Journal of
Cardio - Thoracic Medicine

http://jctm.mums.ac.ir

Impact of Crocin Supplementation on Serum level of Zinc, Coppe, and Magnesium levels in Individuals with Metabolic Syndrome

Maryam Saberi-Karimian [1]*, Parisa Asadiyan-Sohan [2]*, Sahar Ghoflchi [2], Maryam Ghasemi [2], Gordon A. Ferns [3], Malihe Aghasizadeh [2,4]**, Majid Ghayour-Mobarhan [1]**

[1] International UNESCO Center for Health-Related Basic Sciences and Human Nutrition, Mashhad University of Medical Sciences, Mashhad, Iran.
[2] Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
[3] Brighton & Sussex Medical School, Division of Medical Education, Falmer, Brighton, Sussex BN1 9PH, UK.
[4] Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

ARTICLEINFO

Article type:
Original Article

Article history:
Received: 21 January 2025
Accepted: 17 May 2025

Keywords:
Crocin
Copper
Magnesium
Metabolic syndrome
Zinc

ABSTRACT

Introduction and Objectives: Current evidence on the association between serum trace element levels and the development of Metabolic Syndrome (MetS) is limited and inconsistent. Recently, investigators have examined saffron supplementation that, which could increase serum trace elements in individuals with MetS. This paper will focus on determining the impact of crocin capsules on the effectiveness of serum Zn, Cu, and Mg in people diagnosed with MetS.

Methods: In this study, a double-blind clinical trial was a conducted, comprising 44 individuals with MetS aged18-70 years. Patients were categorized into a treatment group receiving crocin capsules (1g/day) or a placebo group for a period of 30 days. Levels of serum Zn, Mg, and Cu were measured using an automated analysis system (Model BT3000, Nica Instruments Biotech, Rome, Italy) at the baseline and end of the study.

Results: Forty-four subjects completed the clinical trial. The investigation showed that baseline characteristics revealed no notable differences between the placebo and crocin groups ($p > 0.05$). According to our analysis, it was visibly apparent that there was an increase in serum Zinc levels following crocin supplementation for 30 days. Crocin supplementation had no significant effects on serum. Mg, Zn/Cu, or Cu concentrations.

Conclusion: Metabolic disorders can be modulated by increasing the supply of dietary compounds with antioxidant properties such as crocin.

► *Saberi-Karimian, M., Asadiyan-Sohan, P., Ghoflchi, S., Ghasemi, M., Ferns, G.A., Aghasizadeh, M., Ghayour-Mobarhan, M. Impact of Crocin Supplementation on Serum level of Zinc, Coppe, and Magnesium levels in Individuals with Metabolic Syndrome. J Cardiothorac Med. 2025; 13(2): 1537-1544. Doi : 10.22038/jctm.2025.80591.1483*

*Equal first author
**Corresponding authors: Malihe Aghasizadeh, Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran, Email: maliagh20@gmail.com.
MajidGhayour-Mobarhan, International UNESCO center for Health-Related Basic Sciences and Human Nutrition, Mashhad University of Medical Sciences, Mashhad, Iran, Email: ghayourm@mums.ac.ir

Introduction

Metabolic Syndrome (MetS) refers to a clusterof interrelated risk factors that increase the risk of Cardiovascular Disease (CVD), includeing insulin resistance, central obesity, or disrupted glucosemetabolism, dyslipidemia, and hypertension (1). Epidemiological studies show that genetic and lifestyle factors play a fundamental role in the progression of MetS (2). MetS occurs most often in populations with by excessive nutrient intake and physical inactivity (3). Global prevalence is reported to be between 14% and 32%, depending on age and sex. Additionally, approximately 30% of the Iranian population is reported to suffer from MetS (4). Several studies have indicated that the status of certain trace elements, including copper and zinc, is associated with MetS (5). The regulation of inflammatory processes is significantly influenced by essential metals, particularly zinc and copper (6). Studies have shown that copper and zinc supplementation can reduce chronic inflammation by preventing the activation of NF-κb induced by lipopolysaccharides (7). According to the analysis, systemic inflammation may be a potential underlying mechanism linking the prevalence of MetS to exposure to essential metals (5).

Zinc is essential for various metabolic functions in humans, including the reduction of oxidative stress, the management of inflammation, and the synthesis and secretion of insulin. Therefore, it may have implications for the development of MetS (8, 9). In Iranian individuals, serum zinc levels were clearly higher in men with MetS than in those without MetS (10, 11). Copper also play a role in several antioxidant enzymes, including catalase, cytochrome oxidase and superoxide dismutase (12). Some studies indicate that copper may be related to MetS (13-16). Additionally, several reports have demonstrated a relationship between copper consumption and an increased risk of MetS (17, 18). Magnesium is essential for the absorption and utilization of several nutrients. In some meta-analysis studies, it has been mentioned that there is a negative relationship between magnesium consumption and MetS (19, 20). However, in individual studies, it has been shown that there is a significant relationship only in women, which is controversial (21, 22). Understanding how these metals are affected by lifestyle factors is likely to be important in understanding the etiology and management of MetS (23,24).

Crocin has powerful antioxidant and anti-inflammatory propertiesand has been studied for its potential benefits in conditions related to oxidative stress (25). Derived from saffron, crocin has various reported health benefits (26), including cardioprotective, anti-cancer, anti-inflammatory, neuroprotective, antihypertensive, and anti–oxidant actions (27). Furthermore, it has been suggested that crocin can affect glucose metabolism and insulin sensitivity (28, 29). Evidence suggests that crocin treatment significantly corrected atypical changes in serum cholesterol, LDL-c, HDL-c, and triglyceride levels in diabetic rats, with the higher dose of crocin showing a modestly improved outcome compared to the lower dose. Consequently, the antidiabetic effects of crocin, along with its capacity to improve lipid profiles in diabetic individuals affected by these changes, are of substantial significance (29). However, there is limited quantity of research evaluating the effects of crocin on trace elements in subjects with MetS (30). Trace elements, such as zinc, copper, and selenium, play crucial roles in metabolic processes, oxidative stress regulation, and inflammation, all of which are implicated in MetS. Crocin, a key bioactive compound in saffron, is known for its anti-inflammatory, antioxidant, and metabolic regulatory features. Previous studies suggest that crocin supplementation may influence serum trace element levels, potentially improving metabolic health by restoring balance (31).

Hence, the purpose of this trial was to evaluate the effect of crocin on serum zinc, copper, and magnesium levels in subjects with MetS.

Materials and Methods

Study population

For this randomized controlled clinical trial (RCT), participants were recruited from obese individuals who had been referred to the Nutrition Department of Ghaem Hospital

between August 2010 and August 2012. The study flow chart is shown in Figure 1.

The study protocol received approval from Mashhad University of Medical Sciences (IRCT2013080514279N1). All individuals provided informed consent. This form was obtained from all participants in accordance with protocols granted by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.fm.REC.1397.018). This study enrolled 44 subjects with metabolic syndrome (aged 18 to 70 years) between April and June 2014 who fulfilled the eligibility requirements described previously (32). Participants were included based on the criteria established by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) criteria for MetS: waist circumference greater than 102 cm in males and greater than 88 cm in females, insulin resistance (fasting blood glucose (FBG)> 100 mg/dl) impaired glucose tolerance dyslipidemia with elevated serum triglyceride levels (TG)> 150mg/dl, reduced serum high-density lipoprotein cholesterol levels HDL-C < 50 mg/dl in females and HDL-C < 40 mg/dl in males, and high blood pressure (> 130/85 mmHg).

Randomization and Blinding

Computer generated random numbers were used to perform random allocation to groups in this trial. Sequentially numbered sealed envelopes were also used to perform the random allocation sequence by an anonymous person in the project. The intervention group used crocin capsules while the control group used placebo capsules containing starch. It is worth noting that the placebo capsules were identical in shape and color to the crocin capsules. The production of crocin tablets followed the methodology outlined by Nikbakht-Jam et al. (33). Curcumin capsules contained 5 mg of piperine and 500 mg of curcuminoids, while placebo capsules contained 5 mg of piperine (like the curcumin capsules).

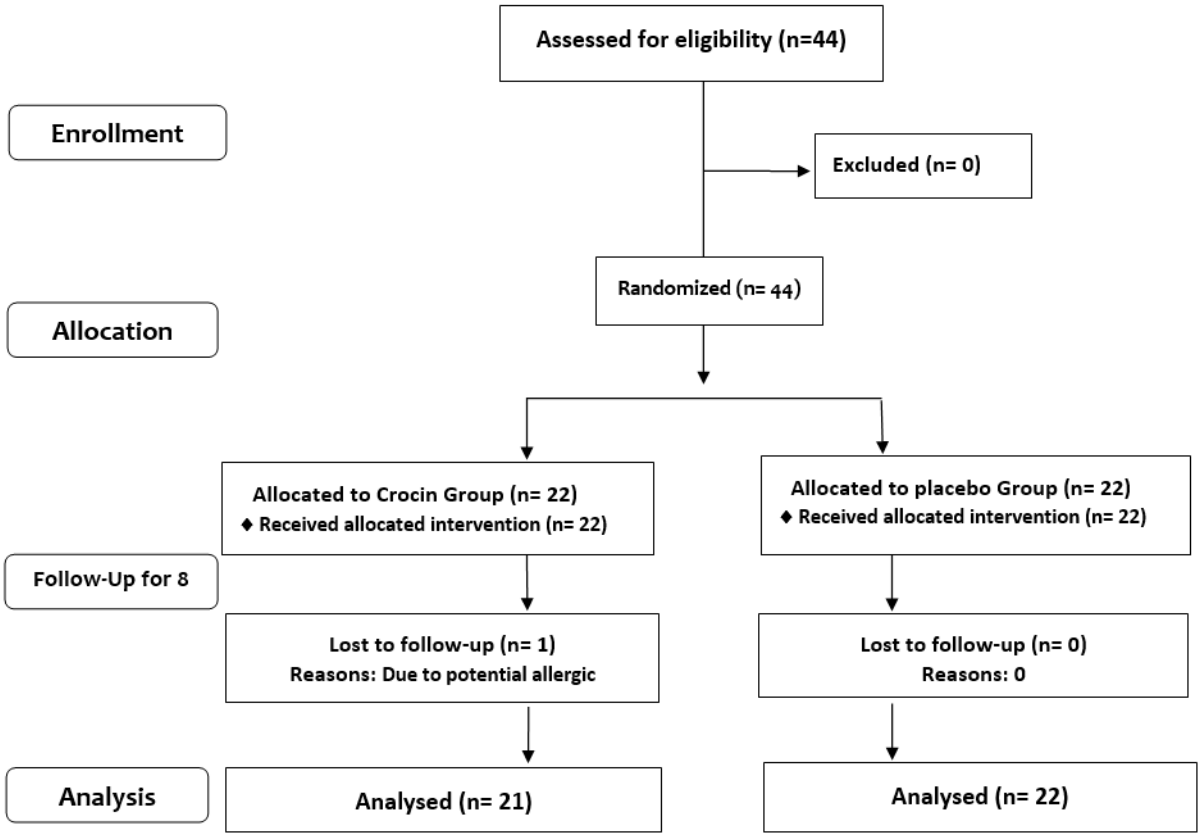

Figure 1. Flow chart of study.

The dosage of crocin (1 g/day) for individuals with Metabolic Syndrome (MetS) is likely based on previous studies evaluating its efficacy in improving metabolic factors. A meta-analysis and systematic review of randomized controlled trials found that Crocus sativus and crocin supplementation improved systolic blood pressure, hemoglobin A1C, and fasting blood glucose in cases with metabolic disorders. Additionally, a clinical trial assessing crocin's effects on MetS components used 100 mg/day for six weeks, suggesting that different dosages have been explored (34). The choice of 1 g/day is based on optimizing therapeutic effects while ensuring safety and tolerability.

Outcome Measurements

All subjects underwent blood sampling after a 12-hour fasting period, both before the intervention began and at the end of the intervention. A total of 44 subjects were allocated to two distinct groups: 22 individuals received crocin and 22 individuals received a placebo. All participants took 2 tablets of 30 mg each of both crocin and placebo per day for a period of eight weeks. Standard protocols were used to measure anthropometric indices and subjects were asked to complete a questionnaire that included questions on demographic information.

Laboratory measurements

The concentration of magnesium, zinc, and copper was evaluated using an auto-analyzer (model BT3000, Biotech nica Instruments, Rome, Italy) and commercial kits (Zn: 462-01-111/3, Mg: 1028, Cu: 341-01-038/1).

Statistical analysis

Statistical analyses were conducted using SPSS software version 18. To assess variables that did not follow a normal distribution, t-tests, Mann-Whitney and U tests were utilized. The level of statistical significance was set at <0.05.

Results

Forty-four subjects completed the clinical trial. Table 1 displays the baseline clinical factors of the participants .The investigations revealed no significant differences in Cu, Mg, Zn/Cu, and Zn between the crocin and placebo groups (p> 0.05).

The influence of crocin on serum levels of Zn, Cu, and Mg in the study groups is presented in Table 2. The data showed a significant difference (P = 0.03). However, no significant difference was observed between the study groups after the intervention (P > 0.05).

Table 1. Baseline biochemical variables in the study groups.

Variable	Crocin (N=21)	Placebo (N=22)	P-value
Serum Zn, µg/dl	93.34±24.56	96.37±25.19	0.801
Serum Cu, µg/dl	104.55±34.44	86.00±18.10	0.164
Serum Zn/Cu	1.05(0.78 to 1.23)	1.10(0.94 to 1.42)	0.374
Serum Mg, µg/dl	1.76(1.72 to 1.89)	1.77(1.65 to 1.87)	0.703

*Data are presented as Mean ± SD or median and interquartile range.

Table 2. Crocin's effects on serum levels of Cu, Zn and Mg in the study groups.

	Variable	Crocin (N=21)	Placebo (N=22)	P-value
After the intervention period	Zn, µg/dl	99.56±17.12	97.69±24.82	0.462
	Cu, µg/dl	100.16±33.45	83.14±13.42	0.085
	Zn/Cu	0.92(0.76 to 1.23)	1.14(0.97 to 1.40)	0.060
	Mg, µg/dl	1.90(1.86 to 1.95)	1.85(1.69 to 2.01)	0.444
Difference between values before and after intervention	Zn, µg/dl	6.22±19.85	1.32±28.31	0.03*
	Cu, µg/dl	-5.21±17.53	-6.16±26.16	0.941
	Zn/Cu	0.50(-0.07 to 3.01)	0.37(-1.33 to 1.45)	0.628
	Mg, µg/dl	0.10(-0.14 to 0.16)	-0.03(-0.48 to 0.12)	0.297

Therefore, there were no meaningful effects of crocin at 1 g per day for 30 days on serum Mg, Zn/Cu, and Cu concentrations.

Discussion

This double-blind randomized controlled trial study was the first to examine the impact of crocin on serum levels of Cu, Mg, and Zn in subjects with MetS in the Iranian population. Crocin, the main carotenoid in saffron, has potent antioxidant properties that can neutralize some free radicals (35, 36). A study on individuals how had MetS (by Nikbakht-Jam et al.) showed people taking 30 mg/day of crocin for 8 weeks had an effect on oxidant status in individuals with MetS (33). Crocin has various properties, such as potential positive effects on hyperlipidemia, high blood pressure, and hyperglycemia and it may also affect MetS (35). However, a controlled, double-blind study administering 100 mg/day of crocin tablets for less than 2 months had no effect on the components of MetS (37).

Due to the important effects of magnesium, zinc and copper on human metabolism, we examined crocin's effect on the levels of Mg, Zn, and Cu in subjects with MetS. Zinc has antioxidant and anti-inflammatory properties (38, 39). An imbalance between zinc and copper levels has been documented to cause oxidative stress and their deficiency is effective in a greater likelihood of developing cardiovascular disease and diabetes (40). Some studies indicate a correlation between serum Zn and Cu levels and MetS (41-43). In 2012, Yu et al. demonstrated in Chinese men with MetS that serum zinc levels were higher (44). Additionally, in another study, results showed that the level of serum zinc was significantly higher in men with MetS compared to those without it, but in women with MetS, this trend was reported to be negative (10, 45). Based on the double-blind clinical trial showeda Relationship between MetS and concentration of magnesium (46). A cohort study demonstrated Characters with serum Zn in the lower quartile compared to higher quartile levels had a Elevated fasting blood glucose level (FBG) and degree of insulin resistance (47). Darroudi et al. showed that Serum levels ofserum Zn and Cu in normal BMI persons in an Iranian populationwere related to the prevalence of MetS (48). Serum concentrations of Cu, Zn, and Mg have been reported to be associated with the prevalence of MetS, although there have been conflicting results in different populations (48). In our study, administering crocin at a dosage of 60 mg per day for eight weeks showed no significant impact on serum Zn and Mg levels. However, the time constraints of the study as well as the low amounts of crocin consumed may be responsible for our negative result.

Conclusion

A total of forty-four subjects were included in this clinical trial. According to our analysis, a notable rise in serum zinc levels was demonstrated following crocin supplementation for a period of 30 days. Nevertheless, no notable effects of crocin supplementation on serum Mg also Cu Mg concentrations were observed. Therefore, metabolic disorders can be modulated by increasing the supply of dietary compounds with antioxidant properties such as crocin.

Declarations

Ethics Approval and Consent to Participate

Informed consent was obtained from all subjects using protocols approved by the Ethics Committee of Mashhad University of Medical Science. (IR.MUMS.fm.REC.1397.018).

Availability of Data and Materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing Interests

The authors declare no conflict of interest.

Acknowledgments

We gratefully acknowledge the contributions of the data collection team and the individuals who participated in this study.

Funding

This work was supported by a grant from Islamic Azad University, Iran.

References

1. Yeh WT, Weng LC. Epidemiology of metabolic syndrome in Asia. Asia Pacific journal of clinical nutrition. 2008;17:37-42.
2. Zaribaf F, Falahi E, Barak F, Heidari M, Keshteli AH, Yazdannik A, et al. Fish consumption is inversely associated with the metabolic syndrome. European journal of clinical nutrition. 2014 Apr;68(4):474-80.
3. Johnson RJ, Segal MS, Sautin Y, Nakagawa T, Feig DI, Kang DH, et al. Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease2. The American journal of clinical nutrition. 2007 Oct 1;86(4):899-906.
4. Farmanfarma KK, Kaykhaei MA, Adineh HA, Mohammadi M, Dabiri S, Ansari-Moghaddam A. Prevalence of metabolic syndrome in Iran: A meta-analysis of 69 studies. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019 Jan 1;13(1):792-9.
5. Ma J, Zhou Y, Wang D, Guo Y, Wang B, Xu Y, et al. Associations between essential metals exposure and metabolic syndrome (MetS): exploring the mediating role of systemic inflammation in a general Chinese population. Environment international. 2020 Jul 1;140:105802.
6. Milanino R, Marrella M, Gasperini R, Pasqualicchio M, Velo G. Copper and zinc body levels in inflammation: an overview of the data obtained from animal and human studies. Agents and actions. 1993 Jul;39:195-209.
7. von Bülow V, Dubben S, Engelhardt G, Hebel S, Plümäkers B, Heine H, et al. Zinc-dependent suppression of TNF-α production is mediated by protein kinase A-induced inhibition of Raf-1, IκB kinase β, and NF-κB. The Journal of Immunology. 2007 Sep 15;179(6):4180-6.
8. Hara T, Takeda TA, Takagishi T, Fukue K, Kambe T, Fukada T. Physiological roles of zinc transporters: molecular and genetic importance in zinc homeostasis. The Journal of Physiological Sciences. 2017 Mar 1;67(2):283-301.
9. Olechnowicz J, Tinkov A, Skalny A, Suliburska J. Zinc status is associated with inflammation, oxidative stress, lipid, and glucose metabolism. The journal of physiological sciences. 2018 Jan 1;68(1):19-31.
10. Ghasemi A, Zahediasl S, Hosseini-Esfahani F, Azizi F. Gender differences in the relationship between serum zinc concentration and metabolic syndrome. Annals of human biology. 2014 Sep 1;41(5):436-42.
11. Rashidmayvan M, Mansoori A, Aghasizadeh M, Dianati M, Barati S, Sahranavard T, et al. Prediction of cardiovascular disease risk by serum zinc and copper concentrations and anthropometric measurements. Journal of Trace Elements in Medicine and Biology. 2024 May 1;83:127385.
12. Uauy R, Olivares M, Gonzalez M. Essentiality of copper in humans. The American journal of clinical nutrition. 1998 May 1;67(5):952S-9S.
13. Xu J, Zhou Q, Liu G, Tan Y, Cai L. Analysis of serum and urinal copper and zinc in Chinese northeast population with the prediabetes or diabetes with and without complications. Oxidative medicine and cellular longevity. 2013;2013(1):635214.
14. Freitas EP, Cunha AT, Aquino SL, Pedrosa LF, Lima SC, Lima JG, et al. Zinc status biomarkers and cardiometabolic risk factors in metabolic syndrome: a case control study. Nutrients. 2017 Feb 22;9(2):175.
15. Qu R, Jia Y, Liu J, Jin S, Han T, Na L. Dietary flavonoids, copper intake, and risk of metabolic syndrome in Chinese adults. Nutrients. 2018 Jul 29;10(8):991.
16. La SA, Lee JY, Kim DH, Song EL, Park JH, Ju SY. Low magnesium levels in adults with metabolic syndrome: a meta-analysis. Biological trace element research. 2016 Mar;170:33-42.
17. Lu CW, Lee YC, Kuo CS, Chiang CH, Chang HH, Huang KC. Association of serum levels of zinc, copper, and iron with risk of metabolic syndrome. Nutrients. 2021 Feb 7;13(2):548.
18. de Oliveira Otto MC, Alonso A, Lee DH, Delclos GL, Bertoni AG, et al. Dietary Intakes of Zinc and Heme Iron from Red Meat, but Not from Other Sources, Are Associated with Greater Risk of Metabolic Syndrome and Cardiovascular Disease3. The Journal of nutrition. 2012 Mar 1;142(3):526-33.
19. Ju SY, Choi WS, Ock SM, Kim CM, Kim DH. Dietary magnesium intake and metabolic syndrome in the adult population: dose-response meta-analysis and meta-regression. Nutrients. 2014 Dec 22;6(12):6005-19.
20. Dibaba DT, Xun P, Fly AD, Yokota K, He K. Dietary magnesium intake and risk of metabolic syndrome: a meta-analysis. Diabetic Medicine. 2014 Nov;31(11):1301-9.
21. Choi MK, Bae YJ. Relationship between dietary magnesium, manganese, and copper and metabolic syndrome risk in Korean adults: the Korea National Health and Nutrition Examination Survey (2007–2008). Biological Trace Element Research. 2013 Dec;156:56-66.

22. Noori N, Nafar M, Poorrezagholi F, Ahmadpoor P, Samadian F, Firouzan A, et al. Dietary intakes of fiber and magnesium and incidence of metabolic syndrome in first year after renal transplantation. Journal of Renal Nutrition. 2010 Mar 1;20(2):101-11.
23. Maekawa M, Watanabe A, Iwayama Y, Kimura T, Hamazaki K, Balan S, et al. Polyunsaturated fatty acid deficiency during neurodevelopment in mice models the prodromal state of schizophrenia through epigenetic changes in nuclear receptor genes. Translational psychiatry. 2017 Sep;7(9):e1229-.
24. Burns KA, Vanden Heuvel JP. Modulation of PPAR activity via phosphorylation. Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids. 2007 Aug 1;1771(8):952-60.
25. Ghoushi E, Poudineh M, Parsamanesh N, Jamialahmadi T, Sahebkar A. Curcumin as a regulator of Th17 cells: Unveiling the mechanisms. Food Chemistry: Molecular Sciences. 2024 Mar 12:100198.
26. Li X, Jiang C, Zhu W. Crocin reduces the inflammation response in rheumatoid arthritis. Bioscience, biotechnology, and biochemistry. 2017 May 4;81(5):891-8.
27. Hazman Ö, Aksoy L, Büyükben A. Effects of crocin on experimental obesity and type-2 diabetes. Turkish journal of medical sciences. 2016;46(5):1593-602.
28. Shirali S, Zahra Bathaie S, Nakhjavani M. Effect of crocin on the insulin resistance and lipid profile of streptozotocin-induced diabetic rats. Phytotherapy Research. 2013 Jul;27(7):1042-7.
29. Rajaei Z, Hadjzadeh MA, Nemati H, Hosseini M, Ahmadi M, Shafiee S. Antihyperglycemic and antioxidant activity of crocin in streptozotocin-induced diabetic rats. Journal of medicinal food. 2013 Mar 1;16(3):206-10.
30. Mohajer A, Ghayour-Mobarhan M, Parizadeh SM, Tavallaie S, Rajabian M, Sahebkar A. Effects of supplementation with curcuminoids on serum copper and zinc concentrations and superoxide dismutase enzyme activity in obese subjects. Trace Elem. Electrolytes. 2014;32:16-21.
31. Javandoost A, Afshari A, Nikbakht-Jam I, Khademi M, Eslami S, Nosrati M, et al. Effect of crocin, a carotenoid from saffron, on plasma cholesteryl ester transfer protein and lipid profile in subjects with metabolic syndrome: A double blind randomized clinical trial. ARYA atherosclerosis. 2017 Sep;13(5):245.
32. Mohammadi A, Sahebkar A, Iranshahi M, Amini M, Khojasteh R, Ghayour-Mobarhan M, et al. Effects of supplementation with curcuminoids on dyslipidemia in obese patients: a randomized crossover trial. Phytotherapy Research. 2013 Mar;27(3):374-9.
33. Nikbakht-Jam I, Khademi M, Nosrati M, Eslami S, Foroutan-Tanha M, Sahebkar A, et al. Effect of crocin extracted from saffron on pro-oxidant–anti-oxidant balance in subjects with metabolic syndrome: A randomized, placebo-controlled clinical trial. European journal of integrative medicine. 2016 Jun 1;8(3):307-12.
34. Yan X, Zhao S, Feng X, Li X, Zhou Q, Chen Q. Effects of Crocus sativus on glycemic control and cardiometabolic parameters among patients with metabolic syndrome and related disorders: a systematic review and meta-analysis of randomized controlled trials. Nutrition & Metabolism. 2024 May 25;21(1):28.
35. Alavizadeh SH, Hosseinzadeh H. Bioactivity assessment and toxicity of crocin: a comprehensive review. Food and chemical toxicology. 2014 Feb 1;64:65-80.
36. Goli SA, Mokhtari F, Rahimmalek M. Phenolic compounds and antioxidant activity from saffron (Crocus sativus L.) petal. Journal of Agricultural Science. 2012;4(10):175-.
37. Kermani T, Kazemi T, Molki S, Ilkhani K, Sharifzadeh G, Rajabi O. The efficacy of crocin of saffron (Crocus sativus L.) on the components of metabolic syndrome: A randomized controlled clinical trial. Journal of research in pharmacy practice. 2017 Oct 1;6(4):228-32.
38. Vallee BL, Falchuk KH. The biochemical basis of zinc physiology. Physiological reviews. 1993 Jan 1;73(1):79-118.
39. Prasad AS. Zinc: role in immunity, oxidative stress and chronic inflammation. Current Opinion in Clinical Nutrition & Metabolic Care. 2009 Nov 1;12(6):646-52.
40. Hamasaki H, Kawashima Y, Yanai H. Serum Zn/Cu ratio is associated with renal function, glycemic control, and metabolic parameters in Japanese patients with and without type 2 diabetes: a cross-sectional study. Frontiers in endocrinology. 2016 Nov 15;7:147.
41. Miao X, Sun W, Fu Y, Miao L, Cai L. Zinc homeostasis in the metabolic syndrome and diabetes. Frontiers of medicine. 2013 Mar;7:31-52.
42. Viktorínová A, Tošerová E, Križko M, Ďuračková Z. Altered metabolism of copper, zinc, and magnesium is associated with increased levels of glycated hemoglobin in patients with diabetes mellitus. Metabolism. 2009 Oct 1;58(10):1477-82.
43. Seo JA, Song SW, Han K, Lee KJ, Kim HN. The associations between serum zinc levels and metabolic syndrome in the Korean population: findings from the 2010 Korean National Health and Nutrition Examination Survey. PloS one. 2014 Aug 25;9(8):e105990.

44. Yu Y, Cai Z, Zheng J, Chen J, Zhang X, Huang XF, et al. Serum levels of polyunsaturated fatty acids are low in Chinese men with metabolic syndrome, whereas serum levels of saturated fatty acids, zinc, and magnesium are high. Nutrition research. 2012 Feb 1;32(2):71-7.
45. Mohamadian M, Parsamanesh N, Chiti H, Sathyapalan T, Sahebkar A. Protective effects of curcumin on ischemia/reperfusion injury. Phytotherapy Research. 2022 Dec;36(12):4299-324.
46. Guerrero-Romero F, Jaquez-Chairez FO, Rodríguez-Morán M. Magnesium in metabolic syndrome: a review based on randomized, double-blind clinical trials. Magnesium research. 2016 Dec 1;29(4).
47. Yang HK, Lee SH, Han K, Kang B, Lee SY, Yoon KH, et al. Lower serum zinc levels are associated with unhealthy metabolic status in normal-weight adults: the 2010 Korea National Health and Nutrition Examination Survey. Diabetes & metabolism. 2015 Sep 1;41(4):282-90.
48. Darroudi S, Fereydouni N, Tayefi M, Esmaily H, Sadabadi F, Khashyarmanesh Z, et al. Altered serum Zinc and Copper in Iranian Adults who were of normal weight but metabolically obese. Scientific Reports. 2019 Oct 16;9(1):14874.