., Fowler, K. M., Dreyfuss, J. M., Pan, H., Kozuka, C., Lee, A., Basu, R., Pober, D. M., Gerstein, R. E., & Goldfine, A. B. (2018). Metabolic Effects of Betaine: A Randomized Clinical Trial of Betaine Supplementation in Prediabetes. <i>The Journal of Clinical Endocrinology and Metabolism</i> , 103(8), 3038–3049. https://doi.org/10.1210/clinem.2018.00507 | No |
| 14 | Betaine | 2016 | Long term betaine supplementation regulates genes involved in lipid and cholesterol metabolism of two muscles from an obese pig breed | Animal study | fourteen purebred AL pigs surgically castrated. Pigs were randomly assigned into two experimental groups, Group C (n=6), consuming the C diet, and Group CB (n=8), consuming the Cdiet supplemented with betaine (1 g/kg-1) | Control | Total intramuscular lipids from both muscles were significantly higher (P<0.05) on CB (C diet supplemented with betaine)- when compared to (commercial) C-fed pigs, mainly due to higher contents on intramuscular neutral lipids | This study examined the effect of a long term betaine supplementation (1 g/kg-1) on the regulation of genes involved in lipid and cholesterol metabolism. Betaine supplementation did not affect the FA profile of neutral intramuscular lipids from L. lumborum/and b. femoris/or AL pigs. | Betaine consumption by AL obese pigs led to an increase in intramuscular fat (IMF) of both muscles analyzed. | https://www.sciencedirect.com/science/article/pii/S0309174016302420 | Albuquerque, A., Neves, J. A., Redondo, M., Laranjo, M., Félix, M. R., Freitas, A., Tirapicos, J. L., & Martins, J. M. (2017). Long term betaine supplementation regulates genes involved in lipid and cholesterol metabolism of two muscles from an obese pig breed. <i>Meat Science</i> , 124, 25–33. https://doi.org/10.1016/j.meatsci.2016.10.012 | No |
| 15 | Betaine | 2021 | Effects of betaine supplementation on cardiovascular markers: A systematic review and Meta-analysis | Systematic review and Meta-analysis | This systematic review and meta-analysis compared the effects of betaine supplementation on cardiovascular disease (CVD) markers. Betaine supplementation had a significant effect on concentrations of betaine | Not Applicable | Betaine supplementation had a significant effect on concentrations of betaine, total cholesterol (TC), low-density lipoprotein (LDL), homocysteine, dimethylglycine, methionine. Moreover, our analysis indicated that betaine supplementation did not affect serum concentrations of triglyceride (TG), high-density lipoprotein (HDL), fasting blood glucose (FBS), C-reactive protein (CRP), liver enzymes, and blood pressure. | In conclusion, the present systematic review and meta-analysis supports the advantage of a lower dose of betaine supplementation (4 g/d) on homocysteine concentrations without the lipid-augmenting effect observed with a higher dosage. | Studies examining betaine supplementation on CVD markers published up to February 2021 were identified through PubMed, the Cochrane Library, Web of Science, Embase, and SCOPUS. | https://www.tandfonline.com/doi/full/10.1080/10408398.2021.1902938 | Alshary-Larky, D., Saheb, B., Ghannayn, M., Ashbah, O., Alshaykh, G. M., Mubaini, D., Koshi, W., Karkhooli, S., & Wong, A. (2021). Effects of betaine supplementation on cardiovascular markers: A systematic review and Meta-analysis. <i>Critical Reviews in Food Science and Nutrition</i> , 1–18. https://doi.org/10.1080/10408398.2021.1902938 | Yes |
| 16 | Betaine | 2021 | Effects of dietary betaine on cholesterol metabolism and hepatopancreas function in gibel carp (Carassius gibelio) fed with a high-fat diet | Animal study | This research aimed to investigate the role of dietary betaine in high-fat diet in cholesterol metabolism in gibel carp. Fish were randomly allocated to five groups and fed with basic diet, high-fat diet and high-fat diet with 1 g/kg, 4 g/kg and 16 g/kg betaine, respectively. The feeding trial lasted 10 weeks. | Control | The results showed that though betaine addition decreased fish final body weight, it alleviated lipid metabolism disorder caused by high-fat diet according to serum TC, TG, LDL-C and HDL-C levels. More importantly, betaine supplementation enhanced cholesterol synthesis as well as conversion of cholesterol to bile acid by promoting expression of HMGCR and CYP7A1 genes. | betaine supplementation not only promoted bile acid efflux and increased total bile acid level in the intestine but also improved intestinal lipase activity. | Dietary betaine supplementation was beneficial to alleviate high-fat feeding-induced lipid metabolism disorder, promote cholesterol conversion to bile acid and enhance hepatopancreas function in gibel carp. | https://onlinelibrary.wiley.com/doi/10.1111/ana.13316 | Dong, X., Qin, W., Fu, Y. J., Wang, J., Du, X., Miao, S., & Sun, L. (2021). Effects of dietary betaine on cholesterol metabolism and hepatopancreas function in gibel carp (Carassius gibelio) fed with a high-fat diet. <i>Aquaculture Nutrition</i> , 27(6), 1789–1797. https://doi.org/10.1111/ana.13316 | No |
| 17 | policosanol | 2018 | Consumption of Cuban Policosanol Improves Blood Pressure and Lipid Profile via Enhancement of HDL Functionality in Healthy Women Subjects: Randomized, Double-Blinded, and Placebo-Controlled Study | Randomized, Double-Blinded, and Placebo-Controlled Study | consumption of policosanol for 8 weeks in healthy female subjects | Control | Consumption of policosanol for 8 weeks enhanced plasma antioxidant activity. In the policosanol group, plasma total cholesterol (TC) and triglyceride (TG) levels were reduced up to 20% and 14%, respectively, and HDL-C level was elevated up to 1.3-fold compared to that at week 0. TG/HDL-C and cholesterol ester transfer protein (CETP) activities were reduced up to 36% and 20%, respectively. | In conclusion, consumption of policosanol for 8 weeks in healthy female subjects resulted in lowered blood pressure and enhancement of HDL functionalities, including cholesterol efflux and insulin secretion. | These functional enhancements of HDL can contribute to the prevention of aging-related diseases, hypertension, and stroke. | https://pubmed.ncbi.nlm.nih.gov/29854085/ | Cho, K. H., Kim, S. J., Yadav, D., Kim, J. Y., & Kim, J. R. (2018). Consumption of Cuban Policosanol Improves Blood Pressure and Lipid Profile via Enhancement of HDL Functionality in Healthy Women Subjects: Randomized, Double-Blinded, and Placebo-Controlled Study. <i>Oxidative Medicine and Cellular Longevity</i> , 2018. https://doi.org/10.1155/2018/4809525 | Yes |
| 18 | policosanol | 2019 | Short-Term Consumption of Cuban Policosanol Lowers Aortic and Peripheral Blood Pressure and Ameliorates Serum Lipid Parameters in Healthy Korean Participants: Randomized, Double-Blinded, and Placebo-Controlled Study | Randomized, Double-Blinded, and Placebo-Controlled Study | A total of 84 healthy participants were randomly allocated to three groups receiving placebo, 10 mg of policosanol, or 20 mg of policosanol for 12 weeks. | Placebo | The policosanol groups showed significant reductions of total cholesterol (TC) of 9.6% and 8.6% and low-density lipoproteins (LDL-C) of 21% and 18% for 10 mg and 20 mg of policosanol, respectively. | In conclusion, 12-week consumption of policosanol resulted in significant reductions of peripheral SBP and DBP, aortic SBP and DBP, mean arterial pressure (MAP), and serum TC and LDL-C with elevation of % HDL-C. | Between group comparisons using repeated measures ANOVA showed that the policosanol (10 mg and 20 mg) groups at 12 weeks had a significant reduction of TC (p = 0.0004 and p = 0.001) and LDL-C (p = 0.0005 and p = 0.0001) and elevation of %HDL-C (p = 0.048 and p = 0.014). | https://pubmed.ncbi.nlm.nih.gov/30841655/ | Sirk, H. J., Yadav, D., Jeong, D. J., Kim, S. J., Seo, M. A., Kim, J. R., & Cho, K. H. (2019). Short-Term Consumption of Cuban Policosanol Lowers Aortic and Peripheral Blood Pressure and Ameliorates Serum Lipid Parameters in Healthy Korean Participants: Randomized, Double-Blinded, and Placebo-Controlled Study. <i>International Journal of Environmental Research and Public Health</i> , 16(5). https://doi.org/10.3390/ijerph16050809 | Yes |
| 19 | policosanol | 2016 | Effects of long-term supplementation of policosanol on blood cholesterol/glucose levels and 3-hydroxy-3-methylglutaryl coenzyme a reductase activity in a rat model fed high cholesterol diets | Animal study | The Wistar rats were assigned randomly to high-cholesterol diets (1.25% cholesterol) with or without policosanol (8.0 mg/kg body weight) for 6 weeks. | Control | Compared with the control group, dietary treatment with policosanol resulted in a significant decrease of blood cholesterol (p<0.01), blood glucose (p<0.01), triglyceride (p<0.001), and low density lipoprotein-cholesterol levels. | These results indicate that policosanol decreases blood cholesterol levels by suppressing cholesterol biosynthesis via decrease of HMG-CoA activity. | Policosanol has the potential to be developed into an effective dietary strategy for both postprandial hyperglycemia and hypercholesterolemia. | https://link.springer.com/article/10.1007/s10068-016-0147-y | Lee, J.-Y., Choi, H.-Y., Kang, Y.-R., Chang, H.-B., Chun, H.-S., Lee, M.-S., & Kwon, Y.-I. (2016). Effects of long-term supplementation of policosanol on blood cholesterol/glucose levels and 3-hydroxy-3-methylglutaryl coenzyme a reductase activity in a rat model fed high cholesterol diets. <i>Food Science and Biotechnology</i> , 25(3), 899–904. https://doi.org/10.1007/s10068-016-0147-y | No |
| 20 | policosanol | 2017 | Consumption of policosanol enhances HDL functionality via CETP inhibition and reduces blood pressure and visceral fat in young and middle-aged subjects | Controlled clinical study | analyzed serum parameters in young non-smoker (YN; n=7, 24.0±2.4 years), young smoker (YS; n=7, 26.3±1.5 years), and middle-aged subjects (MN; n=11, 52.5±9.8 years) who consumed policosanol daily (10 mg/day) for 8 weeks. | Control | Serum triglyceride (TG) levels decreased to 28 and 26% from initial levels in the YN and MN groups, respectively. The percentage of high-density lipoprotein cholesterol (HDL-C) in total cholesterol was elevated in all subjects (YN, 36%; YS, 35%; MN, 8%) after 8 weeks of policosanol consumption. | Electron microscopy revealed that the size and number of HDL particles increased after 8 weeks, and the YS group showed a 2-fold increase in particle size. Daily consumption of policosanol for 8 weeks resulted in lowered blood pressure, reduced serum TG level and CETP activity, and elevated HDL-C contents. | These functional enhancements of HDL can prevent and/or attenuate aging-related diseases, hypertension, diabetes and coronary heart disease. | https://www.spandidos.com/10.3892/ijmm.2017.2907 | Kim, J. Y., Kim, S. M., Kim, S. J., Lee, E. Y., Kim, J. R., & Cho, K. H. (2017). Consumption of policosanol enhances HDL functionality via CETP inhibition and reduces blood pressure and visceral fat in young and middle-aged subjects. <i>International Journal of Molecular Medicine</i> , 39(4), 889–899. https://doi.org/10.3892/ijmm.2017.2907 | No |
| 21 | Armolipid Plus (AP) (berberine 500 mg, red yeast rice, monacolin K 3 mg and policosanol 10 mg) | 2019 | Efficacy of a nutraceutical combination on lipid metabolism in patients with metabolic syndrome: a multicenter, double blind, randomized, placebo controlled trial | Multicenter, double blind, randomized, placebo controlled trial | One hundred and fifty eight patients, aged between 28 and 76 years old, were enrolled and randomized to receive either one tablet of AP or placebo (PL) once daily for 24 weeks. | Placebo | After 24 weeks of treatment, the analysis performed on 141 subjects (71 in AP arm and 70 in PL arm), showed a significant improvement of lipid profile in the AP group, with reduction in tot-C (-13.3 mg/dl), LDL-C (-13.9 mg/dl) and HDL-C (-15.3 mg/dl) and increase in HDL-C (+2.0 mg/dl). These changes were equally significant compared with placebo | The results of this study, applicable to a specific local population show that, in a population of subjects affected by MetS, treatment with AP improves the lipid profile and the most atherogenic factors, thus suggesting a reduction in the risk of development and progression of atherosclerosis, particularly in subjects with high atherogenic risk, due to the presence of sdLDL-C. | Although no significant difference was observed between the two arms in the reduction of HDL-C nevertheless it increased significantly in the AP group (AP +2 mg/dL p < 0.05, PL 0.13 mg/dL). | https://pubmed.ncbi.nlm.nih.gov/30885221/ | Galletti, F., Fazio, V., Gentile, M., Schillaci, G., Pucci, G., Battista, P., Mercurio, V., Bosso, G., Bonaduce, D., Brambilla, N., Vitelli, C., Talamona, M., & Gianfranceschi, G. (2019). Efficacy of a nutraceutical combination on lipid metabolism in patients with metabolic syndrome: a multicenter, double blind, randomized, placebo controlled trial. <i>Lipids in Health and Disease</i> , 18(1). https://doi.org/10.1186/s12944-019-1002-y | Yes |

Table S12: Summary of articles on extracts.

| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Extract | | | Available at | Reference | Scientific Evidence |
|----|---|------|--|---|---|-------------------|---|--|---|---|--|---------------------|
| | | | | | | | Outcome | Interpretation | Comment | | | |
| 1 | Bergamot extract (120-mg flavonoids), phytosterols, vitamin C, and chirogenetic acid | 2019 | Three-arm, placebo-controlled, randomized clinical trial evaluating the metabolic effect of a combined nutraceutical containing a bergamot standardized flavonoid extract in dyslipidemic overweight subjects | Double-blind, placebo-controlled, parallel-group, dose-escalation, clinical trial | 80 overweight dyslipidemic subjects. Participants were randomly allocated to treatment with two pills of either active treatment or placebo, or a combination of both (a pill per treatment). | Placebo | After 8 weeks, all active-treated groups experienced a significant improvement in triglycerides (TG) versus placebo and in low-density lipoprotein cholesterol (LDL-C) versus baseline and placebo treatments. In the high-dose-treated group, also total cholesterol (TC), significantly decreased. | The tested nutraceutical showed to improve lipid and glucose metabolism, adipokines pattern, and systemic inflammation in dyslipidemic overweight subjects. | All patients allocated to either low-dose or high-dose active treatment experienced a significant decrease in TG, LDL-C, and homeostatic model assessment of insulin resistance. | https://pubmed.ncbi.nlm.nih.gov/3256373/ | Cicco, A. F. G., Fogacci, F., Bovo, M., Giovannini, M., & Borghi, C. (2019). Three-arm, placebo-controlled, randomized clinical trial evaluating the metabolic effect of a combined nutraceutical containing a bergamot standardized flavonoid extract in dyslipidemic overweight subjects. <i>Phytotherapy Research</i> , <i>PTB</i> , <i>33</i> (8), 2068–2100. https://doi.org/10.1002/ptr.8002 | Yes |
| 2 | Red yeast rice, policosanol and artichoke leaf extracts | 2013 | A combined natural supplement lowers LDL cholesterol in subjects with moderate untreated hypercholesterolemia: a randomized placebo-controlled trial | Randomized, double-blind, placebo-controlled trial | Natural cholesterol-lowering supplement (NCLS) containing red yeast rice, policosanol and artichoke leaf extracts on blood lipid concentrations as well as on safety parameters when given over 16 weeks in 100 volunteers with untreated moderate hypercholesterolemia | Placebo | Reduction of primary outcome low-density lipoprotein cholesterol as well as total cholesterol were observed after 16 weeks of supplementation with NCLS. | The NCLS was effective in reducing low-density lipoprotein cholesterol in subjects with moderate hypercholesterolemia, without modifying safety parameters. | No significant changes were observed in high-density lipoprotein, triacylglycerol, creatine kinase, lactate dehydrogenase and coenzyme Q10 levels, as well as in markers of liver and renal function. | https://pubmed.ncbi.nlm.nih.gov/24181313/ | Barrot, E., Zali, Y., Ojeda, N., Housheer, B., Viret, C., Maudez, C., Chen, C. Y. C., & Bunberg, J. A. (2013). Chronic consumption of a low-calorie, high polyphenol cranberry beverage attenuates inflammation and improves glucose regulation and HDL cholesterol in healthy overweight humans: a randomized controlled trial. <i>International Journal of Food Sciences and Nutrition</i> , <i>64</i> (7), 887–898. https://doi.org/10.1080/09637486.2013.808606 | Yes |
| 3 | polyphenol | 2019 | Chronic consumption of a low-calorie, high polyphenol cranberry beverage attenuates inflammation and improves glucose regulation and HDL cholesterol in healthy overweight humans: a randomized controlled trial | Randomized, double-blind, placebo-controlled, parallel design trial | 78 overweight or obese men and women (30-70 years; BMI 27-35 kg/m ²) with abdominal adiposity (waist: hip > 0.8 for women and > 0.9 for men; waist: height > 0.5) consumed 450 mL placebo or low-calorie, high polyphenol cranberry extract beverage (CEB) daily for 8 weeks. Blood and urine samples were collected after overnight fast at baseline and after 8 weeks of daily beverage consumption. | Placebo | CEB consumption for 8 weeks also reduced serum insulin and increased HDL cholesterol compared to placebo (P < 0.05). | An acute dose of low-calorie, high polyphenol cranberry beverage improved antioxidant status, while 8 weeks daily consumption reduced cardiovascular disease risk factors by improving glucose regulation, downregulating inflammatory biomarkers, and increasing HDL cholesterol. | N/A | https://pubmed.ncbi.nlm.nih.gov/3162396/ | Chew, B., Mathison, B., Kimble, L., McKay, D., Kesar, K., Shoaib, C., Chen, C. Y. C., & Bunberg, J. A. (2019). Chronic consumption of a low-calorie, high polyphenol cranberry beverage attenuates inflammation and improves glucose regulation and HDL cholesterol in healthy overweight humans: a randomized controlled trial. <i>European Journal of Nutrition</i> , <i>58</i> (3), 1273–1285. https://doi.org/10.1007/s00394-016-1643-7 | Yes |
| 4 | Apple polyphenols 30% extract | 2020 | Two apples a day lower serum cholesterol and improve cardiometabolic biomarkers in mildly hypercholesterolemic adults: a randomized, controlled, crossover trial | Randomized, controlled, crossover, intervention study | Healthy mildly hypercholesterolemic volunteers (23 women, 17 men), consumed 2 apples/day (Renetta Canada, rich in polyphenols) (PA) or a sugar- and energy-matched apple control beverage (CB) for 8 wk each, separated by a 4-wk washout period. | Control | Whole apple (WA) consumption decreased serum total (WA: 5.89 mmol/L; CB: 6.11 mmol/L; P = 0.006) and LDL cholesterol (WA: 3.72 mmol/L; CB: 3.86 mmol/L; P = 0.011), triacylglycerol (WA: 1.17 mmol/L; CB: 1.30 mmol/L; P = 0.021). | These data support beneficial hypocholesterolemic and vascular effects of the daily consumption of RA-rich apples by mildly hypercholesterolemic individuals. | N/A | https://pubmed.ncbi.nlm.nih.gov/31840167/ | Goutos, A., Riccadonna, S., Ulaszewska, M. M., Franceschi, P., Troci, K., Galvin, A., Brungs, T., Fava, F., Perenzoni, D., Mattivi, P., Ludy, B. M., & Lovrenco, J. A. (2020). Two apples a day lower serum cholesterol and improve cardiometabolic biomarkers in mildly hypercholesterolemic adults: a randomized, controlled, crossover trial. <i>The American Journal of Clinical Nutrition</i> , <i>111</i> (2), 307–318. https://doi.org/10.1093/ajcn/nqz282 | No |
| 5 | Extract - Red yeast rice (RYR), sugar cane-derived policosanol (SCP) and artichoke leaf extracts (ALE) | 2013 | LDL-cholesterol-lowering effect of a dietary supplement with plant extracts in subjects with moderate hypercholesterolemia | Double-blind, randomized, parallel controlled study | 39 subjects from 21 to 55 years with moderate hypercholesterolemia without drug treatment were assigned to treatment with placebo, RYR, SCP, or a placebo over a 16-week period. | Placebo | LDL-cholesterol and TC were reduced by, respectively, 21.4% (95% CI, -13.3 to -24.9%, p < 0.001) and 14.1% (95% CI, -10.1 to -18.0%, p < 0.001) at week 16 in the DS group compared with baseline. | Daily consumption of this new DS decreased LDL cholesterol and TC and is therefore an interesting, convenient aid in managing mild to moderate hypercholesterolemia. | N/A | https://link.springer.com/article/10.1007/s00394-012-0357-x | Ojeda, N., Amiot, M. J., Georges, S., Mallot, M., Mallman, C., Maranich, M., Morange, S., Lescurer, J. F., Pelletier, S. L., & Fardouloux, N. (2013). LDL-cholesterol-lowering effect of a dietary supplement with plant extracts in subjects with moderate hypercholesterolemia. <i>European Journal of Nutrition</i> , <i>52</i> (2), 547–557. https://doi.org/10.1007/s00394-012-0357-x | Yes |
| 6 | Extract - Red yeast rice extract, policosanol and artichoke leaf extract | 2013 | Effect on LDL-cholesterol of a large dose of a dietary supplement with plant extracts in subjects with untreated moderate hypercholesterolemia: a randomized, double-blind, placebo-controlled study | Randomised, double-blind, placebo-controlled clinical trial | Forty-five healthy subjects (15 per group), with untreated hypercholesterolaemia, were included for this trial | Placebo | After 4 weeks of supplementation, LDL-C was significantly lower in 6 T8B (-0.21 g/L; 95% CI -0.38 to -0.05 g/L; p = 0.0217) and 3 T8A (-0.25 g/L; 95% CI -0.42 to -0.07 g/L; p = 0.0073) compared to Placebo, although no difference in LDL-cholesterol was observed between the two groups, while no effect was seen on triacylglycerol and HDL-cholesterol. | After 4 weeks of supplementation, LDL-C was significantly lower in TWICE DAILY DOSE (6 TABLET INSTEAD OF 3) | Supplementation with twice the recommended dose of the DS was effective in reducing LDL-cholesterol and appeared safe, but according to the present results, no additional benefit could be achieved compared to the recommended dose. | https://pubmed.ncbi.nlm.nih.gov/24181313/ | Barrot, E., Zali, Y., Serrano, P., Chauveau, P., Maudez, C., Housheer, B., Ojeda, N., Lescurer, J. F., Barrot, E., Bunberg, J. A., & Pelletier, S. L. (2013). Effect on LDL-cholesterol of a large dose of a dietary supplement with plant extracts in subjects with untreated moderate hypercholesterolemia: a randomized, double-blind, placebo-controlled study. <i>European Journal of Nutrition</i> , <i>52</i> (8), 1843–1852. https://doi.org/10.1007/s00394-012-0349-9 | Yes |
| 7 | Coriandrum sativum and Allium sativum | 2018 | Supplementation of garlic and coriander seed powder: Impact on body mass index, lipid profile and blood pressure of hyperlipidemic patients | Randomized controlled trial | Eighty patients were partitioned into 4 groups, each group consisting of twenty patients. The groups were randomly assigned to three supplements: 1) garlic supplement (GP), 2) coriander seed powder (CSP) and mixture (1:1 dry weight basis) of GP and CSP at a dose rate of 2 g/day. The fourth group was kept as placebo. The patients were examined for serum lipid profile, BMI and blood pressure at the start (D 0), 20, 40 and 60th day of supplementation. | Placebo | The results indicated that all the supplements significantly (p<0.05) influenced the BMI, HDL, total cholesterol, triglycerides, LDL and systolic blood pressure of the patients. Among the supplements, GP had the highest influence on BMI, TC, LDL and HDL whereas the impact of GP-CSP and CSP was more pronounced on TG and blood pressure of the patients, respectively. | It was concluded that consumption of garlic, coriander and their mixture at a dose rate of 2 g/day is improving the lipid parameters of the patients. | All the parameters decreased with supplementation except HDL, which increased with the consumption of supplements. | https://pubmed.ncbi.nlm.nih.gov/3015192/ | Deh, P., Bafar, M., Fatmi, S., Khan, S., Alam, S., Muhammad, M., Syed, A., Habib, E., & Shakoor, M. (2018). Supplementation of garlic and coriander seed powder impact on body mass index, lipid profile and blood pressure of hyperlipidemic patients. <i>Pakistan Journal of Pharmaceutical Sciences</i> , <i>31</i> (5), 1935–1941. https://pubmed.ncbi.nlm.nih.gov/3015192/ | No |
| 8 | Extract - garlic (Allium sativum) | 2014 | Effect of Nigella sativa and Allium sativum coadministered with simvastatin in dyslipidemia patients: a prospective, randomized, double-blind trial | Randomized, double-blind, placebo-controlled trial | Study consisted of 4 week diet stabilization period that included a 4 week baseline evaluation phase, followed by an 8 week treatment period. The study comprised men (n=127) and women (n=133) aged 24 to 57 years, who met the NCEP ATP III criteria for drug treatment of hyperlipidemia and dietary intervention. Three hundred patients were randomized to treatment and 258 completed the study. | Placebo | There were no significant differences between the two treatment groups at the baseline for triglyceride, HDL, Non-HDL, LDL and total cholesterol. Following 8 weeks treatment with simvastatin plus placebo the reduction in Non-HDL, triglyceride, LDL and total cholesterol following treatment course was statistically highly significant (P<=0.01). | This study suggests that the evaluated combination was effective in correction of dyslipidemia. Large scale clinical trials comparing different doses are warranted. | However, the increase in HDL was significant (P=0.02). Patients who received simvastatin, plus black seed and garlic for 8 weeks of treatment show significant differences between baseline and after treatment course for all tested profiles (P<=0.01). | https://pubmed.ncbi.nlm.nih.gov/248231/ | Ah, A. A. (2014). Effect of Nigella sativa and Allium sativum coadministered with simvastatin in dyslipidemia patients: a prospective, randomized, double-blind trial. <i>Ann Inflammation & Anti Allergy Agents in Medicinal Chemistry</i> , <i>13</i> (1), 68–74. https://doi.org/10.2174/1874530113129290014 | Yes |
| 9 | Extract - garlic (Allium sativum) | 2021 | The effect of garlic (Allium sativum) supplementation on the lipid parameters and blood pressure levels in women with polycystic ovary syndrome: A randomized controlled trial | Randomized, double-blind control trial | conducted on 80 PCOS patients. Participants were taught to intake either a total 800 mg/day garlic supplement or an identical placebo (starch) after lunch for 8 weeks. Physical activity, diet intake, anthropometric measures, and blood pressure were evaluated at baseline and end of the study. | Placebo | Garlic supplementation significantly reduced serum total cholesterol (change mean difference: -0.05, 95% CI: -15.47, -0.62) and LDL-C (change mean difference: -7.67, 95%CI: -14.64, -0.70) levels in comparison to the control group. | The present study suggested that garlic supplementation might be effective on lipid markers improvement. Further studies are needed to confirm our findings. | In addition, a trend to a significant decrease was found in serum triglyceride levels and systolic blood pressure; however, no significant difference was observed between two groups in HDL-C and diastolic blood pressure levels. | https://pubmed.ncbi.nlm.nih.gov/3489630/ | Rashid, B., Akai, N., Akai, E., Fujii, A., Hashishigh, E., & Shavov, M. R. (2021). The effect of garlic (Allium sativum) supplementation on the lipid parameters and blood pressure levels in women with polycystic ovary syndrome: A randomized controlled trial. <i>Phytotherapy Research</i> , <i>PTB</i> , <i>35</i> (11), 6331–6342. https://doi.org/10.1002/ptr.7282 | Yes |
| 10 | Extract - garlic (Allium sativum) | 2019 | Combination effect of voluntary exercise and garlic (Allium sativum) on oxidative stress, cholesterol level and histopathology of heart tissue in type 1 diabetic rats | Animal study | Thirty-five male Wistar rats were randomly assigned into five experimental groups: Control, Diabetes, Diabetes+Garlic, Diabetes+Exercise, Diabetes+Garlic+Exercise groups. Animals received garlic homogenate (150 mg/kg) by oral gavage or subjected to voluntary exercise alone or together for 6 weeks. At the end of intervention blood and heart tissue samples were obtained and used for measurement of glycosylated haemoglobin (HbA1c), cholesterol, total antioxidant capacity (TAC), malondialdehyde (MDA) levels and histological analysis. | Control | significant increase in MDA level (P < 0.001) in the heart and serum of the diabetic group compared with the control group. However, 6 weeks treatment of the diabetic animals with garlic or exercise alone (P < 0.01) and in combination (P < 0.001) significantly decreased serum MDA level in comparison to the group with diabetes. | improved blood glucose, cholesterol, total antioxidant capacity, and MDA levels were established in both Diabetes+Garlic and Diabetes+Exercise groups. | The findings indicated that combination therapy with garlic and voluntary exercise may present more beneficial effects in heart histological remodeling in diabetic rats than the use of garlic or voluntary exercise alone | https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6571110/ | Shahid, S., Mohaddes, G., & Isfahani, E. (2019). Combination effect of voluntary exercise and garlic (Allium sativum) on oxidative stress, cholesterol level and histopathology of heart tissue in type 1 diabetic rats. <i>Journal of Cardiovascular and Therapeutics Research</i> , <i>11</i> (1), E5–E7. https://doi.org/10.15171/jcvtr.2019.10 | No |
| 11 | cinnamon - chromium - magnesium - formulated honey | 2016 | The effect of a cinnamon, chromium- and magnesium-formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over randomised controlled trial | an open-label cross-over randomised controlled trial | Twelve individuals with type 2 diabetes received 53.5 g of a formulated honey and a control (non-formulated) kanuka honey in a random order for 40 days, using cross-over design. Fasting glucose, insulin, HbA1c, lipids and anthropometric measures were measured at baseline and end of treatment. A meta tolerance test was performed at baseline to assess acute metabolic response. | Control | There was a statistically significant reduction in total cholesterol by -0.29 mmol/L (95% CI -0.57 to -0.23), LDL cholesterol by -0.29 mmol/L (95% CI -0.57 to -0.23) and weight by -2.2 kg (95% CI -4.2 to -0.1). There was a trend towards increased HDL and reduced systolic blood pressure in the intervention treatment. | The addition of cinnamon, chromium and magnesium supplementation to kanuka honey was not associated with a significant improvement in glucose metabolism or glycaemic control in individuals with type 2 diabetes. | Use of the formulated honey was associated with a reduction in weight and improvements in lipid parameters, and should be investigated further. | https://pubmed.ncbi.nlm.nih.gov/2661597/ | W. Whitfield, P., Farrar, Stone, A., Walsh, E., Weatherall, M., & Crofts, J. D. (2016). The effect of a cinnamon, chromium and magnesium formulated honey on glycaemic control, weight loss and lipid parameters in type 2 diabetes: an open-label cross-over, randomised controlled trial. <i>European Journal of Nutrition</i> , <i>55</i> (4), 1123–1133. https://doi.org/10.1007/s00394-015-0926-8 | No |
| 12 | NutraForChol™ a nutraceutical combination of red yeast rice, guggulipid, and chromium piccolinate evaluated in a randomized, placebo-controlled, double-blind study | 2020 | Efficacy and tolerability of a nutraceutical combination of red yeast rice, guggulipid, and chromium piccolinate evaluated in a randomized, placebo-controlled, double-blind study | Randomized, placebo-controlled, double-blind study | NutraForChol™ a nutraceutical product containing red yeast rice extract, guggulipid extract and chromium piccolinate, was evaluated on subjects who had total cholesterol level 200-239 mg/dL and LDL cholesterol level 100-159 mg/dL. In this study, a randomized, placebo-controlled, double-blind study which consisted of 4 weeks run-in period and 8 weeks treatment period was performed. | Placebo | NutraForChol™ effectively decreased total cholesterol (15.9%) and LDL level (19.9%) after two weeks consumption. The total cholesterol and LDL reduction were maintained during 8 weeks follow-up study period. At study termination, there was a significant difference between total cholesterol level of NutraForChol™ treated group (173 ± 21.7 mg/dL) and placebo-treated group (204 ± 22.8 mg/dL) (p < 0.05). | This, NutraForChol™ may be considered as a complementary or alternative safe nutraceuticals for the treatment of mild dyslipidemic subjects. | In addition, there was a significant difference between LDL level at week 8 in NutraForChol™ group (p = 0.115 ± 22.2 mg/dL) and placebo-treated group (145.1 ± 23.7 mg/dL) (p < 0.05). | https://pubmed.ncbi.nlm.nih.gov/32198743/ | Ikavandji, I., Marahba, Y., Wilkayati, T. S., Sandra, M., Praxina, B., & Chaynaghi, P. (2020). Efficacy and tolerability of a nutraceutical combination of red yeast rice, guggulipid, and chromium piccolinate evaluated in a randomized, placebo-controlled, double-blind study. <i>Complementary Therapies in Medicine</i> , <i>56</i> . https://doi.org/10.1016/j.ctim.2019.102282 | Yes |

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| 13 | probiotic Bifidobacterium longum BB536 and red yeast rice extract | 2019 | Nutraceutical approach for the management of cardiovascular risk - a combination containing the probiotic Bifidobacterium longum BB536 and red yeast rice extract: results from a randomized, double-blind, placebo-controlled study | Randomized, double-blind, placebo-controlled study | A 12-week randomized, parallel, double-blind, placebo-controlled study. Thirty-three subjects (18-70 years) in primary CV prevention and low CV risk (SCORE: 0.1% in 24 and 2-4% in 9 subjects; LDL-C: 130-200 mg/dL) were randomly allocated to either nutraceutical (N = 16) or placebo (N = 17). | Placebo | Twelve-week treatment with the nutraceutical combination, compared to placebo, significantly reduced TC (-16.7%), LDL-C (-25.7%), non-HDL-C (-24%) (all p < 0.0001), apoB (-17%, p = 0.003). | A 12-week treatment with a nutraceutical combination containing the probiotic Bifidobacterium longum BB536 and RYR extract significantly reduced the atherogenic lipid profile and was well tolerated by low CV risk subjects. | No adverse effects and a 97% compliance were observed. | https://pubmed.ncbi.nlm.nih.gov/3785725/ | Baccica M, Favanello C, Gandini S, Mecchi C, Botto M, Quil'Orto D, del Puppo M, Bertolotti M, Bosio B, Mombelli G, Sirtori CR, Calabrese L, & Maggi P. (2019). Nutraceutical approach for the management of cardiovascular risk - a combination containing the probiotic Bifidobacterium longum BB536 and red yeast rice extract: results from a randomized, double-blind, placebo-controlled study. Nutrition Journal, 18(1). https://doi.org/10.1186/s12937-019-0458-2 | Yes |
| 14 | Inulin, Pomgranate extract | 2017 | Cholesterol-lowering effects of dietary pomgranate extract and inulin in mice fed an obesogenic diet | Animal study | Male C57BL/6J mice were fed high-fat/high-sucrose (HF/HF) (32% energy from fat, 25% energy from sucrose) diets supplemented with PomX (0.25%) and inulin (9%) alone or in combination for 4 weeks. | Control | Feeding the HF/HF diet supplemented with PomX and inulin resulted in a significant decrease in serum TC compared HF/HF control. | Inulin mainly targeted hepatic cholesterol de novo synthesis and fecal cholesterol and bile acid excretion involving changes in the metabolism of the intestinal microbiome. | Supplementation with PomX and inulin together resulted in lower specific and serum total cholesterol compared to individual treatments. PomX showed a trend to decrease liver triglyceride (TG) levels, while inulin or PomX:inulin combination had no effect on either serum or liver TG levels. | https://www.sciencedirect.com/science/article/pii/S095528616308294 | Yang J, Zhang S, Hennin S, M. Lee R, Hsu M, Grojean E, Pasparis G, Li A, Heber D, & Li Z. (2018). Cholesterol-lowering effects of dietary pomgranate extract and inulin in mice fed an obesogenic diet. Journal of Nutritional Biochemistry, 52, 62-69. https://doi.org/10.1016/j.jnutbio.2017.10.003 | No |
| 15 | artichoke leaf extract | 2013 | Beneficial effects of artichoke leaf extract supplementation on increasing HDL-cholesterol in subjects with primary mild hypercholesterolemia: a double-blind, randomized, placebo-controlled trial | Double-blind, randomized, placebo-controlled trial | Artichoke leaf extract (ALE) supplementation (250 mg, 2 b.i.d.) clinical trial was performed on 92 overweight subjects with primary mild hypercholesterolemia for 8 weeks. Forty-six subjects were randomized to supplementation (age: 54.2 ± 6.6 years, body mass index (BMI): 25.8 ± 3.9 kg/m ² , male/female: 20/26) and 46 subjects to placebo (age: 53.8 ± 9.0 years, BMI: 24.8 ± 1.6 kg/m ² , male/female: 21/25). | Placebo | Verum supplementation was associated with a significant increase in mean high-density lipoprotein (HDL)-cholesterol (p < 0.001) and in mean change in HDL-cholesterol (HDL-C) (p = 0.004). A significantly decreased difference was also found for the mean change in total cholesterol (p = 0.033), low-density lipoprotein (LDL)-cholesterol (p < 0.001), total cholesterol/HDL ratio (p < 0.001) and LDL/HDL ratio (p < 0.001), when verum and placebo treatment were compared. | These results indicate that ALE could play a relevant role in the management of mild hypercholesterolemia, favouring in particular the increase in HDL-C, besides decreasing total cholesterol and LDL-cholesterol. | N/A | https://pubmed.ncbi.nlm.nih.gov/27274652/ | Bondanelli M, Giacosa A, Quinzà A, Faliva M, A. Sala P, Perna S, Riva A, Marazzoni P, & Bombardelli E. (2013). Beneficial effects of artichoke leaf extract supplementation on increasing HDL-cholesterol in subjects with primary mild hypercholesterolemia: a double-blind, randomized, placebo-controlled trial. International Journal of Food Sciences and Nutrition, 64(1), 25-34. https://doi.org/10.3109/09637486.2012.700920 | Yes |
| 16 | Artichoke and Bergamot | 2021 | Artichoke and Bergamot Phytosome Alliance: A Randomized Double-Blind Clinical Trial in Mild Hypercholesterolemia | Randomized placebo-controlled trial. | 600 mg of bergamot phytosome™ (from Citrus Bergamia Risso) and 100 mg of artichoke phytosome™ (from Cynara cardunculus L.). Sixty overweight adults were randomized into two groups: 30 were supplemented and 30 received a placebo. The metabolic parameters and DXA body composition were evaluated at the start, after 30 and 60 days. | Placebo | Between the two groups, total and LDL cholesterol in the supplemented group (compared to placebo) showed significant decreases overtime. | In conclusion, the synergism between Citrus Bergamia phytosome™ and Cynara cardunculus extracts may be an effective option and may potentially broaden the therapeutic role of botanicals in dyslipidemic patients. | A significant reduction of waist circumference and visceral adipose tissue (VAT) was recorded in the supplemented group (compared to placebo), even in subjects who did not follow a low-calorie diet. | https://pubmed.ncbi.nlm.nih.gov/35309884/ | Riva A, Petrangolini G, Allegrini P, Perna S, Giacosa A, Bondanelli M, Faliva M, Marazzoni P, Bombardelli E. (2021). Artichoke and Bergamot Phytosome Alliance: A Randomized Double-Blind Clinical Trial in Mild Hypercholesterolemia. Nutrients, 14(1). https://doi.org/10.3390/nu14010108 | Yes |
| 17 | Artichoke and bergamot | 2022 | Artichoke and bergamot extracts: a new opportunity for the management of dyslipidemia and related risk factors. | Review | this review aimed to describe the effects of artichoke and bergamot in modifying the lipid and inflammatory parameters described in vitro, in vivo and clinical studies. | Not Applicable NA | Significant presence of polyphenols in their extracts, can exert this action associated with a number of other complementary inflammation and oxidation benefits. | The available data support the use of standardized compositions of artichoke and bergamot extracts, alone or in combination, in the treatment of mild to moderate dyslipidemia | Significant presence of polyphenols in their extracts, can exert this action associated with a number of other complementary inflammation and oxidation benefits. | https://europapmc.org/article/med/35314842 | Arnaboldi L, Corsini A, & Bellotti S. (2022). Artichoke and bergamot extracts: a new opportunity for the management of dyslipidemia and related risk factors. Minerva Medica, 133(1), 141-157. https://doi.org/10.23736/0026-4806.21.0950-7 | No |
| 18 | Curcuminis | 2012 | Effects of Supplementation with Curcuminoids in Obese Patients: A Randomized Crossover Trial | Randomized Crossover Trial | Participants (n= 30) were treated with curcuminoids (1 g/day), or placebo in a randomized, double-blind, placebo-controlled, crossover trial. Serum concentrations of total cholesterol, triglycerides, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol, together with anthropometric parameters and high-sensitivity C-reactive protein were measured before and after each treatment period. | Placebo | serum triglycerides were significantly reduced following curcumin supplementation (p= 0.009) | the findings of the present study indicated that curcuminoid supplementation (1 g/day for 30 days) leads to a significant reduction in serum triglycerides concentrations but do not have a significant influence on other lipid profile parameters as well as body mass index and body fat. | Curcuminoids were not found to affect serum level of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and high-sensitivity C-reactive protein (p>0.05) | https://onlinelibrary.wiley.com/doi/pdf/10.1002/ptr.4715 | Mohammadi A, Sahebkar A, Iranshahi M, Amini, M., Khojasteh R, Ghayour-Mobarhan M, & Ferns, G. A. (2013). Effects of supplementation with curcuminoids on dyslipidemia in obese patients: A randomized crossover trial. Phytotherapy Research, 27(3), 374-379. https://doi.org/10.1002/ptr.4715 | Yes |
| 19 | Apium graveolens | 2019 | The Effect of Celery (Apium graveolens L.) Leaf Infusion on Blood Cholesterol Levels in White Male Rat (Rattus norvegicus) Induced by Alloxan | Animal study | The sample used in this study were 25 white male rats Wistar strain aged 3-4 months with a bodyweight of 150-200 grams. The design used are were unidirectional pattern of completely randomized design with 5 treatments and 5 replications. Treatment 1 (P1) rats were given with the standard feed. Treatment 2 (P2) rats were induced by alloxan. Treatment 3 (P3) rats were induced by alloxan and given 2 ml of 5% celery leaf infusion therapy. Treatment 4 (P4) rats were induced by alloxan and given 2 ml of 10% celery leaf infusion therapy. Treatment 5 (P5) rats were induced by alloxan and given 2 ml of 15% celery leaf infusion therapy. Celery leaf infusion was given every morning and evening. Administration of alloxan with a single dose of 150 mg / kg in IP and celery leaf infusion therapy were given for 14 days. | Control | The results showed that the infusion of celery leaves was not showing any effect (P>0.05) on blood cholesterol levels of white male rats induced by alloxan. | Administration of celery leaves (Apium graveolens L.) infusion for 14 days with a concentration of 5%, 10% and 15% have no effect on blood cholesterol levels in male rats induced by alloxan. | Administration of celery leaves (Apium graveolens L.) infusion for 14 days with a concentration of 5%, 10% and 15% have no effect on blood cholesterol levels in male rats induced by alloxan. | http://202.4.186.66/IMV/article/view/48309/11584 | Moeviani, K. & Armansyah, T. T. (2019). The Effect of Celery (Apium graveolens L.) Leaf Infusion on Blood Cholesterol Levels in White Male Rat (Rattus norvegicus) Induced by Alloxan. Jurnal Medika Veterinaria FEBRUARI, 3(3), 108-113. https://doi.org/10.21517/jmedvet.v1 | No |
| 20 | Bauhinia variegata | 2019 | Antidiabetic, anti-hyperlipidemic and antioxidant activities of Bauhinia variegata flower extract | Animal study | Ethanic extract of B. variegata was administered orally to Streptozotocin (STZ) induced diabetic rats once daily for 21 days. Blood glucose levels were estimated at day 0, 7, 14 and 21 by glucometer (one touch) and lipid profile and histopathological examination of isolated organs (kidney, liver and pancreas) were also estimated on 21 day. | Control | The levels of triglycerides, total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL) were restored while administering B. variegata. | It can be concluded from the present study that B. variegata possesses significant antidiabetic, anti-hyperlipidemic and antioxidant activities. | To evaluate antidiabetic, anti-hyperlipidemic and antioxidant activities of ethanolic extract of Bauhinia variegata flower. | https://www.sciencedirect.com/science/article/abs/pii/S1878818119302526 | Tripathi A. K., Gupta P. S., & Singh S. K. (2019). Antidiabetic, anti-hyperlipidemic and antioxidant activities of Bauhinia variegata flower extract. Biocatalysis and Agricultural Biotechnology, 13, 101142. https://doi.org/https://doi.org/10.1016/j.cbab.2019.101142 | No |
| 21 | Coriandrum Sativum | 2021 | The Effectiveness of Coriander Seed Extract (Coriandrum Sativum) on Lowering Cholesterol Levels in Elderly Patients with Hypercholesterolemia | Quasi-experimental study with coriander seed extract as a treatment. | The treatment group was given an intervention in the form of coriander seed extract for 14 days which was recorded on the observation sheet while the control group was given health education about healthyeating patterns and lifestyles. This study was 15 elderly people per group. The data analysis technique used an independent T-test. | Control | The results showed that the significance value of the treatment group and the control group before was 0.063, while the significance value after treatment was 0.038. | Based on the results of the independent t test, the significance value in the treatment group and the control group before being given coriander seed extract was 0.063 (p value > 0.05), which means there was no difference in cholesterol levels between the treatment group and the control group. Meanwhile, the significance value in the treatment group and the control group after treatment was 0.038 (p value < 0.05), which means that there was a difference in cholesterol levels between the treatment group and the control group. | Based on the results of the study above, it shows that there is a significant effect of coriander seed extract on cholesterol reduction in the elderly with hypercholesterolemia with p-value before 0.063 and p-value after 0.038. | https://jurnal.uns.ac.id/plantum/article/view/54727 | Setyowati A., & Lilya, mauli. (2021). The Effectiveness of Coriander Seed Extract (Coriandrum Sativum) on Lowering Cholesterol Levels in Elderly Patients with Hypercholesterolemia. PACENTUM (Jurnal Ilmiah Kesehatan, Dan Aplikasinya, 2(3)). https://jurnal.uns.ac.id/plantum/article/view/54727 | Yes |
| 22 | Curcuma longa | 2020 | Antidyslipidemic and cardioprotective effects of turmeric (Curcuma longa) in rat fed a high cholesterol diet | Animal study | Twenty (20) rats were randomly grouped into four groups: A-D of five animals per group. Group A: C received HCD (2000mg/kg, oral) and carbimazole (60mg/kg, oral) daily for eight weeks. Group B served as negative control. Group B (positive control) was treated with atorvastatin (20mg/kg), while group C served as treatment group and received Curcuma longa (400mg/kg) daily for eight weeks. Group D served as normal control and received no treatment. After the administration, biochemical markers of lipid profiles (total cholesterol (TC), triglycerides (TG) and high density lipoprotein cholesterol (HDL-C)) were assayed using standard methods. | Control | Curcuma longa significantly induced hypolipidaemia and stabilized lipid biochemical markers (p<0.05 or p<0.01); and protected the cardiac muscle fibers from injuries. | Curcuma longa significantly induced hypolipidaemia and stabilized lipid biochemical markers (p<0.05 or p<0.01); and protected the cardiac muscle fibers from injuries. Turmeric (Curcuma longa) has antidyslipidemic and cardioprotective effects. | This study showed that the aqueous extract of Curcuma longa (ACL) has effect on lipid metabolism and prevents cardiomyopathy in albino rats fed a high cholesterol diet and high dose Carbimazole. | http://www.ijdtonline.info/index.php/ijdt/article/view/3869 | Uchendu I. E., Ekeogwu L. B., & Nwilo E. B. (2020). Antidyslipidemic and cardioprotective effects of turmeric (Curcuma longa) in rat fed a high cholesterol diet. Journal of Drug Delivery and Therapeutics, 10(1-3), 178-181. https://doi.org/10.22770/ijdt.v10i1-3-3869 | No |
| 23 | Cyperus rotundus | 2015 | Hypolipidemic Properties of Ethanolic Extract of Cyperus rotundus Rhizome | Animal study | This study investigated the effect of ethanolic extract of Cyperus rotundus rhizome on hyperlipidemia induced with carbimazole and cholesterol in male wistar rats. Hyperlipidemia was induced using 400 mg/kg cholesterol and 2 mg/kg carbimazole. The lipemic control group was administered cholesterol and carbimazole but not the normal control group. | Control | Cholesterol and carbimazole administration caused a significant (p = 0.05) increase in the Total Cholesterol, Triglyceride (TG), Low Density Lipoprotein (LDL), and High Density Lipoprotein (non-HDL) Cholesterol and LDL/HDL ratio and a significant (p = .05) decrease in the levels of HDL cholesterol in the lipemic control when compared to the normal control. | Treatment with ethanolic extract of Cyperus rotundus at 250 mg/kg, 500 mg/kg and the standard hypolipidemic drug (simvastatin) 5mg/kg significantly (p < 0.05) reduced total cholesterol, TG, LDL, LDL/HDL ratio, total non-HDL Cholesterol and also significantly (p= .05) increased the level of HDL cholesterol when compared to the non-treatment group (the lipemic control group). | Results of the present study indicate that Cyperus rotundus rhizome contains principles that have hypolipidemic potentials and which compare effectively with standard clinically used therapeutic Hypolipidemic agent simvastatin | https://www.researchgate.net/profile/Oluwa-G-Ahambisi-S-Nwadi-U-Iloosunu-C-&Ene-A-2015/publication/276546633_Hypolipidemic_Properties_of_Ethanol_Extract_of_Cyperus_rotundus_Rhizome/links/54945851548472588b1/ijdt-vol10-no1-3-178-181.pdf | Oluwa, G. Ahambisi, S., Nwadi, U., Iloosunu, C., & Ene, A. (2015). Hypolipidemic Properties of Ethanolic Extract of Cyperus rotundus Rhizome. International Journal of Biochemistry Research & Review, 10(1), 178-180. https://doi.org/10.9794/ijbr.2015.17158 | No |

Table S13: Summary of articles on fats.

| Fat | | | | | | | | | | | | |
|------------|--------------|------|--|--|--|-------------------|---|---|--|---|--|---------------------|
| No | Ingredients | Year | Title | Type of study | Method/Design of study | Control / Placebo | Outcome | Interpretation | Comment | Available at | Reference | Scientific Evidence |
| 1 | soy lecithin | 2016 | Effect of soy lecithin on total cholesterol content, fatty acid composition and carcass characteristics in the Longissimus dorsi of Hanwoo steers (Korean native cattle) | Animal study | Hanwoo steers (24 head) were fed two diets: Control (CON) (concentrate + alcohol-fermented feed (AFF)) and soy lecithin treatment (CON + soy lecithin at 0.5% of the AFF). | Control | A lower cholesterol concentration was found in the Longissimus dorsi for the soy lecithin diet compared to the CON diet. | Soy lecithin supplementation would alter the total cholesterol content, polyunsaturated fatty acid profile and meat quality of Longissimus dorsi. | N/A | https://onlinelibrary.wiley.com/doi/abs/10.1111/asi.12660 | Li, X. Z., Park, B. K., Hong, B. C., Ahn, J. S., & Shin, J. S. (2017). Effect of soy lecithin on total cholesterol content, fatty acid composition and carcass characteristics in the Longissimus dorsi of Hanwoo steers (Korean native cattle). <i>Animal Science Journal</i> , 88(6), 847–853. https://doi.org/https://doi.org/10.1111/asi.12660 | No |
| 2 | soy lecithin | 2018 | Protective role of soybean lecithin in reducing hypercholesterolemia and DNA fragmentation inducing by high cholesterol in adult male rats | Animal study | Thirty two adult male rats have been used in this study, were randomly selected and equally divided in to four groups as follows C, T1, T2, T3 for 42 days. C:control group, were given distilled water by gavage needle, rats of this group were given soybean lecithin only (430mg/kg/day). T2:rats of this groups were given only cholesterol (10gm/day). T3: rats of this groups were given soybean lecithin (430mg/kg/day). | Control | The daily supplementation of soybean lecithin induces a significant decrease ($p > 0.05$) in total cholesterol (TC) and triglyceride (TG) in both intact and hypercholesterolemic infected rats respectively. | soybean lecithin supplementation to rats has an important protective role on cardiovascular system and liver in hypercholesterolemic infected rats. | This supplementation can overcome the deleterious effect of hypercholesterolemia on heart and liver basically. | https://journals.uokufa.edu.iq/index.php/kjvs/article/view/7403 | Alshammari, S. M., & Khalil, L. W. (2018). Protective role of soybean lecithin in reducing hypercholesterolemia and DNA fragmentation in adult male rats. <i>Kufa Journal for Veterinary Medical Sciences</i> , 9(1), 35–45. https://journals.uokufa.edu.iq/index.php/kjvs/article/view/7403 | No |
| 3 | soy product | 2021 | A Non-Probiotic Fermented Soy Product Reduces Total and LDL Cholesterol: A Randomized Controlled Crossover Trial | Randomized Controlled Crossover Trial | In a randomized, crossover, intervention study, 27 men and women (aged 29-75 y) exhibiting at least two risk factors, consumed two packets (12.5 g each) daily of a fermented powdered soy product, or an isoenergic control powder made from germinated brown rice for 12 weeks each. | Control | The consumption of the fermented soy product resulted in a significantly greater mean change from baseline (compared to the germinated rice, all $p < 0.05$) in total cholesterol of -0.23 mmol/L (CI: -0.40, -0.06) compared with 0.14 mmol/L (CI: -0.03, 0.31), respectively; and low density lipoprotein (LDL) cholesterol -0.18 mmol/L (CI: -0.32, -0.04) compared with 0.04 mmol/L (CI: -0.01, 0.018) respectively. | The fermented soy powder consumed by participants in this study without implementing other changes in their typical diets, decreased the total and LDL cholesterol, and may serve as a dietary strategy to manage blood lipids. | N/A | https://pubmed.ncbi.nlm.nih.gov/33562090/ | Jung, S. M., Haddad, E. H., Kaur, A., Sirfat, R., Kim, A. Y., Oda, K., Rajaram, S., & Sabaté, J. (2021). A Non-Probiotic Fermented Soy Product Reduces Total and LDL Cholesterol: A Randomized, Controlled Crossover Trial. <i>Nutrients</i> , 13(7), 1–16. https://doi.org/10.3390/nu13070535 | Yes |
| 4 | Soy Product | 2016 | Probiotic Soy Product Supplemented with Isoflavones Improves the Lipid Profile of Moderately Hypercholesterolemic Men: A Randomized Controlled Trial | Randomized placebo-controlled double-blind trial | 49 male healthy men with total cholesterol (TC) >5.17 mmol/L and <6.21 mmol/L Intervention: The volunteers have consumed 200 ml of the probiotic soy product (group SP-10(10) CFU/day), isoflavone-supplemented probiotic soy product (group ISP-probiotic plus 50 mg of total isoflavones/100 g) or unfermented soy product (group USP-placebo) for 42 days in a randomized, double-blind study. | Control | After 42 days, the ISP consumption led to improved total cholesterol, non-HDL-C (LDL + IDL + VLDL cholesterol fractions) and electronegative LDL concentrations (reduction of 13.8%, 14.7% and 24.2%, respectively, $p < 0.05$). The ISP and SP have prevented the reduction of HDL-C level after 42 days. The C-reactive protein and fibrinogen levels were not improved. The equal production by the ISP group subjects was inversely correlated with electronegative LDL concentration. | The results suggest that a regular consumption of this probiotic soy product, supplemented with isoflavones, could contribute to reducing the risk of cardiovascular diseases in moderately hypercholesterolemic men, through the an improvement in lipid profile and antioxidant properties. | N/A | https://pubmed.ncbi.nlm.nih.gov/26797632/ | Cavallini, D. C. U., Manzoni, M. S. J., Bedani, R., Roselino, M. N., Celliberto, L. S., Vendramini, R. C., de Valdez, G. F., Abdalla, D. S. P., Pinto, R. A., Rosetto, D., Valentini, S. R., & Rossi, F. A. (2016). Probiotic Soy Product Supplemented with Isoflavones Improves the Lipid Profile of Moderately Hypercholesterolemic Men: A Randomized Controlled Trial. <i>Nutrients</i> , 8(1). https://doi.org/10.3390/nu8010052 | Yes |