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File: ■ Cardamom (*Elettaria cardamomum*, Zingiberaceae)
■ Lipid Profile
■ Systematic Review/Meta-analysis

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RE: Systematic Review: Clinical Use of Cardamom to Improve Lipid Profiles

Shekarchizadeh-Esfahani P, Arab A, Ghaedi E, Hadi A, Jalili C. Effects of cardamom supplementation on lipid profile: A systematic review and meta-analysis of randomized controlled clinical trials. *Phytother Res*. March 2020;34(3):475-485. doi: 10.1002/ptr.6543.

Cardiovascular disease (CVD) remains the leading cause of death worldwide. Dyslipidemia – commonly brought on by lifestyle factors such as an unhealthy diet, physical inactivity, and the use of tobacco (*Nicotiana tabacum*, Solanaceae) and consumption of alcohol – is a major risk factor for the development of CVD. Dyslipidemia is characterized by elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), or triglycerides (TG), and reduced levels of high-density lipoprotein cholesterol (HDL-C). Nutrition therapy and pharmacotherapy are the primary treatment options for treating dyslipidemia and decreasing the risk of CVD. Lipid-lowering drugs, or statins, however, can have adverse effects like muscle pain and digestive system problems. Increasingly, nutraceuticals have gained interest as adjunctive treatment options for treating dyslipidemia. Cardamom (*Elettaria cardamomum*, Zingiberaceae), known as the "queen of spices," is a good source of phenolic compounds that may exert beneficial effects on serum lipids and lipoproteins; however, available studies have yielded inconsistent results. The purpose of this systematic review and meta-analysis was to review randomized controlled trials (RCTs) that examined the effect of cardamom supplementation on lipid profiles.

The databases PubMed, Scopus, Web of Science, Google Scholar, and the Cochrane library were searched from inception to March 2019 using search terms related to cardamom, lipoproteins, triglycerides, and dyslipidemia. RCTs that investigated the effects of cardamom on blood lipid concentrations and provided sufficient information on baseline and post-trial blood lipid concentrations in treatment and placebo groups were eligible for inclusion. The methodological quality of the studies was assessed using Cochran collaboration's tool, with each domain classified as low, high, or unclear risk of bias. Study quality was considered good (low risk for more than two domains), fair (low risk for two domains), and weak (low risk for less than two domains). Analyses were repeated using correlation coefficients of 0.2 and 0.8, and a random effect model was

used if heterogeneity was present between studies. Publication bias was assessed using Begg and Egger's regression tests. Subgroup analyses were performed for participants' mean age (≥ 50 years and < 50 years), intervention duration (≤ 8 weeks and > 8 weeks), and health status (diagnosis of diabetes and no diagnosis of diabetes).

A total of 256 articles were identified. After the removal of duplicates (n = 165), nonrelevant studies based on title or abstract (n = 158) and studies not meeting the inclusion criteria (n = 2), five studies were included in the final analysis. Studies were conducted in Iran (n = 4) and India (n = 1) and included patients with type 2 diabetes mellitus (T2DM; n = 2), pre-diabetes (n = 1), ischemic heart disease (n = 1), and nonalcoholic fatty liver disease (n = 1). All patients were overweight based on body mass index (BMI), except those from one study. The mean age of the patients (n = 361; n = 181 cardamom group; n = 180 placebo group) ranged from 45 to 60 years. The duration of the studies ranged from eight to 12 weeks, and all studies administered 3 grams per day of cardamom powder. All trials were considered to have high methodological quality based on the Cochrane collaboration's tool.

Both the pooled and subgroup analyses (age, supplementation duration, or health status) revealed no significant effect of cardamom supplementation on TC concentrations with no heterogeneity observed. A significant reduction was found in TG concentrations following cardamom supplementation (weighted mean difference [WMD]: −20.55 mg/dl, 95% confidence interval [CI; −32.48, −8.63], P < 0.001) with no heterogeneity (I^2 = 0.0%, P = 0.47) observed. No significant effect of cardamom supplementation on TG was found in any subgroup analysis. Combined effect size from the included studies demonstrated no significant effect of cardamom supplementation on LDL-C or HDL-C. Subgroup analysis for the effect of cardamom supplementation on LDL-C showed no significant effect; whereas, a significant increase in HDL-C was found in trials performed in patients without diabetes compared with those with the disease (WMD: 6.57 mg/dl, 95% CI [1.42, 11.73], I^2 = 25.2%). For the sensitivity analysis, the removal of one study changed the effect of cardamom on TG to nonsignificant. No evidence was found for publication bias on any of the measured indices.

To the authors' knowledge, this is the first quantitative review of RCTs on the effect of cardamom supplementation on serum blood lipids. Cardamom supplementation demonstrated significant reductions in TG without significantly affecting TC, LDL-C, or HDL-C. This effect of cardamom supplementation was observed only in studies with an intervention period ≥ 8 weeks and in patients ≥ 50 years without T2DM. A significant decrease in HDL-C was observed in patients without diabetes, which may be related to the patients' higher TG level at baseline. While the exact mechanisms for the hypotriglyceridemic effect of cardamom remain to be explored, the authors explain the effects may be linked with cardamom's ability to ameliorate insulin resistance – despite the hypotriglyceridemic effect occurring in patients without T2DM – and its antioxidant activity. While the safety of cardamom was not reported in the present analysis, few adverse effects have been reported, including nausea, constipation, and glossitis. The authors cite limitations related to the small number of studies included in the analysis, the max duration of the intervention (12 weeks), an inability to perform a subgroup analysis based on BMI, and lack of assessment for cardamom supplementation compliance.

Because the studies were conducted in Iran and India, the generalizability of the results to include other populations remains limited. Other limitations not cited by the authors

include whether the patients were taking medications or nutraceuticals that have lipid-lowering effects such as n-3 fatty acids and niacin or consideration for other lifestyle factors that may have confounded the results such as diet and physical activity or assessment of baseline and post-treatment bodyweight. Further investigation into the bioactive compounds and their mechanistic role in modulating the lipid profile is also needed. In either case, the authors call for further investigation of cardamom supplementation – especially in patients with dyslipidemia – with consideration for lipid lowering agents for improving blood lipid profiles and reducing the risk of CVD. The authors report no conflicts of interest. The initial analysis did find both clinically and statistically significant reductions in TG, but it should also be noted that 20 mg/DL is less than the other medications (including fish oil) which lower TG by 20-50%

–Gavin Van De Walle, MS, RDN

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