

# openheart Effects of spirulina on weight loss and blood lipids: a review

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## ABSTRACT

Spirulina, a cyanobacteria commonly referred to as a blue-green algae, is one of the oldest lifeforms on Earth. Spirulina grows in both fresh and saltwater sources and is known for its high protein and micronutrient content. This review paper will cover the effects of spirulina on weight loss and blood lipids. The currently literature supports the benefits of spirulina for reducing body fat, waist circumference, body mass index and appetite and shows that spirulina has significant benefits for improving blood lipids.

## INTRODUCTION

Spirulina is both a salt and fresh water blue-green algae, which is being increasingly studied recently. Spirulina was initially classified under the plant kingdom due to its rich plant pigments and its ability to photosynthesize, but was later placed into bacterial kingdom (cyanobacteria) due to its genetic, physiological and biochemical makeup.<sup>1</sup> Spirulina grows naturally in high salt alkaline water reservoirs in subtropical and tropical areas of America, Mexico, Asia and Central Africa.<sup>1</sup>

Among the many varieties of spirulina, the most commonly studied species are *Spirulina platensis* (*Arthrospora platensis*), *Spirulina maxima* (*Arthrospora maxima*) and *Spirulina fusiformis* (*Arthrospora fusiformis*). Spirulina is composed of numerous antioxidants, including beta-carotene, phycocyanin, tocopherols, micronutrients, polyunsaturated fatty acids, particularly gamma-linolenic acid and phenolic compounds. The high nutritive values of spirulina were recognised by the Intergovernmental Institution for the use of Microalgae *Spirulina* Against Malnutrition in the 1970s, where they launched Spirulina to fight against starvation and malnutrition.<sup>2</sup> Spirulina has also been recognised and recommended by National Aeronautics and Space Administration and the European Space Agency for food supplementation during long-term space travels. Since then, there have been numerous animal and human clinical trials

to determine its beneficial effects as a supplement. Spirulina is a low-cost nutritional supplement and has not been established to have any significant side effects. Metabolic syndrome is currently on rise<sup>3</sup> and dyslipidaemia and obesity are an integral component of its causation. While there are several other supplements being evaluated for lipid lowering and weight loss effects, benefits from supplementation of spirulina are not limited to the above benefits but also extends to its antiviral, anticancer, antioxidant, anti-diabetic, anti-inflammatory, hepatoprotective, cardioprotective and immunity boosting properties.<sup>4,5</sup> The primary aim of this article is to review the effects of spirulina on obesity and dyslipidaemia. Additionally, we also discuss the potential mechanism of action for the aforementioned effects.

## Anti-inflammatory effects of spirulina

The prevalence of obesity has nearly tripled since 1975.<sup>6</sup> According to the 2016 global health report, more than 1.9 billion adults were categorised as overweight; 650 million among them being obese.<sup>7</sup> Globally, approximately 2.8 million adults are estimated to die every year from it.<sup>8</sup> Obesity has been closely linked to inflammation, hyperlipidaemia and insulin resistance.<sup>9,10</sup> This may be due to the fact that adipose tissue secretes numerous biologically active substances like adipokines and chemokines, which play an important role in inflammation and the development of atherosclerosis.<sup>11</sup>

Although caloric restriction and exercise are the mainstay treatments for obesity, spirulina has shown significant benefits in aiding weight loss. The phycocyanin in spirulina contains a light-harvesting chromophore called phycocyanobilin, which is capable of inhibiting nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) oxidase, a significant source of oxidative stress in adipocytes playing a key role in inducing insulin resistance and shifting adipokine and cytokine production in hypertrophied adipocytes. Thus, by suppressing adipocyte



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oxidative stress, spirulina may lead to systemic anti-inflammatory and insulin-sensitising effects.<sup>12–20</sup>

### Weight loss and blood lipids

Several clinical and preclinical trials have been conducted to test the benefits of spirulina on weight loss. Yousefi *et al* studied 52 obese participants with a body mass index (BMI)  $\geq 25$ – $40 \text{ kg/m}^2$  who were randomised to 2 g spirulina per day with a restricted caloric diet versus placebo consisting of a restricted calorie diet for 12 weeks. Participants in the spirulina group had significantly lower body weight of  $-3.22 \pm 1.97 \text{ kg}$ , waist circumference  $-3.37 \pm 2.65 \text{ kg}$ , body fat of  $-2.28 \pm 1.74 \text{ kg}$  and BMI of  $-1.23 \pm 0.79 \text{ kg/m}^2$  ( $p < 0.001$ ,  $p = 0.049$ ,  $p = 0.049$  and  $p = 0.02$ , respectively). Additionally, triglycerides (TG) reduced by  $-18 \text{ mg/dL}$  and high-sensitivity C reactive protein levels were lower by  $-1.66 \pm 1.9 \text{ ng/mL}$  towards the end of the study period ( $p = 0.03$  and  $p = 0.02$ , respectively).<sup>21</sup>

Zeinalian *et al* studied 62 obese subjects after administering 1 g spirulina for 12 weeks and observed a significant reduction in appetite by  $-4.16\%$  ( $p = 0.008$ ), BMI by  $-1.9\%$  ( $p < 0.001$ ), body weight by  $-1.79\%$  ( $p < 0.001$ ) and a reduction in total cholesterol (TC) by  $-4.67\%$  ( $p = 0.002$ ).<sup>22</sup> Additionally, high density lipoprotein-cholesterol (HDL-C) was noted to increase by  $1.73\%$  ( $p = 0.05$ ) with no significant change in TG or low density lipoprotein (LDL).

Several trials have also used *Spirulina maxima* to assess its beneficial effects. In one study, 50 obese subjects with hypertension under antihypertensive treatment were given 2 g spirulina per day or placebo for 3 months. Those given spirulina were found to have significant improvements in their body mass from  $92.96 \pm 18.58 \text{ kg}$  to  $88.97 \pm 17.13 \text{ kg}$  ( $p < 0.001$ ), BMI from  $33.5 \pm 6.7 \text{ kg/m}^2$  to  $31.7 \pm 5.8 \text{ kg/m}^2$  ( $p < 0.001$ ) and waist circumference from  $105.2 \pm 15.3$  to  $103.4 \pm 14.1 \text{ cm}$  ( $p < 0.002$ ) versus baseline, a benefit that was not shown with the placebo. Compared with placebo-treated individuals, those given spirulina had significantly lowered LDL-cholesterol (LDL-C) from  $3.5 \pm 0.9 \text{ mmol/L}$  to  $3.0 \pm 0.6 \text{ mmol/L}$  ( $p < 0.001$ ) and interleukin-6 from  $4.3 \pm 0.6 \text{ mmol/L}$  to  $3.9 \pm 0.4 \text{ mmol/L}$  ( $p = 0.002$ ) and improved total antioxidant status from  $1.8 \pm 0.3$  to  $2.2 \pm 1.0 \text{ mmol/L}$  ( $p = 0.001$ ) and insulin sensitivity ratio from  $3.2 \pm 1.8 \text{ mg/kg/min}$  to  $4.3 \pm 2.1 \text{ mg/kg/min}$  ( $p < 0.001$ ).<sup>23</sup>

Mizcke *et al* in 2016 demonstrated benefits of spirulina maxima in 40 hypertensive patients without evidence of cardiovascular disease when supplemented with 2 g of spirulina per day versus placebo for 3 months. In those given spirulina, there was significant reduction in BMI ( $26.9 \pm 3.1$  vs  $25.0 \pm 2.7 \text{ kg/m}^2$ ,  $p = 0.0032$ ), weight ( $75.5 \pm 11.8 \text{ kg}$  vs  $70.5 \pm 10.3 \text{ kg}$ ,  $p < 0.001$ ), systolic blood pressure ( $149 \pm 7 \text{ mm Hg}$  vs  $143 \pm 9 \text{ mm Hg}$ ,  $p = 0.0023$ ) and arterial stiffness index ( $7.2 \pm 0.6$  vs  $6.9 \pm 0.7 \text{ m/s}$ ,  $p < 0.001$ ), thus proving beneficial cardiovascular effects with short-term low-dose spirulina supplementation (table 1).<sup>24</sup>

## BLOOD LIPIDS

### Animal studies

Spirulina has been speculated to have lipid lowering capabilities since 1981.<sup>25</sup> Hypocholesterolaemic effect was initially shown in animal trials.<sup>26</sup> Later in 1990, Iwata *et al* conducted the first preclinical trial on young and healthy Wistar rats, which were artificially induced with hyperlipidaemia by feeding a high-fructose diet. The groups were either on high fructose diet alone (68%) or on high-fructose diet with spirulina at 5%, 10% and 15% concentrations for 4 weeks. Towards the end of the study period, blood samples were obtained after administration of intravenous heparin injection at the dose of 200 U per 100 g body weight. The results revealed a significant improvement in the lipid profile with concomitant increased activity of lipoprotein lipase (LPL), although the difference in lipid levels or LPL was not significantly different between 5%, 10% or 15% spirulina concentration groups.<sup>27</sup>

The hypolipaeamic effect of spirulina was also shown in artificially induced diabetes in mice with administration of alloxan ( $250 \text{ mg/kg}$  body weight). With administration of 5% spirulina, hepatic triacylglycerols decreased. Improvement in serum HDL and lowered serum LDL as well as VLDL was also noted.<sup>28</sup>

Li *et al* found that spirulina given for 8 weeks increased HDL-C and lowered LDL-C, TG and TC levels when fed a high fat diet.<sup>29</sup> Similar to other previous studies, it was also shown to normalise hepatic steatosis with improvements in liver function tests, including transaminases, free fatty acids and overall lipid profile. This action was thought to be secondary to activation of AMP-activated protein kinase signalling pathway which subsequently downregulates the expression of lipid synthesising genes, namely sterol regulatory element-binding transcription factor-1c, 3-hydroxy-3-methyl glutaryl coenzyme A reductase and acetyl CoA carboxylase which ultimately reduce TG levels and subsequently inhibit synthesis of fatty acids.

Additionally, spirulina can alter gut microbiota to have lipid lowering effects. Studies have revealed an increase in abundance of *Prevotella*, *Porphyromonadaceae*, *Barnesiella* and *Paraprevotella*. *Prevotella* increases bile metabolism to reduce blood lipid levels. *Alloprevotella* and *Ruminococcus* are short chain fatty acid producers which can be digested by the intestine. They regulate energy metabolism and improve insulin sensitivity via specific receptors to ultimately reduce lipid metabolism disorders and prevent non-alcoholic liver disease. *Firmicutes* are another group of bacteria which have been associated with reduction in body weight and serum LDL-C levels, which improved with spirulina supplementation.<sup>29</sup>

### Clinical trials

The clinical trials on humans using spirulina include healthy patients and those with dyslipidaemia, hypertension, postischaemic heart disease, diabetes, the nephrotic syndrome and elderly patients. The response to spirulina supplementation has been noted to differ between

**Table 1** Spirulina clinical studies: antiobesity benefits

Year	Author	Participants	Spirulina dose	Changes in lipids	Changes in diabetes	Changes in blood pressures	Changes in body weight
2018	Yousefi <i>et al</i> <sup>21</sup>	52 obese participants what BMI>25 to 40 kg/m <sup>2</sup>	2 g spirulina per day with restricted caloric diet vs placebo consisting of restricted calorie diet for 12 weeks	Triglycerides reduced by -18 mg/dL and high-sensitivity C reactive protein levels by -1.66±1.9 ng/mL vs placebo	-	-	Significantly lower body weight of -3.22±1.97 kg, waist circumference -3.37±2.65 kg, body fat of -2.28±1.74 kg and BMI of -1.23±0.79 kg/m <sup>2</sup>
2017	Zeinalian <i>et al</i> <sup>22</sup>	62 obese	1 g per day spirulina for 12 weeks	HDL-C increased by 1.73% (p=0.05)	-	-	Appetite reduced by -4.16% (p=0.008), BMI by -1.9% (p<0.001), body weight by -1.79% (p<0.001)
2017	Szulinska <i>et al</i> <sup>23</sup>	50 obese subjects with hypertension	2 g per day spirulina or placebo for 3 months	Significantly lowered LDL-C from 3.5±0.9 mmol/L to 3.0±0.6 mmol/L (p<0.001) and interleukin-6 from 4.3±0.6 mmol/L to 3.9±0.4 mmol/L (p=0.002); improved total antioxidant status from 1.8±0.3 to 2.2±1.0 mmol/L (p=0.001)	Insulin sensitivity ratio improved from 3.2±1.8 mg/kg/min to 4.3±2.1 mg/kg/min (p<0.001)	-	Body mass reduced from 92.96±18.58 kg to 88.97±17.13 kg (p<0.001), BMI reduced from 33.5±6.7 kg/m <sup>2</sup> to 31.7±5.8 kg/m <sup>2</sup> (p<0.001) and waist circumference reduced from 105.2±15.3 to 103.4±14.1 cm (p<0.002) vs baseline
2016	Mizcke <i>et al</i> <sup>24</sup>	40 hypertensive patients	2 g of spirulina vs placebo for 3 months	-	-	Reduction in SBP (149±7 mm Hg vs 143±9 mm Hg, p=0.0023) and arterial stiffness index (7.2±0.6 vs 6.9±0.7 m/s, p<0.001) vs placebo	Significant reduction in BMI (26.9±3.1 vs 25.0±2.7 kg/m <sup>2</sup> , p=0.0032), weight (75.5±11.8 kg vs 70.5±10.3 kg, p<0.001)

BMI, body mass index; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; SBP, systolic blood pressure.

**Table 2** Hyperlipidaemia-related clinical trials

Year	Author	Participants	Spirulina	Blood lipids	BG	BP	Other effects
1988	Nakaya <i>et al</i> <sup>30</sup>	30	4.2 g per day×8 weeks in group 1; 4.2 g per day spirulina×4 weeks in group 2	Significant reduction in TC; predominately higher among those with higher serum TC and those with higher dietary content of TC.	–	–	No change in BW
1996	Ramamoorthy <i>et al</i> <sup>31</sup>	30 patients with hypercholesterolaemia (TC>250 mg/dL) with ischaemic heart disease	2g×3 months in group 1; 4g×3 months in group 2 and group three being control	Significant lowering in TC, LDL, VLDL, TG and increase in HDL as compared with the control group.	–	–	Significant reduction in BW as compared with control group.
2000	Mani <i>et al</i> <sup>34</sup>	15 T2DM	2 g spirulina×2 months	Significant lowering in TC, LDL, VLDL, TG and HDL-C; LDL-C ratio.	Significant reduction in BG.	–	–
2001	Parikh <i>et al</i> <sup>35</sup>	25 T2DM	2 g per day×2 months	Significant reduction in TG by 6.4 mg. LDL-C by 7.1 mg. TC by 21.3 mg (p<0.05) and atherogenic indices of TC:HDL-C from 5.4±1.0 to 5.0±1.0 (p<0.05) and LDL-C; HDL-C from 3.5±0.8 to 2.9±0.5 (p<0.05). Apolipoprotein B lowered by 16.1 mg (p<0.05); apolipoprotein A1 levels increased by 11.4 mg (p<0.05).	Reduced fasting blood glucose by 19.3 mg (p<0.05), postprandial blood glucose by 16.1 mg (p<0.05), HbA1c by 1.0% (p<0.05)	–	–
2008	Lee <i>et al</i> <sup>36</sup>	37 T2DM	8 g×12 weeks	Significant reduction in TGs (125.8–98.5 mg/dL, p<0.05).	–	Reduced BP	Antioxidant effects by lowering plasma malondialdehyde levels (p<0.05) and increasing plasma adiponectin levels (p<0.1)
2002	Samuels <i>et al</i> <sup>37</sup>	23 paediatric Indian patients with nephrotic syndrome	Steroid medications alone or with 1 g/day×2 months	TC decreased significantly by 116.33 mg/dL vs 69.87 mg/dL in control; LDL by 94.14 mg/dL vs 61 mg/dL in controls and triglycerides by 67.72 mg/dL vs 22.6 mg/dL in controls. LDL-C:HDL-C ratio decreased by 1.66 vs 1.13 (p<0.05) and TC:HDL-C decreased by 1.96 vs 1.19.	–	–	–
2003	Kim <i>et al</i> <sup>39</sup>	12 elderly patients aged 60–75 years	7.5 g/day for 24 weeks	Significant reductions in TG, TC and LDL fraction.	–	–	No anthropometric changes
2005	Kim <i>et al</i> <sup>40</sup>	51 elderly females with hypercholesterolaemia (TC>200 mg/dL) aged 60 years and above	7.5 g/day for 8 weeks	Significant reduction in TC, LDL-C, oxidised LDL and apolipoprotein B.	–	–	–
2008	Park <i>et al</i> <sup>42</sup>	78 individuals aged 60–87 year	8 g/day spirulina vs placebo for 16 weeks	Significant reduction in plasma TC and LDL noted. IL-2 increased and IL-6 reduced.	–	–	–
2014	Mazokopakis <i>et al</i> <sup>32</sup>	Cretan Greek newly diagnosed with dyslipidaemia	1 g per day for 3 months	Significant reduction in TGs by 16.3% (p<0.0001), LDL-C by 10.1% (p<0.0001), TC by 8.9% (p<0.0001), non-HDL-C by 10.8% (p<0.0001) and TC/HDL ratio by 11.5% (p=0.0006). HDL-C increased by 3.5%.	–	–	HellenicSCORE revealing a reduction in risk from 15.4% to 1.9%.

BG, blood glucose; BP, blood pressure; BW, body weight; HDL-C, high density lipoprotein-cholesterol; IL, interleukin; LDL-C, low density lipoprotein-cholesterol; TC, total cholesterol; TG, triglyceride; VLDL, very low density lipoprotein.

different ages, races, genders, comorbidities and dose/duration of treatment.

One of the first clinical trials ever done using spirulina was carried out in 1988 consisting of 30 healthy volunteers with mild hypertension or hyperlipidaemia. They were treated in two groups, one of the groups received 8 weeks of 4.2 g of spirulina versus the other group which received the same amount of spirulina for 4 weeks followed by observation for another 4 weeks without any supplementation. Results were notable for a significant reduction in TC in the initial 4 weeks of spirulina supplementation, which returned to baseline with its discontinuation. These changes in TC were directly proportional to serum TC and dietary TC concentrations. There were no changes in HDL, TG or body weight.<sup>30</sup>

Ramamoorthy *et al* established the hypolipaeamic effects of spirulina in patients with ischaemic heart disease and hypercholesterolaemia (serum cholesterol levels >250 mg/dL), where a total of 30 patients were split into three groups. Groups 1 and 2 were treated with 2 g or 4 g of spirulina for 3 months, while group 3 was a control arm. Towards the end of the study period, plasma TC was lowered by 22.4% and 33.5% in group 1 and 2, respectively ( $p<0.01$ ) and LDL by 31% and 45% ( $p<0.01$ ), which were both statistically significant reductions. Higher reductions in both LDL and TC were noted among those treated with 4 g spirulina/day. In addition, HDL-C increased, while TG and VLDL decreased in both the experimental groups. However, there was no statistical significance between the two experimental groups while there was significant change when compared with the control group. Similarly, body weight was reduced in both the treatment groups while there were no changes in lipid profiles or body weight in the control arm. The reduction in body weight in both groups given spirulina (-2.2 kg) was highly significant compared with control (0.7 kg;  $p<0.01$ ).<sup>31</sup>

Supplementation of 1 g spirulina for 3 months among Cretan Greek patients with newly diagnosed dyslipidaemia also revealed significant improvements in dyslipidaemia. Mean levels of TGs reduced by 16.3% ( $p<0.0001$ ), LDL-C by 10.1% ( $p<0.0001$ ), TC by 8.9% ( $p<0.0001$ ), non-HDL-C by 10.8% ( $p<0.0001$ ) and TC/HDL ratio by 11.5% ( $p=0.0006$ ). Additionally, HDL-C increased by 3.5%, without any significant changes in weight, BMI or blood pressures.<sup>30</sup> The TG levels reduced by 17.2% on an average; the reduction was higher (at 21.3%) among women over 47 years old and those with TG>150 mg/dL (18.6% reduction). HellenicSCORE is a scoring system designed to assess risk for development of cardiovascular disease and associated mortality among the Greek population, and the overall cardiovascular risk level on HellenicSCORE in this study projected a reduction in risk from 15.4% to 1.9% during the study period.<sup>32,33</sup>

In 15 patients with non-insulin dependent diabetes mellitus, supplementation of 2 g/day of spirulina for 2 months leads to significant reductions in TG, TC, LDL-C, VLDL-C and LDL-C/HDL-C ratio.<sup>34</sup> Similarly, Parikh *et*

*al* enrolled 25 type 2 diabetics and established that 2 g/day of spirulina for 2 months in this population can lower fasting blood glucose by 19.3 mg ( $p<0.05$ ), postprandial blood glucose by 16.1 mg ( $p<0.05$ ), HbA1c by 1.0% ( $p<0.05$ ) in addition to lowering in TG by 6.4 mg, LDL-C by 7.1 mg, TC by 21.3 mg ( $p<0.05$ ) and overall reduction in atherogenic indices of TC:HDL-C from  $5.4\pm 1.0$  to  $5.0\pm 1.0$  ( $p<0.05$ ) and LDL-C:HDL-C from  $3.5\pm 0.8$  to  $2.9\pm 0.5$  ( $p<0.05$ ). Additionally, apolipoprotein B was lowered by 16.1 mg ( $p<0.05$ ) with subsequent increases in apolipoprotein A1 levels by 11.4 mg ( $p<0.05$ ), thus a favourable increase in A1:B ratio. However, the increase in apo B levels with reduction in apo A1 level was also significant among the control group. Nevertheless, this study was able to establish improved short-term control from spirulina on glucose and lipid profiles among diabetics.<sup>35</sup>

Lee *et al* in 2008 tested 8 g/day of spirulina on 37 Korean subjects with T2DM (Type 2 diabetes mellitus) for 12 weeks, which resulted in a significant reduction in TGs (125.8–98.5 mg/dL,  $p<0.05$ ). Those with higher plasma TG showed greater reductions in TG levels. Similarly, the subjects with higher TC and LDL-C levels showed greater reductions in TC, LDL-C and improvement in blood pressure. The study also revealed lowering in plasma malondialdehyde levels ( $p<0.05$ ) and increased plasma adiponectin levels ( $p<0.1$ ), which are indicative of a reduction in oxidative stress with spirulina supplementation.<sup>36</sup>

Dyslipidaemia is a common comorbidity in patients with nephrotic syndrome. Loss of plasma proteins in the urine can cause low oncotic pressure, which leads to hepatic production of albumin and other proteins including lipoproteins, which can contribute to hyperlipidaemia. In this study, 23 paediatric patients with hypercholesterolaemia and nephrotic syndrome, between the age of 2 and 13 years were treated with steroid medications alone or in combination with 1 g/day spirulina for 2 months. At the end of study period, TC decreased by 116.33 mg/dL vs 69.87 mg/dL in control; LDL by 94.14 mg/dL vs 61 mg/dL in controls and triglycerides by 67.72 mg/dL vs 22.6 mg/dL in controls. LDL-C:HDL-C ratio decreased significantly by 1.66 vs 1.13 ( $p<0.05$ ) and TC:HDL-C decreased by 1.96 vs 1.19. Thus, the overall findings concluded that spirulina has significant hypolipidaemic effects in patients with nephrotic syndrome.<sup>37</sup>

Hyperlipidaemia and coronary vascular disease (CVD) are known to increase with advancing age.<sup>38</sup> Most of the clinical trials testing spirulina supplementation on the elderly population has been in Korea. One study included 12 Korean patients between the age 60 and 75 years old who were supplemented with 7.5 g/day of spirulina for 24 weeks. The study found significant reductions in TGs, TC and LDL after 4 weeks of spirulina supplementation. There was no difference in the reduction among patients with mild hypercholesterolaemia (TC at or above 200 mg/dL) vs normocholesterolaemia.<sup>39</sup> In 2005, another study involved 51 elderly females with hypercholesterolaemia

(TC >200 mg/dL) aged 60 years and above, where they were supplemented with 7.5 mg/day spirulina for 8 weeks in half of the study population and the other half were given placebo. Findings were significant for reductions in TC, LDL-C, oxidised LDL and apolipoprotein B.<sup>40</sup> The most recent randomised controlled trial included 78 individuals aged 60–87 years, who were randomly assigned to 8 g/day spirulina versus placebo for 16 weeks. The female were noted to have higher mean TC and LDL-C and also showed significant reductions in their plasma levels, TC from 200.5 to 184.8 mg/dL (p=0.03) and LDL from 126.7 to 112.1 mg/dL (p=0.05).<sup>41</sup> In addition, interleukin-2 (IL-2) was significantly increased (p<0.0001) and IL-6 was reduced (p<0.05) at the end of the study period. IL-2 has anti-inflammatory properties and is an important regulator of chronic inflammatory response. IL-2 levels reduce with increasing age; thus, supplementation with spirulina may help to boost immunity in the elderly.<sup>42</sup>

A systematic review published in 2015 encompassing eight humans studies concluded that spirulina has blood lipid lowering benefits and antioxidant effects.<sup>43</sup> Furthermore, a recent 2018 meta-analysis of 12 clinical studies in humans showed that spirulina supplementation (1 g up to 19 g per day) significantly lowered TC (−36.60 mg/dL; p=0.0001), low-density lipoprotein cholesterol (−33.16 mg/dL; p=0.0002), triglycerides (−39.2 mg/dL; p=0.0001), very-low-density lipoprotein cholesterol (−8.02 mg/dL; p=0.0001), fasting blood glucose (−5.01 mg/dL; p=0.04) and diastolic blood pressure (−7.17 mm Hg; p=0.001).<sup>41</sup>

Overall, the evidence in the literature suggests that spirulina improves several well-established CVD risk factors including hyperlipidaemia and seems to provide benefits around weight loss. The variation in response in the clinical trials is likely due to the difference in dose, duration of treatment and responsiveness among patients based on their comorbidities. As a whole, supplementing spirulina at 2–8 g/day may improve lipid profiles, particularly by reducing TC, TG and LDL-c and improving HDL-c; improving apolipoprotein A1 and reducing apolipoprotein B, aiding weight loss and reducing BMI. Spirulina also seems to improve insulin resistance, antioxidant/anti-inflammatory properties, blood glucose and blood pressure as discussed in this article (table 2).

## SUMMARY OF THE MECHANISMS OF ACTION OF SPIRULINA

- ▶ **Faecal excretion of cholesterol and bile.** In 2005, Nagoaka *et al* demonstrated lower micellar solubility of cholesterol with bile acids and as a result reduced absorption of fats in the small intestine with higher faecal excretion of cholesterol and bile acid when fed with spirulina concentrates. Additionally, phycocyanin residue diet increased the proportion of cholesterol excretion, thus indicating the hypolipaeamic effects of spirulina, particularly from phycocyanin.<sup>44</sup>
- ▶ **Anti-inflammatory properties.** Reactive oxygen species are frequently associated with tissue inflammation

and damage. Due to Spirulina's composition of the blue-green pigments, particularly phycocyanobilin, a water-soluble photosynthetic pigment possessing extensive anti-inflammatory and antioxidant properties. Phycocyanobilin is structurally similar to bilirubin and can inhibit NADPH oxidase. The antioxidant activity of spirulina has been proven to be directly proportional to the quantity of phycocyanin (which contains phycocyanobilin).<sup>12–14 45</sup>

- ▶ **Weight loss:** The proposed mechanism of action of spirulina is a reduction in macrophage infiltration into visceral fat, prevention of hepatic fat accumulation, reduction in oxidative stress, improvement in insulin sensitivity and satiety.
- ▶ **Improves satiety:** Reduction in appetite may be due to an improvement in leptin resistance in the arcuate nucleus.
- ▶ **Pancreatic lipase inhibition:** One of the components of spirulina is noted to be glycolipid H-b2, which inhibits pancreatic lipase activity in a dose depended way, thus reducing postprandial TG levels.<sup>46</sup> Similar effects may be exerted by phycocyanin as well.<sup>46</sup>
- ▶ **Prevention of cholesterol accumulation by gamma-linolenic acid:** Spirulina is also composed of gamma-linolenic acid (GLA). GLA is mostly formed from conversion of LA in the presence of enzyme delta-6-desaturase, which may be inhibited with mineral deficiencies, alcohol/tobacco abuse, infections, ageing and other severe medical conditions. Moreover, GLA deficiencies may worsen arterial thickness, hypertension and dyslipidaemia.<sup>47 48</sup> Additionally, spirulina also contains vitamin B3, also called niacin, which is also known to improve dyslipidaemia.<sup>49</sup>

Overall, spirulina has several benefits for improving weight loss, dyslipidaemia and obesity. However, further research including larger clinical trials would be warranted for confirming these benefits.

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