

1 **The Effects of Spirulina (*Arthrospira platensis*) Supplementation on Anthropometric**
2 **Indices, Blood Pressure, Sleep Quality, Mental Health, Fatigue Status, and Quality of Life**
3 **in Patients with Ulcerative Colitis: A Randomized, Double-blinded, Placebo-controlled**
4 **Trial**

5
6 *Sajjad Moradi¹, Mehdi Zobeiri², Awat Feizi³, Cain C. T. Clark⁴, Mohammad Hassan Entezari^{1*}*

7
8
9 *¹Department of Clinical Nutrition, School of Nutrition and Food Science, Isfahan University of*
10 *Medical Sciences, Isfahan, Iran*

11 *²Department of Internal Medicine, School of Medicine, Kermanshah University of Medical*
12 *Sciences, Iran*

13 *³Department of Biostatistics and Epidemiology, School of Health, Isfahan University of Medical*
14 *Sciences, Isfahan, Iran*

15 *⁴Centre for Intelligent Healthcare, Coventry University, Coventry, CV1 5FB, U.K.*

16
17 **Running title:** The Effects of Spirulina on Ulcerative Colitis Patients

18
19 ***Corresponding Author:** Mohammad Hassan Entezari, PhD

20 Department of Clinical Nutrition, School of Nutrition and Food Science, Isfahan University of
21 Medical Sciences, Isfahan, Iran, Email: entezari@hlth.mui.ac.ir

22
23

24

25

26

27

28

29

30

31

32List of Abbreviations:

33BMI: Body mass index

34DASS: Depression, Anxiety, Stress Scale

35DBP: Diastolic blood pressure

36FFS: Fatigue Severity Scale

37HC: Hip circumference

38IBD: Inflammatory bowel disease

39IPAQ: Physical Activity Questionnaire

40NC: neck circumference

41PSQI: Pittsburgh Sleep Quality Index

42SBP: Systolic blood pressure

43SCCA I: Simple Clinical Colitis Activity Index

44SIBDQ: Short IBD Questionnaire

45WC: Waist circumference

46WHR: Waist to hip ratio

47

48

49

50

51

52

53

54

55

56

57

58

59

61ABSTRACT

62**Background:** An emerging body of evidence has highlighted the protective role of spirulina in
63human health. Thus, we conducted a randomized controlled trial to discern the effects of
64spirulina supplementation on anthropometric indices, blood pressure, sleep quality, mood,
65fatigue status, and quality of life among ulcerative colitis patients.

66**Methods:** Eighty participants with ulcerative colitis were randomly allocated to receive, either, 1
67g/day (two 500 mg capsules) spirulina (n=40) or placebo (n=40), in a clinical trial for eight
68weeks. Dietary intake, physical activity, sleep quality, mental health, fatigue status, and quality,
69were assessed for each participant at baseline and trial cessation. Anthropometric indices and
70blood pressure were also assessed.

71**Results:** Seventy-three participants completed the intervention. Our results revealed that
72spirulina supplementation significantly reduced sleep disturbances ($p=0.03$), while no significant
73changes occurred in the sleep quality score or other sleep parameters, vs. the placebo group ($p>$
740.05). Furthermore, a significant reduction in stress score ($p=0.04$) and increase in quality of life
75($p=0.03$) was detected, but not anxiety, depression, or fatigue scores ($p> 0.05$). Additionally,
76anthropometric indices and blood pressure did not significantly change ($p> 0.05$).

77**Conclusion:** An improved quality of life was observed among ulcerative colitis patients
78following spirulina supplementation, which could be attributed to improved sleep disturbance
79and stress status. Further clinical studies, with longer duration interventions and suitably
80powered sample sizes, are necessary to elucidate the veracity of our findings.

81**Keywords:** Spirulina; Ulcerative Colitis; Clinical trial; Sleep quality; Mood

82

83What's already known about this topic?

- 84 • An emerging body of evidence has highlighted the protective role of spirulina in human
85 health.
- 86 • There have been no study on the effects of spirulina supplementation on ulcerative colitis
87 patients.

88

89 What does this article add?

- 90 • This study is the first clinical trial that was designed to evaluate the effects of spirulina
91 supplementation on anthropometric indices, blood pressure, sleep quality, mood, fatigue
92 status, and quality of life among ulcerative colitis patients.
- 93 • An improved quality of life was observed among ulcerative colitis patients following
94 spirulina supplementation, which could be attributed to improved sleep disturbance and
95 stress status

96INTRODUCTION

97

98In recent decades, the prevalence of inflammatory bowel disease (IBD), a chronic immune-
99mediated disorder, has been rising steadily ¹. Ulcerative colitis is one of the most common types
100of IBD and is characterized by clinically intermittent periods of exacerbation and remission ².
101Ulcerative colitis may lead to several additional problems, including, sudden weight loss,
102abdominal and joint pain, rectal pain and bleeding, cramping, constipation, frequent loose bowels
103^{3,4}, severe fatigue ⁵, poor sleep quality ⁶, and mental disorders ⁷. However, the pathogenesis of
104this disease is not completely understood; indeed, several studies have documented that the
105interactions between genetic, environmental factors, gut microbiota, and immunopathologic
106responses are associated with the triggering of ulcerative colitis ⁸⁻¹¹. Typically,
107immunosuppressive and anti-inflammatory drugs are used to control the immune-inflammatory
108reaction in ulcerative colitis patients ¹²; however, these drugs tend to cause a number of short-
109term or long-term side effects, such as increased risk of infection, hepatotoxicity, osteoporosis,
110tremor, eyes problems, gastrointestinal problems, pancreatitis, mental disorders, and antigen-
111antibody reactions ^{13,14}. Hence, the use of comparably safer complementary therapies, with fewer
112side effects and lower toxicities, may be efficacious in ulcerative colitis management.

113Indeed, growing evidence posits that the use of herbal medicines, and their extracted compounds,
114with protective and antioxidant properties, can also be effective and safe for the management of
115ulcerative colitis disease ¹⁵⁻²⁰. Instance nigella sativa ¹⁵ silymarin ¹⁶, ginger ¹⁷, ferulago²¹,
116curcumin ¹⁸, resveratrol ¹⁹ have been shown as potentially effective agents in improving,
117managing, or ameliorating ulcerative colitis and/or its accompanying comorbidities. Spirulina
118(*Arthrospira platensis*), as eco-friendly cyanobacterium (*Oscillatoriaceae* family), is a spiral
119blue-green microalgae ^{22,23}, which is edible and widely consumed as food or nutritional

supplement²⁴. It is a good source of essential nutrients, especially amino acids, phytochemicals (carotenoids and phycocyanins), vitamins (vitamin B12 and provitamin A), essential fatty acids, minerals (calcium and iron), and fiber²⁵⁻²⁷. Spirulina administration has been posited as a complementary therapy for the management of several diseases, owing to its antioxidant, liver-protecting, anti-inflammatory, anti-hypertension, cancer prevention, anti-viral, and antibacterial activities^{25,26,28}. Further, contemporary studies have indicated that spirulina represents a good source of tryptophan, which can viably lead to improvements in the mental health of patients²⁹. Moradi-Kor et al.³⁰ also reported that spirulina supplementation may reduce adolescent stress, anxiety, depression-related neuroanatomical biochemical, and molecular deficits in adult female rats. Concordantly, Madhu et al.³¹ showed that spirulina supplementation has dose-dependent antidepressant properties in murine models.

Therefore, we sought to conduct a randomized, double-blinded, placebo-controlled trial to discern the effect of spirulina (*Arthrospira platensis*) powder on anthropometric indices, blood pressure, sleep quality, anxiety, stress, depression, quality of life, and fatigue status in ulcerative colitis patients.

135

136 MATERIALS AND METHODS

137

138 *Subjects characteristics*

A total of 426 ulcerative colitis patients, who were referred to the Imam Khomeini Hospital (Kermanshah, Iran), were interviewed during the trial period between November 2019 and December 2020. Among these patients, 80 individuals were eligible and volunteered to participate in the clinical trial. During the two months trial, seven participants dropped out of the

143study. The inclusion criteria were; having diagnosed ulcerative colitis according to colonoscopy,
144clinical records, and pathology; being in the age range of 18–65 years; having symptoms of
145active mild-to-moderate ulcerative colitis disease ($5 \leq$ Simple Clinical Colitis Activity Index
146(SCCAI) ≤ 12 score)³². These individuals were excluded: patients with severe ulcerative colitis
147(SCCAI) < 5 or > 12 scores, individuals in pregnancy or breastfeeding condition; taking
148antidepressants, anxiety, and stress drugs; taking antioxidant and omega-3 supplements in the
149last three months; smokers or alcohol consumers; patients with heart disease, liver, kidney,
150cancer disease, thyroid and parathyroid or other gastrointestinal diseases; participants with poor
151compliance (using less than 90% of the supplements). =

152The present clinical trial was conducted according to the Helsinki Declaration, and written
153informed consent was signed by all patients prior to participation in the study. The protocol of
154this study was certified by the ethical committee at the Isfahan University of Medical Sciences
155(code: IR.MUI.RESEARCH.REC.1398.436, approval date Oct. 23 2019) and registered at:
156<http://www.IRCT.ir> (code: IRCT20191204045612N1).

157*Experimental Setting*

158

159The current work was a randomized, double-blind, placebo-controlled clinical trial. By simple
160sampling method, 80 participants, with active mild to moderate ulcerative colitis, were allocated
161to spirulina (n= 40) or the control (n= 40) groups, randomly. The intervention group
162supplemented with a 500 mg capsule of Spirulina, two times a day, before lunch and dinner for
163eight weeks, and the other group received placebo capsules, of inert contents, but of equivalent
164weight and appearance. Patients visited twice during the trial (at the baseline and end of
165intervention). All patients were requested to continue their habitual physical activity, dietary

intake, and their current drug regimen throughout the follow-up period. Finally, compliance was evaluated through weekly phone calls and monitoring the number of used packages.

168

169*Sample size calculation*

170

Sample size was calculated considering type I and statistical power of 5% and 80%, respectively. Minimum detectable effect size (i.e. Δ of clinical response) was considered to be of 0.3 for according to a similar clinical trials in ulcerative colitis patients ^{33,34}. Sample size was calculated as 33 participants in each intervention/placebo group and considering about 20% dropout rate, 40 patients were determined for each group.

176*Randomization and blinding*

177

In the current study, a simple randomization method, using a random number table, was used,, where patients, laboratory staff, researchers, and participants were blinded to the supplement allocation, until the end of the study.

181*Assessments*

182

Anthropometric parameters were assessed at the start of the intervention and at study cessation. The participants' height was evaluated via a nonelastic wall-mounted stadiometer, measured to the nearest 0.5 cm. The individuals' body weight was assessed, with participants dressed in minimal clothes, using a digital scale, with an accuracy of 0.1 kg. Neck circumference (NC), Hip circumference (HC), and The Waist circumference (WC) was measured using a non-stretch tape measure, without any pressure on the body surface. Waist to hip ratio (WHR) was calculated as WC/HC, and body mass index (BMI) was estimated as weight (kg)/square of height (m).

Moreover, blood pressure was assessed, with participants in a seated position and after 5 min rest, at the beginning and end of the intervention, based on the European Society of Hypertension³⁵ guidelines, using a mercury sphygmomanometer (Riester)

All measurements were taken at the beginning and end of the study. To evaluate the dietary intakes of each patient, food diaries for 3 days (including one weekend day) were recorded. Nutrient intakes were computed using Nutritionist IV software (First Databank, San Bruno, CA) modified for Iranian foods. Physical activity levels were assessed via the short form of International Physical Activity Questionnaire (IPAQ)³⁶, whilst the sleep quality and duration were evaluated using the Pittsburgh Sleep Quality Index (PSQI) questionnaire³⁷. Depression, Anxiety, Stress Scale (DASS-21-items) questionnaire was applied to evaluate mood scores in ulcerative colitis patients, where the reliability and validity of the questionnaire has been demonstrated in Iranian populations³⁸. To evaluate the fatigue level of ulcerative colitis patients, the Fatigue Severity Scale (FFS) questionnaire, validated in Iranian populations, was used³⁹. The short IBD Questionnaire (SIBDQ) score was used to assess the quality of life of patients, where its' validity and reliability have been confirmed, first, by Jowett et al. for patients with ulcerative colitis ($r = 0.83$)⁴⁰, and second, in an Iranian population⁴¹.

Statistical Methods

Data analyses were conducted using SPSS Version 22 (Inc., Chicago IL., USA.) Q-Q plot and skewness test normality tests were used to evaluate the distribution. All variables were reported as mean \pm standard deviation (SD). Participants' characteristics and micro-nutrients and macro-nutrients intake were evaluated between spirulina and the placebo groups, using independent t-tests for quantitative and Chi-square for qualitative variables. The within-group analysis was

carried out using paired t-tests. Multiple linear regression (adjusted for baseline value of age, disease length, and beginning BMI) was applied to find any differences between the spirulina and the placebo groups at the end of the intervention. Bonferroni correction was used for multiple testing adjustments. We considered a p value < 0.05 to represent statistical significance, *a priori*, for all the efficacy measures.

RESULTS

Subjects' Baseline Characteristics

A total of 80 participants, with mild or moderate levels of ulcerative colitis, were registered in our study and randomly dichotomized into a spirulina and a placebo group. Among the 80 patients who were included in the study, seven participants withdrew; personal reasons (n = 3) and alteration of supplementation (n = 4) (Figure 1). Ultimately, analyses were conducted on 73 patients (36 in the Spirulina group and 37 in the control group), with a compliance of >90%.

Table 1 details the participants' characteristics at the beginning of the study. No significant differences in baseline characteristics of ulcerative colitis patients between intervention and control groups, for age, sex, height, weight, BMI, WC, HC, NC, SBP, DBP, disease duration, the dose of mesalazine, family history, sleep quality, anxiety, stress, depression, fatigue scores, and current medication (all p> 0.05), (Table 2). Further, the differences in macronutrient and micronutrient intake and physical activity was not significantly different between group (p> 0.05), (**Table 2**).

Effects of Spirulina Supplementation on Anthropometric Parameters and Blood pressure

236

237The efficacy of spirulina administration on anthropometric parameters are shown in **Table 3**.
238Within-group comparison revealed a significant increase in body weight ($p= 0.02$) and BMI ($p=$
2390.02) among participants who supplemented with spirulina. However, after correcting for
240multiple testing, no significant effects were detected in the body weight, BMI, WC, HC, NC,
241WHR, systolic blood pressure (SBP), diastolic blood pressure (DBP), in comparison with the
242placebo group (all $p> 0.05$).

243*Effects of Spirulina Administration on Sleep quality*

244

245The results of spirulina supplementation on sleep quality score and its parameters are reported in
246**Table 3**. Within-group comparison demonstrated a significant decrease in sleep quality score
247($p=0.01$ for spirulina group and $p=0.01$ for the placebo group) and sleep disturbances ($p=0.004$)
248for the spirulina group. After correcting for multiple testing, there was a significant reduction in
249sleep disturbances ($p= 0.03$) in the spirulina group, while no significant changes occurred in the
250sleep quality score, sleep duration, subjective sleep quality, sleep latency, sleep efficiency, use of
251sleep medication, and daytime dysfunction parameters, in comparison with the control group ($p>$
2520.05).

253

254*Effects of Spirulina Supplementation on Mood and Fatigue status and Quality of life*

255

256Within-group comparison indicated a significant decrease in stress score ($p<0.001$ for spirulina
257group and $p= 0.04$ for placebo group) and depression score ($p= 0.01$ for spirulina group and $p=$
2580.02 for placebo group) among tow group (**Table 3**). Further, within-group comparison
259demonstrated a significant increase in quality of life ($p= p<0.001$ for spirulina group and $p= 0.01$

for the placebo group) in both groups. After correcting for multiple testing, the stress score ($p=10.04$) remained statistically significant in comparison with the control group. Furthermore, a significant increase in quality of life remained after correcting for multiple comparisons ($p=0.03$) vs. the placebo group (**Table 3**). However, there were no significant changes regarding anxiety, depression, and fatigue scores in comparison with the control group ($p> 0.05$).

Side effects

The participants did not report any allergic or serious adverse events during the clinical trial. Some of the patients reported mild bloating at the beginning of supplementation during the study; however, all bloating events resolved during the supplementation period.

DISCUSSION

An emerging body of evidence has highlighted the beneficial effects of spirulina in human health. Indeed, this spiral blue-green microalgae is a good source of important nutrients²⁵⁻²⁷, and could be used as a complementary therapy for health improvement in several non-communicable diseases^{25,26,28}. To the best of our knowledge, the current work is the first randomized, double-blinded, placebo-controlled trial to comprehensively assess the efficacy of spirulina (*Arthrospira platensis*) supplementation on anthropometric indices, blood pressure, sleep quality, anxiety, stress, depression, and fatigue status in ulcerative colitis patients. Accordingly, our results revealed that no significant effects were detected in the anthropometric indices or blood pressure, after spirulina supplementation, among patients with ulcerative colitis, in comparison with the placebo group. However, spirulina supplementation significantly reduced sleep disturbances at the end of eight weeks, although no significant changes occurred in the sleep quality score or other sleep parameters, in comparison with the control group. In addition, a significant reduction

283in stress score and an increase in quality of life was observed following eight weeks of
284administration with spirulina in comparison with the placebo group, but not for depression,
285anxiety, or fatigue scores.

286The present study indicated that 1 g/day spirulina supplementation did not affect anthropometric
287indices in ulcerative colitis patients. A previous systematic review and meta-analysis of
288randomized clinical trials ²⁴, incongruent to our results, posited that >2 g/day spirulina
289administration can significantly decrease anthropometric indices among overweight or obese
290subjects. The authors reported that spirulina supplementation may lead to decreases weight or
291other anthropometric indices through reduction of oxidative stress and free radicals, anti-
292inflammatory effects, decreasing liver-lipid accumulation, and a mediatory effect on appetite ²⁴.
293Although, a more recent meta-analysis ⁴², concordant with our results, suggested that relatively
294low doses of spirulina supplementation did not affect weight or BMI, respectively. Although, in
295quantities >2g/day, some anthropometric changes were observed⁴². Nevertheless, given that loss
296of appetite and weight loss are the common symptoms in patients with ulcerative colitis ^{43,44},
297more than 2 g/day of spirulina supplementation may exacerbate the symptoms and complications
298of ulcerative colitis. .

299We observed that eight weeks of 1 g/day Spirulina administration did not significantly change
300blood pressure in ulcerative colitis patients. Previous clinical studies have reported conflicting
301outcomes regarding the efficacy of spirulina on blood pressure ^{45,46}. Driessche et al ⁴⁵ indicated
302that a daily intake of 4.8 g spirulina did not affect SBP or DBP among non-hypercholesterolemic
303adults. In contrast, several studies revealed that 2 to 4.5 g/day spirulina supplementation
304significantly reduced the SBP or DBP ⁴⁷⁻⁵¹. However, Huang et al.⁴⁶, in their meta-analysis,
305observed that spirulina administration has a beneficial effect on DBP improvement, but not SBP.

306Indeed, the extant literature posits that spirulina contains phycocyanin and peptides with
307antihypertensive properties which may able to decrease the SBP or DBP via increases nitric
308oxide synthase, inhibition of angiotensin I-converting enzymes, and consequently inhibiting
309renin–angiotensin–aldosterone system ⁴⁷⁻⁵¹. However, the effective spirulina dosage and its'
310mechanism of action on blood pressure are still controversial, and therefore, more clinical trials
311with a longer length of intervention and suitably powered sample sizes are essential.

312Several studies have shown that sleep and its parameters may be related to some symptoms and
313severe exacerbations of ulcerative colitis ^{6,52,53}. Hood et al.⁶ reported that poor sleep quality is
314prevalent in ulcerative colitis patients, whilst Ananthakrishnan et al.⁵² also, in their prospective
315cohort study, indicated that less than six hours/day or higher than nine hours/day sleep were each
316related with an enhanced risk of ulcerative colitis. Moreover, Sobolewska-Wlodarczyk et al. ⁵³
317revealed that sleep disturbance was prevalent among ulcerative colitis patients. Therefore, the
318monitoring and management of sleep abnormalities can help colitis patients to improve their
319health status. The results of the current trial, for the first time, suggested that spirulina
320administration for eight weeks could significantly diminish sleep disturbances in ulcerative
321colitis patients, albeit no significant differences were detected in the sleep quality score or other
322sleep parameters in comparison with the control group. Spirulina can putatively improve sleep
323disturbances via various proposed mechanisms. First, spirulina manufactures extracellular
324products with microbial-modulating properties ⁵⁴, where it has been reported that non-normal
325microbial diversity was observed among participants who had poor sleep quality ⁵⁵. The
326microbial-modulating properties of spirulina via inhibit the growth of some Gram-negative or
327Gram-positive bacteria ⁵⁴, which may help achieve normal intestinal bacterial distribution in
328poor sleep quality individuals. Second, spirulina as functional food has several bioactive contents

329with anti-inflammatory or antioxidant functions ⁵⁶⁻⁵⁸. According to previous literature, a higher
330oxidative or inflammatory condition in patients is strongly associated with poor sleep quality and
331sleep disturbance problems ^{59,60}. Spirulina bioactive components, including phycobiliprotein, β -
332carotene, and phycocyanin, can elicit decreases in lipid peroxidation or attenuate expression of
333inflammatory genes, which can ameliorate oxidative or inflammatory status ⁵⁶⁻⁵⁸, and
334consequently enhance sleep quality. Third, spirulina can increase leptin secretion from adipose
335tissue ⁶¹; indeed, Hirota et al suggested that plasma leptin concentrations were positively related
336to higher sleep quality⁶². It is possible that the increased leptin levels may lead to a higher sleep
337quality. Notwithstanding the posited mechanisms, further clinical trials are necessary to confirm
338the precise mechanism of action.

339The main therapeutic strategies in ulcerative colitis patients are to sustain a good quality of life
340by preventing relapse, and treating symptomatic periods when they happen ⁶³. Langhorst et al. ⁶⁴
341reported that short-term stress was positively related to higher risk of relapse among ulcerative
342colitis patients, whilst Levenstein et al.⁶⁵ also demonstrated that life stress was related with both
343subjective and objective aspects of relapse in ulcerative colitis. Therefore, stress management
344methods may help to decrease disease relapse risk in ulcerative colitis patients and increase the
345quality of life ^{64,66}. Indeed, a novel finding in our study was that a significant reduction in stress
346score and increase in quality of life was observed following supplementation with spirulina in
347comparison with the control group. Spirulina supplementation, via potential mechanisms, may
348conceivably affect stress status of ulcerative colitis patients through anti-oxidative or anti-
349inflammatory features ^{67,68}. In addition, spirulina can help to maintain normal intestinal bacterial
350distribution and decrease potential disorders from opportunistic pathogens, like E.coli and
351Candida albicans, and subsequently lower leakage into the bloodstream ²², which, in turn, can

352reduce inflammatory load and stress risk ⁶⁹. C-phycocyanin, a bioactive component of spirulina,
353selectively inhibits cyclooxygenase-2 ⁷⁰, which is involved stress-related psychiatric disorders ⁷¹,
354in addition to possessing bio-absorptive attributes against environmental heavy metals exposure,
355such lead or cadmium ^{72,73}, and may reduce risk of heavy metals-induced neurotoxicity ⁷⁴.
356Furthermore, spirulina supplementation, through an inhibitory effect on pancreatic lipase
357enzymes and jejunal cholesterol absorption ²⁴, may lead to improvements in cholesterol-induced
358mood disorders ⁷⁵. Despite the apparent effect of spirulina supplementation on reducing stress, it
359did not yield on changes in depressive and anxiety symptoms or fatigue score of ulcerative colitis
360patients in our study. Considering the potential effects of spirulina on mental health ^{29,31,76,77}, a
361longer course of intervention or a higher dose may improve the efficacy of spirulina
362supplementation on other aspects of mental health, however further trials are warranted
363accordingly.

364Overall, improvements in quality of life observed after spirulina supplementation in the present
365study could be due to improved sleep disturbance ⁷⁸ and stress ⁶³ status in patients with ulcerative
366colitis. Indeed, the enhanced quality of life among individuals with ulcerative colitis might
367potentially decrease disease activity and risk of symptomatic periods ^{63,78}.

368STRENGTHS AND LIMITATIONS

369

370We, for the first time, conducted a parallel randomized, placebo-controlled, and double-blind
371clinical trial that comprehensively examined the efficacy of spirulina supplementation on health
372status among free-living participants with ulcerative colitis disease. Further, the high number of
373participants that completed the clinical trial indicated good compliance of patients with their
374therapy. Additional strengths of this work include the homogeneous population of ulcerative

375colitis patients, and also the assessment of physical activity and dietary intake as important
376confounding factors during the intervention.

377However, notwithstanding the strengths outlined above, our study, like other clinical trials, had
378some limitations. Due to the participants declining post-intervention colonoscopy, because of its
379invasive nature, we were not able to apply colonoscopy or tissue biopsy results to evaluate the
380severity of ulcerative colitis disease. Although, we applied a valid and reliable SCCAI
381questionnaire as an effective tool to counteract this issue. The dose-dependent efficacy of
382spirulina supplementation was not evaluated in the study, meaning that we cannot infer such a
383relationship. Finally, the time of intervention in the current trial was potentially not long-enough
384to elicit anthropometric changes, so a longer duration for spirulina supplementation in ulcerative
385colitis patients is recommended.

386CONCLUSION

387

388In summary, the present study was conducted to assess the efficacy of spirulina ([Arthrospira](#)
389[platensis](#)) supplementation on anthropometric indices, blood pressure, sleep quality, mood, and
390fatigue status among patients with ulcerative colitis. Our results revealed that no significant
391effects were detected in the anthropometric indices or blood pressure, after spirulina
392supplementation in comparison with the placebo group. However, spirulina supplementation
393significantly reduced sleep disturbances, in comparison with the control group. Furthermore, a
394significant reduction in stress score and increase in quality of life was observed following
395spirulina supplementation vs. the placebo group, but not for depression, anxiety, or fatigue
396scores. Further clinical trials, with a longer duration of intervention and suitably powered sample
397sizes are necessary to confirm the veracity of our results.

398**COMPETING INTERESTS**

399The authors declare that they have no competing interests.

400**AUTHORS' CONTRIBUTIONS**

401SM, MZ and ME designed this study. SM, MZ and ME contributed in trail operation. SM and
402AF performed the statistical analysis, and interpretation of data. SM wrote the manuscript. ME
403and CC critically revised the manuscript. All authors approved the final version of the
404manuscript.

405**FUNDING**

406The current work is a part of PhD thesis supported by a grant from Vice-Chancellor for
407Research, Isfahan University of Medical Sciences (No.398533).

408**ACKNOWLEDGEMENTS**

409We would like to thank all participants who kindly contributed in the study.

410**REFERENCES**

411