Effects of resveratrol supplementation on plasma lipids: a systematic review and meta-analysis of randomized controlled trials

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CRD summary
The author concluded that resveratrol had no significant effect on plasma lipid concentrations. This conclusion reflects the evidence, but the lack of evidence and wide confidence intervals mean that its reliability is unclear. The author's recommendation for further research seems justified.

Authors' objectives
To determine the effects of resveratrol on plasma lipid concentrations.

Searching
MEDLINE was searched for articles from inception to June, 2013. Search terms were reported. The reference lists of selected articles were handsearched to locate further studies.

Study selection
Eligible were randomised clinical case-control or case-crossover trials that investigated the effects of purified resveratrol or standardised resveratrol-enriched extracts, on any lipid profile parameter. To be included, trials had to present sufficient data on the plasma or serum lipid levels, in all treatment and control groups, at the start and the end point. Trials with a daily resveratrol intake of less than 5mg were excluded.

The included trials were published between 2010 and 2013, and were conducted in the USA, Japan, India, Spain, Hungary, the Netherlands, or Denmark. Trial populations were healthy people, people who were obese, or people with diabetes, metabolic syndrome, a high risk of coronary artery disease or established coronary artery disease. The age of participants ranged from 40 to 67 years and, where reported, 15% to 64% of participants were smokers. Most trials were of purified \textit{trans}-resveratrol. The daily dose of resveratrol ranged from 8mg to 1,500mg; treatment lasted from one to six months.

The author did not state how many people selected trials for inclusion.

Assessment of study quality
The risk of bias in each trial was assessed using criteria from the Cochrane handbook. For each domain, trials were assessed as having a low, high or unclear risk of bias. The author did not state how many people assessed quality.

Data extraction
Mean changes from initial values for the outcomes were extracted to calculate mean differences and 95% confidence intervals. Where required, published formulae were used to convert millimoles per litre into mg per decilitre (dL), and to convert standard errors into standard deviations.

The author did not state how many people extracted the data.

Methods of synthesis
Mean differences and 95% confidence intervals were pooled using random-effects models. Statistical heterogeneity was assessed using Cochran's Q and $I^2$. In double-arm (2x2) crossover trials, each arm was treated as a single trial.

Sensitivity analyses were performed by removing one trial at a time. Random-effects meta-regression was performed to investigate the influence of resveratrol dose on effect sizes for the different plasma lipids. Publication bias was assessed using several methods (reported in the paper).

Results of the review
Seven trials were included in the review (282 participants; calculated as 236 from Table 1, with 45 crossover
participants included twice, producing 281 total; ranging from 11 twice to 34 twice or 20 to 57). There were five parallel-group trials, one double-arm crossover trial, and one single-arm crossover trial. All of the trials had low risk of bias for selective reporting. Most had an unclear risk of bias for most other domains, and a low risk of other bias.

No statistically significant differences between treatment and control groups were observed for the mean changes in plasma concentrations of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides.

The results were similar in post hoc subgroup analyses for coronary heart disease risk (high or low), and treatment duration (three months or more, or less than three months). The removal of one trial, in a sensitivity analysis, showed a significant reduction of total cholesterol plasma concentration in the treatment groups compared with controls (WMD -14.58, 95% CI -28.47 to -0.69; four trials; I²=0). Meta-regression revealed no significant dose-response associations for the effects of resveratrol on plasma lipid concentrations.

Compared with controls, a statistically significant greater increase in plasma concentration of free fatty acids was observed with resveratrol (WMD 0.09, 95% CI 0.02 to 0.16; three trials; I²=0).

Some evidence of publication bias was found (reported fully in the paper).

Authors’ conclusions
The main finding of this review was that resveratrol had no significant effect on plasma lipid concentrations.

CRD commentary
The review question and inclusion criteria were clearly defined. Only one database was searched and some evidence of publication bias was shown, so it is possible that relevant trials were missed. It was not reported that the review processes were performed by two people, meaning that reviewer error and bias may be present. Suitable quality assessment criteria were employed; the results varied across the domains.

The author acknowledged the differences between the trials in their populations, designs, resveratrol doses, and duration of treatment. Statistical methods of synthesis were appropriate, because attempts were made to explore the influence of between-trial variation on the effect sizes. The author acknowledged that only a few trials, with small samples, could be included in the review, and the changes in plasma lipid levels were not the primary outcome for most trials.

The author’s conclusion reflects the evidence, but the lack of evidence and wide confidence intervals mean that the reliability of the evidence is unclear. The author’s recommendation for further research seems justified.

Implications of the review for practice and research
Practice: The author did not state any implications for future practice.

Research: The author stated that large-scale, well-designed trials were needed. They should include people with dyslipidaemia and assess changes in circulating lipid concentrations as primary outcomes.

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