P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

File: ■ Chlorella (*Chlorella vulgaris*, Oocystaceae)
■ Dyslipidemia
■ Systematic Review/Meta-analysis

052248-701

Date: November 30, 2022

RE: Chlorella Supplementation Has Beneficial Effect on TC and LDL-C Levels: Systematic Review and Meta-analysis

Sherafati N, Bideshki MV, Behzadi M, Mobarak S, Asadi M, Sadeghi O. Effect of supplementation with *Chlorella vulgaris* on lipid profile in adults: a systematic review and dose-response meta-analysis of randomized controlled trials. *Complement Ther Med*. June 2022;66:102822. doi: 10.1016/j.ctim.2022.102822.

Dyslipidemia symptoms include by high levels of total cholesterol (TC), triglycerides (TGs), and low-density lipoprotein cholesterol (LDL-C), and low levels of high-density lipoprotein cholesterol (HDL-C). Non-alcoholic fatty liver disease (NAFLD), coronary heart disease, stroke, type 2 diabetes (T2D), and mortality can occur with dyslipidemia. A high-fiber diet and regular physical activity are needed to prevent and treat dyslipidemia. Some dietary supplements (DSs), e.g., with β-glucan fiber, may be used adjunctively. Chlorella (*Chlorella vulgaris*, Oocystaceae), a one-celled freshwater green alga, is rich in fiber, protein including essential amino acids, carbohydrates, vitamins, minerals, unsaturated fatty acids (FAs) including ω-3 FAs, and carotenoids. Used globally, it is found in almost all geographic regions. Randomized, controlled clinical trials (RCTs) of chlorella report conflicting findings, with some seeing lipid profile benefits; others, none. An earlier meta-analysis (MA) concluded that chlorella significantly reduced TC and LDL-C and had no significant effects on TGs or HDL-C. That MA had methodological flaws, and since its publication, other RCTs were reported. The authors performed a comprehensive systematic review (SR) and MA of chlorella's effects on lipid profiles using the Preferred Reporting Items for SRs and MAs protocol.

A search of electronic databases and the internet included very-low density lipoprotein cholesterol (VLDL-C) among its search terms with no limits on language. Of 1238 initial results, 443 were duplicates, and 777 were excluded in title and abstract screening. Of 18 articles assessed in full-text, eight did not meet SR criteria. Eligible RCTs in adults ≥18 years of age had at least a one-week intervention. The 10 RCTs included used no other *Chlorella* spp. (used in four excluded RCTs), nor aminobutyric acid-rich chlorella (used in one).* RCTs comparing combination therapies (e.g., lipid-lowering medications and/or exercise programs) that differed only in chlorella intake were included; however, those that used chlorella and other nutrients were not. RCTs were published in 2012-2021 and had 264 participants in chlorella groups and 275 in control groups (t = 539). Three were conducted in the Republic of Korea; seven, in Iran. Two studies included only women; one, only men; the rest were gender-inclusive. Four trials had healthy participants, while the others variously included patients with dyslipidemia, T2D, and

NAFLD. Six RCTs were double-blinded; four were not blinded. Interventions lasted three − four weeks. with chlorella dosages of 900-500 mg/d. Of the 10, two studies conducted independent biochemical verification of the chlorella DS. Four studies reported good participant compliance; six, poor or unclear compliance. Mean changes and standard deviations of lipid levels after chlorella intake vs. placebo/control were compared and pooled mean differences (MDs) calculated in a random-effects model. $P < 0.05$ was considered statistically significant. The I^2 statistic was used to rate heterogeneity. Fractional polynomial modeling was used to determine non-linear effects of chlorella dosages on lipid profiles.

Of nine RCTs reporting effects of chlorella supplementation on TGs, two found significant reductions. In the MA, there was a pooled MD of −2.11 mg/dL (P= 0.42; I^2 = 23.5), indicating no effects on TGs. A number of subgroup analyses also found no significant effects on TGs, and the dose-response analysis found no non-linear effects. Of 10 RCTs evaluating TC, five found a significant reduction after chlorella intake. The pooled MD was significant (−7.47; 95% confidence interval [CI] −12.98 to −1.96 mg/dL; P = 0.008), with significant heterogeneity (I^2 = 79.4) explained by differences in participants' gender, health, chlorella dosage, and baseline TC. Significant TC-lowering effects were seen in studies with heathy participants who took < 1500 mg/d chlorella, those using combination treatment, and those that did not control for baseline TC levels. Dose-response analysis found no non-linear effects. All RCTs considered LDL-C levels, with a strong reducing effect for chlorella vs. placebo (pooled MD −7.71, 95% CI −14.5 to −1.37 mg/dL; P = 0.01; I^2 = 88.6). Subgroup analysis identified different gender and health conditions of participants as sources of heterogeneity. Reductions in LDL-C were seen in studies of women and healthy individuals, those using < 1500 mg/d chlorella, those with a combination treatment, and those that did not adjust for baseline levels. Evidence for non-linearity at doses from 0-1500 mg/d supported the LDL-C-lowering effect (P for non-linearity = 0.01). In all ten RCTs, there was no effect of chlorella on HDL-C levels, significant heterogeneity, and no non-linear associations with dosages. No study included reported on VLDL-C.

The reductions in TC and LDL-C were significant at doses <1500 mg/d. It is likely that nonsignificant effects at higher doses are due to chlorella's protein and carbohydrate content. All studies that used a combination treatment used chlorella <1500 mg/d, and the effect of these treatments must be considered. With no significant benefit found in trials that used chlorella alone, findings on chlorella's TC- and LDL-C-lowering effects should be considered cautiously. Further studies should include complete characterization of chlorella products used. No mention is made in this SR of potential adverse effects (AEs).

The Cochrane quality assessment tool was used to assess risk of bias (ROB) in each of seven domains for RCTs included. Four had low ROB in all domains. Risk of publication bias, assessed vie Egger's linear regression test and the Begg test, found no substantial bias except for the effect of chlorella on TC (P = 0.02). Sensitivity analysis did not detect dependency of the overall MD on any one study. The authors had no conflicts of interest.

—Mariann Garner-Wizard

*Also excluded in full-text review were one in vivo and two non-randomized human trials.

Referenced article can be accessed at
https://www.sciencedirect.com/science/article/pii/S0965229922000243?via%3Dihub.