

SARA KASHKOOLI, BSc Nutr.

Dietitian & Nutritionist



H-index: 12 | Citations: 372 | Publications: 14

Kurdistan Province, Iran | Sa.kashkooli@gmail.com | [LinkedIn profile](#) | [ResearchGate profile](#) | [google scholar](#)

Research Statement

My research pathway began with co-authoring systematic reviews and meta-analyses of clinical trials for metabolic diseases, including diabetes, NAFLD, and obesity. This work has resulted in 14 publications, including 5 in Q1 journals. My expertise in statistical analysis and research design has equipped me to contribute to advancing evidence-based nutritional interventions for complex metabolic conditions.

I aim to investigate the critical relationship between **dietary quality, the gut microbiome, and mental health outcomes**. My proposed PhD research will focus on exploring how **ultra-processed foods (UPFs) and non-nutritive additives** modulate key pathways in the **gut-brain axis** to influence susceptibility to **anxiety and depression in adolescents**. I plan to identify specific **inflammatory mechanisms** driven by modern dietary patterns to develop nutritional frameworks that **prevent the onset of mental disorders**. This work seeks to bridge **clinical nutrition with psychiatry** to improve resilience and healthspan in vulnerable populations..

Education

Bachelor of Nutrition and Dietetics Science

Lorestan University of Medical Science, Iran | 2016 - 2020

- **GPA:** 16.31/20 (3.4/4)
- **Relevant Coursework:** Epidemiology, Clinical Nutrition, Research Methodology

Employment History

1. Diet therapist and nutritional consultant (private practice)

Kurdistan Province | Iran | Jul 2024 – present

- Offer personalized dietary consultations and plans for clients.
- Educate clients on healthy eating practices and weight management.

2. Nutrition and Diet Therapy Consultant

Sina Hospital | Kamyaran City | Kurdistan Province | Iran | 14 Feb 2022 – present

- Provide specialized consultation in nutrition and diet therapy to patients.

3. Nutrition and Diet Therapy Consultant

Shohada Hospital | Dehgolan City | Kurdistan Province | Iran | 20 Sep 2020 – 12 Feb 2022

- Provide specialized consultation in nutrition and diet therapy to patients.

Journal Articles

1. * Samavat S, Ashtary-Larky D, Naeini F, Nazarian B, Kashkooli S, Clark CTC, Bagheri R, Asbaghi O, Babaali M, Goudarzi MA, Zamanian A, Emamat H. The effects of green coffee bean extract on blood pressure and heart rate: A systematic review and dose-response meta-analysis of randomized controlled trials. *Diabetes Metab Syndr.* 2024;18(9):103120. DOI: [[10.1016/j.dsx.2024.103120](https://doi.org/10.1016/j.dsx.2024.103120)]
 - **Journal Standing:** Q1, Impact Factor: 6.0
 - **Contribution:** Fifth author. data collection, screening articles (selection based on inclusion/exclusion criteria), extracting numerical data, data standardization, subgroup analyses, and data entry into Excel for meta-analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 6](#)] • **appendix name:** Samavat_et_al_2024_P1

2. Ashtary-Larky, D., Lamuchi-Deli, N., Kashkooli, S., Mombaini, D., Alipour, M., Khodadadi, F., Bagheri, R., Dutheil, F., & Wong, A. (2023). The effects of exercise training on serum concentrations of chemerin in individuals with overweight and obesity: a systematic review, meta-analysis, and meta-regression of 43 clinical trials. *Archives of Physiology and Biochemistry*, 129(5), 1012–1027. First published online: March 12, 2021. DOI: [[10.1080/13813455.2021.1892148](https://doi.org/10.1080/13813455.2021.1892148)]
 - **Journal Standing:** Q2, Impact Factor: 4.3
 - **Contribution:** Third author. data collection, screening articles (selection based on inclusion/exclusion criteria), extracting numerical data, data standardization, subgroup analyses, and data entry into Excel for meta-analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 7](#)] • **appendix name:** Ashtary_Larky_et_al_2023_P1

3. Ashtary-Larky, D., Kashkooli, S., Bagheri, R., Lamuchi-Deli, N., Alipour, M., Mombaini, D., Baker, J. S., Ahmadi, A. R., & Wong, A. (2023). The effect of exercise training on serum concentrations of chemerin in patients with metabolic diseases: a systematic review and meta-analysis. *Archives of Physiology and Biochemistry*, 129(5), 1028–1037. First published online: March 2, 2021. DOI: [[10.1080/13813455.2021.1892149](https://doi.org/10.1080/13813455.2021.1892149)]
 - **Journal Standing:** Q2, Impact Factor: 1.9
 - **Contribution:** Second author. Participated in study design, data extraction, standardization of data units, and subgroup analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 8](#)] • **appendix name:** Ashtary_Larky_et_al_2023b_P1

4. * Ashtary-Larky, D., Bagheri, R., Ghanavati, M., Asbaghi, O., Kashkooli, S., Tinsley, G. M., Mombaini, D., Kooti, W., & Wong, A. (2022). Effects of betaine supplementation on cardiovascular markers: A systematic review and Meta-analysis. *Critical Reviews in Food Science and Nutrition*, 62(23), 6516–6533. First published online: March 25, 2021. DOI: [[10.1080/10408398.2021.1902938](https://doi.org/10.1080/10408398.2021.1902938)]
 - **Journal Standing:** Q1, Impact Factor: 8.8
 - **Contribution:** Fifth author. data collection, screening articles (selection based on inclusion/exclusion criteria), extracting numerical data, data standardization, subgroup analyses, and data entry into Excel for meta-analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 9](#)] • **appendix name:** Ashtary_Larky_et_al_2022_P1

5. Asbaghi O, Moradi S, Kashkooli S, Zobeiri M, Nezamoleslami S, Hojjati Kermani MA, Lazaridi A-V, Miraghajani M. The effects of oral magnesium supplementation on glycaemic control in patients with type 2 diabetes: a systematic review and dose-response meta-analysis of controlled clinical trials. *Br J Nutr.* 2022;128(12):2420–2432. DOI:[[10.1017/S0007114521005201](https://doi.org/10.1017/S0007114521005201)]
 - **Journal Standing:** Q2, Impact Factor: 3.0
 - **Contribution:** Third author. data collection, screening articles (selection based on inclusion/exclusion criteria), extracting numerical data, data standardization, subgroup analyses, and data entry into Excel for meta-analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 10](#)] • **appendix name:** Asbaghi_et_al_2022_P1

6. Ashtary-Larky, D., Bagheri, R., Tinsley, G. M., Asbaghi, O., Salehpour, S., Kashkooli, S., Kooti, W., & Wong, A. (2022). Betaine supplementation fails to improve body composition: a systematic review and meta-analysis. **British Journal of Nutrition**, 128(5), 975-988. DOI: [[10.1017/S0007114521004062](https://doi.org/10.1017/S0007114521004062)]
- **Journal Standing:** Q2, Impact Factor: 3.0
 - **Contribution:** Sixth author. data collection, screening articles (selection based on inclusion/exclusion criteria), extracting numerical data, data standardization, subgroup analyses, and data entry into Excel for meta-analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 11](#)] • **appendix name:** Ashtary_Larky_et_al_2022b_P1
-
7. Asbaghi, O., Hosseini, R., Boozari, B., Ghaedi, E., Kashkooli, S., & Moradi, S. (2021). The Effects of Magnesium Supplementation on Blood Pressure and Obesity Measure Among Type 2 Diabetes Patient: a Systematic Review and Meta-analysis of Randomized Controlled Trials. **Biological Trace Element Research**, 199(2), 413-424. Published online: 8 May 2020. DOI: [[10.1007/s12011-020-02157-0](https://doi.org/10.1007/s12011-020-02157-0)]
- **Journal Standing:** Q1, Impact Factor: 3.6
 - **Contribution:** Fifth author. Screening studies, performing data extraction, managing database in Excel , and contributed to subgroup analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 12](#)] • **appendix name:** Asbaghi_et_al_2021_P1
-
8. * Asbaghi, O., Kashkooli, S., Mardani, M., Kelishadi, M. R., Fry, H., Kazemi, M., & Kavian, M. (2021). The effect of green coffee bean extract supplementation on liver function and inflammatory biomarkers: A meta-analysis of randomized clinical trials. **Complementary Therapies in Clinical Practice**, 43, 101349. DOI: [[10.1016/j.ctcp.2021.101349](https://doi.org/10.1016/j.ctcp.2021.101349)]
- **Journal Standing:** Q1, Impact Factor: 3.5
 - **Contribution:** Second author. Screened articles for eligibility, extracted and validated data, performed data standardization, and contributed to the statistical analysis and manuscript drafting.
 - **Status:** Published.
 - **First Page:** [[View on Page 13](#)] • **appendix name:** Asbaghi_et_al_2021b_P1
-
9. Asbaghi, O., Kashkooli, S., Amini, M. R., Shahinfar, H., Djafarian, K., Clark, C. T. C., & Shab-Bidar, S. (2020). The effects of L-carnitine supplementation on lipid concentrations in patients with type 2 diabetes: A systematic review and meta-analysis of randomized clinical trials. **Journal of Cardiovascular and Thoracic Research**, 12(4), 246-255. DOI: [[10.34172/jcvtr.2020.43](https://doi.org/10.34172/jcvtr.2020.43)]
- **Journal Standing:** Q3
 - **Contribution:** Second author. Conducted systematic search, study selection, data extraction, data conversion, and contributed to the meta-analysis process.
 - **Status:** Published.
 - **First Page:** [[View on Page 14](#)] • **appendix name:** Asbaghi_et_al_2020_P1
-
10. Abbasnezhad, A., Hasanavand, A., Falahi, E., Kashkooli, S., Asbaghi, O., & Choghakhor, R. (2020). The Effect of L Carnitine Supplementation on Lipid Profiles of Patients with Liver Disease: A Systematic Review and Meta-Analysis. **Preventive Nutrition and Food Science**, 25(2), 124-132. DOI: [[10.3746/pnf.2020.25.2.124](https://doi.org/10.3746/pnf.2020.25.2.124)]
- **Journal Standing:** Q2
 - **Contribution:** Fourth author. data collection, screening articles (selection based on inclusion/exclusion criteria), extracting numerical data, data standardization, subgroup analyses, and data entry into Excel for meta-analysis.
 - **Status:** Published.
 - **First Page:** [[View on Page 15](#)] • **appendix name:** Abbasnezhad_et_al_2020_P1

11. Abbasnezhad, A., Choghakhor, R., & Kashkooli, S. (2019). Effect of L-carnitine on liver enzymes and biochemical factors in hepatic encephalopathy: A systematic review and meta-analysis. *Journal of Gastroenterology and Hepatology*, 34(12), 2062-2070. Published online: 28 July 2019. DOI: [[10.1111/jgh.14765](https://doi.org/10.1111/jgh.14765)]

- **Journal Standing:** Q1, Impact Factor: 3.4 (at time of publication)
- **Contribution:** Third author. Involved in study selection based on criteria, data extraction, data management, and subgroup analysis.
- **Status:** Published.
- **First Page:** [[View on Page 16](#)] • **appendix name:** Abbasnezhad_et_al_2019_P1

12. Khosroshahi MZ, Mokhayeri Y, Mardani M, Eslampour E, Mohammadi R, Kashkooli S, Abbasnezhad A. Effect of curcumin supplementation on liver function enzymes: A systematic review and meta-analysis of randomized controlled clinical trials. *Curr Top Nutraceutical Res.* 2019;19(1):1-14. DOI: [[10.37290/ctnr2641-452X.19:1-14](https://doi.org/10.37290/ctnr2641-452X.19:1-14)]

- **Journal Standing:** Q4
- **Contribution:** Sixth author. Contributed to data extraction and data preparation for statistical analysis.
- **Status:** Published.
- **First Page:** [[View on Page 17](#)] • **appendix name:** Khosroshahi_et_al_2019_P1

13. Asbaghi O, Kashkooli S, Choghakhor, R, Abbasnezhad A. Effect of calcium and vitamin D co-supplementation on lipid profile of overweight/obese subjects: a systematic review and meta-analysis of the randomized clinical trials. *Obes Med.* 2019;15:100124. DOI: [[10.1016/j.obmed.2019.100124](https://doi.org/10.1016/j.obmed.2019.100124)]

- **Journal Standing:** Q2
- **Contribution:** Second author. Performed literature screening, data extraction, data conversion, and contributed to the analysis and interpretation of results.
- **Status:** Published.
- **First Page:** [[View on Page 18](#)] • **appendix name:** Asbaghi_et_al_2019_P1

14. Asbaghi O, Khosroshahi MZ, Kashkooli S, Abbasnezhad A. The Effect of Calcium Vitamin D Co Supplementation on Insulin, Insulin Sensitivity, and Glycemia: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Horm Metab Res.* 2019;51(5):288-295. DOI: [[10.1055/a-0887-0205](https://doi.org/10.1055/a-0887-0205)]

- **Journal Standing:** Q2, Impact Factor: 1.8
- **Contribution:** Third author. Involved in applying inclusion/exclusion criteria, data extraction, and data standardization for meta-analysis.
- **Status:** Published.
- **First Page:** [[View on Page 19](#)] • **appendix name:** Asbaghi_et_al_2019b_P1

Poster presentation

- 1) **Sara Kashkooli**, 2018, effect of thyroid hormones and Thyroid-Stimulating Hormone Levels after Bariatric Surgery (BS) in obese patients: A systematic review; **first annual national surgical technologist student research conference**, Tehran, Iran; [External link of poster](#)
- 2) **Sara Kashkooli**, 2018, Effect of FTO polymorphism genes on Leptin levels: a systematic review; **5th Southwestern national Student Research Congress**, Behbahan, Iran. [External link of poster](#)
- 3) **Sara Kashkooli**, 2018, prevalence of zinc deficiency in patients with thalassemia major in Iran; **11th Student Conference on Health Sciences**, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [Link of poster](#)
- 4) **Sara Kashkooli**, 2018, effect of Blood Lead Level on Blood Pressure in Workers with Occupational Exposure to Lead: A Systematic Review; **11th Student Conference on Health Sciences**, Shahid Beheshti University of Medical Sciences, Tehran,Iran. [External link of poster](#)
- 5) **Sara Kashkooli**, 2018, Investigating the Effect of Dill Plant (Anethum graveolens) on Serum Insulin and Glucose Levels in Diabetes: A Systematic Review; **4th Student Research Congress of the South-West Region of Iran**, in Abadan, Iran.

Leadership & Awards

- **Outstanding Researcher (2019, 2020)**
Lorestan University of Medical Sciences | *Top 1% among 5,000 students*
- **Secretary-General, Nutrition Sciences Student Association | 2018–2019**
Led team ranked #2 among 12 university associations
- **Head of Student Research Committee | Health and Nutrition academy | Feb 2018 – Feb 2019**
ranked #2 among 6 university research committee | Lorestan University of Medical Sciences
- **Managing Editor and Editor in Chief, Biotin Scientific Journal | 2019–2020**
Dedicated to the nutrition knowledge

Research Interests

Brain health | NAFLD | Diabetes | Omega-3 | Clinical Trials | Cohorts

Skills & Abilities

Clinical: Medical Nutrition Therapy (MNT) | Chronic Disease Management | Supplementation Protocols

Languages: Persian (Native) | Kurdish (Fluent) | English (C1)

Software: SPSS, EndNote, Python, R, Nutrition IV

Communication: Teamwork spirit and Teamwork Experiences | High ability to speak and lecture | High number of class presentations | Executive Management Ability

References

- **Prof. Ebrahim Falahi**, Professor, LUMS | Email: e_falahi@yahoo.com - falahi.e@lums.ac.ir
- **Dr. Amir Abbasnezhad**, Assistant Professor | LUMS | Iran | Email: abbasnezhad91@gmail.com
- **Dr. Omid Asbaghi**, PhD Candidate, Shahid Beheshti University | Email: omid.asbaghi@gmail.com

Appendix: First Pages of Publications

DSX 18 (2024) 103120



The effects of green coffee bean extract on blood pressure and heart rate: A systematic review and dose-response meta-analysis of randomized controlled trials



Simin Samavat^a, Damoon Ashtary-Larky^b, Fatemeh Naeini^c, Behzad Nazarian^d, Sara Kashkooli^d, Cain C.T. Clark^e, Reza Bagheri^f, Omid Asbaghi^g, Maryam Babaali^h, Mohammad Ali Goudarziⁱ, Ali Zamanian^{j,*}, Hadi Emamat^{k,**}

^a Department of Cellular and Molecular Nutrition, School of Nutrition Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran

^b Nutrition and Metabolic Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

^c Department of Clinical Nutrition, School of Nutritional Science, Tehran University of Medical Science, Tehran, Iran

^d Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran

^e Centre for Intelligent Healthcare, Coventry University, Coventry, CV1 5FB, UK

^f Department of Exercise Physiology, University of Isfahan, Isfahan, Iran

^g Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

^h Department of Sports Physiology, Damghan Branch, Islamic Azad University, Damghan, Iran

ⁱ Shahrekhord Branch, Islamic Azad University, Shahrekhord, Iran

^j Science in Nutrition, Shahid Beheshti University of Medical Sciences, Iran

^k The Persian Gulf Tropical Medicine Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran

ARTICLE INFO

Keywords:

Chlorogenic acid
Green coffee bean extract
Blood pressure
Heart rate
Meta-analysis

ABSTRACT

Background and aims: The existing literature on the effects of green coffee bean extract (GCBE) consumption on systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) is equivocal. This study aimed to summarize the effects of GCBE consumption on SBP, DBP and HR in adults.

Methods: Data were pooled using a random-effects model and expressed as weighted mean difference (WMD) and 95 % confidence intervals (95 % CIs).

Results: Out of 1624 records, 10 studies that enrolled 563 participants were included. GCBE consumption significantly decreased SBP (WMD: -2.95 mmHg; 95 % CI: -4.27 to -1.62; $p < 0.001$) and DBP (WMD: -2.15 mmHg; 95 % CI: -2.59 to -1.72; $p < 0.001$). However, there was no significant effect on HR (WMD: -1.20 bpm; CI: -2.93 to 0.51; $p = 0.170$). Subgroup analysis showed that GCBE consumption had a more significant effect on SBP and DBP in participants with high SBP and DBP and had no effect on blood pressure in females. Linear and non-linear dose-response analyses were conducted to find the optimum GCBE dosage and duration of intervention. However, no significant associations were observed for SBP, DBP, and HR in linear meta-regression and non-linear dose-response based on the dose and duration of the intervention.

Conclusion: GCBE has the potential as a hypertension-reducing supplement in hypertensive patients. However, GCBE did not significantly change HR.

1. Introduction

High blood pressure, or hypertension, is one of the most common

non-communicable diseases globally and recognized as the central risk factor for cardiovascular disease (CVD) [1,2]. Chronic hypertension can lead to numerous complications, such as heart attacks, strokes, kidney

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<https://doi.org/10.1016/j.dsx.2024.103120>

Received 3 August 2022; Received in revised form 13 September 2024; Accepted 14 September 2024

Available online 23 September 2024

1871-4021/© 2024 Research Trust of DiabetesIndia (DiabetesIndia) and National Diabetes Obesity and Cholesterol Foundation (N-DOC). Published by Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

1. Samavat_et_al_2024_P1

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REVIEW ARTICLE



The effects of exercise training on serum concentrations of chemerin in individuals with overweight and obesity: a systematic review, meta-analysis, and meta-regression of 43 clinical trials

Damoon Ashtary-Larky^a, Nasrin Lamuchi-Deli^a, Sara Kashkooli^b, Delsa Mombaini^a, Meysam Alipour^c, Fatemeh Khodadadi^d, Reza Bagheri^e, Frédéric Dutheil^f and Alexei Wong^g

^aNutrition and Metabolic Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; ^bStudent Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran; ^cAlimentary Tract Research Center, Clinical Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; ^dDepartment of Exercise Physiology, Ferdowsi University of Mashhad, Mashhad, Iran; ^eDepartment of Exercise Physiology, University of Isfahan, Isfahan, Iran; ^fUniversité Clermont Auvergne, CNRS, LaPSCo, Physiological and Psychosocial Stress, CHU Clermont-Ferrand, University Hospital of Clermont-Ferrand, Preventive and Occupational Medicine, Witty Fit, France; ^gDepartment of Health and Human Performance, Marymount University, Arlington, TX, USA

ABSTRACT

Context: Elevated serum concentrations of chemerin is a significant factor in the development of metabolic disorders in individuals with overweight and obesity.

Objective: This systematic review, meta-analysis, and meta-regression evaluated the effects of exercise training on serum concentrations of chemerin in individuals with overweight and/or obesity.

Methods: Studies published up to January 2021 were identified through four databases. Forty-three studies including 1271 participants were included and analysed using a random-effects model to calculate weighted mean differences with 95% confidence intervals.

Results: Results indicated that exercise training significantly decreased serum concentrations of chemerin in individuals with overweight and/or obesity. Subgroup analysis showed that all types of exercise (aerobic, resistance, and combined training) interventions but not high-intensity interval training decreased serum concentrations of chemerin. Subgroup analysis based on baseline body mass index (BMI), gender, and intervention duration showed significant declines in serum concentrations of chemerin. Meta-regression analysis indicated a linear relationship between changes in body fat percentage (BFP) with serum concentrations of chemerin.

Conclusion: Exercise training may decrease serum concentrations of chemerin in individuals with overweight and/or obesity. The chemerin-lowering effects of exercise might be related to declines in BFP. Further studies are needed to confirm these findings.

ARTICLE HISTORY

Received 5 January 2021

Revised 8 February 2021

Accepted 12 February 2021

Published online 6 March 2021

KEYWORDS

Chemerin; exercise; overweight; obesity; meta-analysis

Introduction

The high prevalence of obesity continues to be a major public health issue across the world (Ashtary-Larky *et al.* 2020). An excess in body mass and adiposity are often accompanied by a variety of diseases and health complications, including metabolic syndrome, type-2 diabetes mellitus (T2DM), cardiovascular diseases (CVD), musculoskeletal disorders, and cancer (Ashtary-Larky *et al.* 2018, Abdi *et al.* 2020, Wong *et al.* 2020); leading to a decline in quality of life as well as a rise in disability and mortality (WHO 2018, Tremblay *et al.* 2020). Indeed, adipose tissue-secreted molecules called adipokines mediate obesity and its related diseases (Bagheri *et al.* 2020). Adipokines are involved in the regulation of appetite and satiety, energy expenditure, endothelial function, blood pressure, insulin sensitivity, adipogenesis, fat distribution, and insulin secretion (Blüher 2014, Freitas Lima *et al.* 2015). Therefore, adipokines may be a potential treatment to combat obesity and its complications.

Among adipokines, chemerin was described as a marker that is positively related to body mass (BM), fat mass, T2DM, CVD, and pro-inflammatory markers (Helfer and Wu 2018). Epidemiological studies have shown higher serum concentrations of chemerin in individuals with overweight and obesity (Guzel *et al.* 2014, Niklowitz *et al.* 2018). Lifestyle modifications are generally the first line of treatment to decrease excess adiposity and pro-inflammatory adipokines such as chemerin (Lee *et al.* 2013, Kim *et al.* 2014). Among lifestyle modifications, different types of exercise training have been shown to reduce the serum concentrations of chemerin in overweight and obese individuals (Wang 2017, Salesi and Gani 2018, Kazemi and Naderi Pour, 2019, Avazpour *et al.* 2020). However, some investigations have failed to show any alterations in serum concentrations of chemerin following exercise interventions in overweight and obese individuals (Banitalebi *et al.* 2016, Saravani *et al.* 2020). Moreover, a previous study showed that exercise training may increase the serum concentrations of this pro-inflammatory adipokine

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REVIEW ARTICLE



The effect of exercise training on serum concentrations of chemerin in patients with metabolic diseases: a systematic review and meta-analysis

Damoon Ashtary-Larky^a, Sara Kashkooli^b, Reza Bagheri^c, Nasrin Lamuchi-Deli^a, Meysam Alipour^{d,e}, Delsa Mombaini^a, Julien S. Baker^f , Amirhossein Ramezani Ahmadi^g and Alexei Wong^h

^aNutrition and Metabolic Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; ^bStudent Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran; ^cDepartment of Exercise Physiology, University of Isfahan, Iran Isfahan; ^dAlimentary Tract Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; ^eNutrition and Metabolic Disease Research center, Clinical Sciences Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; ^fCentre for Health and Exercise Science Research, Hong Kong Baptist University, Kowloon Tong, Hong Kong; ^gDepartment of Nutrition, School of Applied Medical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; ^hDepartment of Health and Human Performance, Marymount University, Arlington, TX, USA

ABSTRACT

Context: Elevated serum concentrations of chemerin is a significant factor in the development of metabolic disorders.

Objective: This systematic review and meta-analysis evaluated the influence of exercise training on serum concentrations of chemerin in patients with metabolic diseases.

Methods: Thirteen studies including 463 participants were included and analysed using a random-effects model to calculate weighted mean differences with 95% confidence intervals.

Results: Results indicated that exercise training significantly decreased serum concentrations of chemerin in patients with metabolic diseases when compared with controls. Subgroup analysis showed that exercise training resulted in decreases in serum concentrations of chemerin in men, however, this was not significant in women. Moreover, subgroup analyses based on the type of exercise did not reveal differential effects on serum concentrations of chemerin.

Conclusion: Exercise training may produce improvements in serum concentrations of chemerin in patients with metabolic diseases. Further longer-term studies are needed to confirm these findings.

ARTICLE HISTORY

Received 5 December 2020

Accepted 13 February 2021

Published online 1 March 2021

KEYWORDS

Chemerin; exercise; metabolic disease; diabetes; meta-analysis

Introduction

Metabolic disorders including insulin resistance, diabetes, hypertension, and cardiovascular disease are well-known global health care problems with a persistent surge in prevalence among adults (Balakumar *et al.* 2016, Tremblay *et al.* 2020, Wong *et al.* 2020). Previous findings have shown a strong relationship between the development of low-grade inflammatory responses and adipose tissue secreted molecules known as adipokines and the incidence of metabolic disorders (Ouchi *et al.* 2011, Eskandari *et al.* 2020, Bagheri *et al.* 2020a); suggesting that adipokines can be used as therapeutic targets to treat these conditions (Kobayashi and Inoguchi 2005, Dludla *et al.* 2020).

Among the adipokines, chemerin has been described as a pro-inflammatory marker, which is produced by the liver and white adipose tissue (Hosseini *et al.* 2017, Helfer and Wu 2018). Epidemiological studies have reported a positive relationship between circulating chemerin concentrations and obesity (Guzel *et al.* 2014, Niklowitz *et al.* 2018), diabetes (Coimbra *et al.* 2014, Fatima *et al.* 2017, Yang *et al.* 2010), hypertension (Gu *et al.* 2014), metabolic syndrome (Jialal

et al. 2013), and psoriatic pathogenesis (Chiricozzi *et al.* 2018). Chemerin expression specifically marks the early phases of evolving psoriatic skin correlating with plasmacytoid dendritic cell migration and activation (Chiricozzi *et al.* 2018). In addition, it has been observed that low chemerin expression can be detected in chronic stable plaques (Albanesi *et al.* 2009). Recently, Shafer-Eggleton *et al.* examined the validity of two chemerin-related ratios as biomarkers of metabolic syndrome and reported that the chemerin/high-density lipoprotein (HDL-C) ratio is superior to C-reactive protein (CRP) in predicting metabolic syndrome (Shafer-Eggleton *et al.* 2020). Also, this ratio was correlated with body mass index (BMI), waist circumference (WC), triglycerides, and plasma glucose (Shafer-Eggleton *et al.* 2020); which provides further evidence for the importance of reducing serum concentrations of chemerin in metabolic diseases. Studies have demonstrated that lifestyle modifications significantly decrease serum concentrations of chemerin, which is associated with improved insulin sensitivity (Lee *et al.* 2013, Kim *et al.* 2014). Among lifestyle modifications, different types of exercise training have been shown to improve

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REVIEW



Effects of betaine supplementation on cardiovascular markers: A systematic review and Meta-analysis

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ABSTRACT

Controversy regarding the effects of betaine supplementation on cardiovascular markers has persisted for decades. This systematic review and meta-analysis compared the effects of betaine supplementation on cardiovascular disease (CVD) markers. Studies examining betaine supplementation on CVD markers published up to February 2021 were identified through PubMed, the Cochrane Library, Web of Science, Embase, and SCOPUS. Betaine supplementation had a significant effect on concentrations of betaine (MD: 82.14 $\mu\text{mol/L}$, 95% CI: 67.09 to 97.20), total cholesterol (TC) (MD: 14.12 mg/dL, 95% CI: 9.23 to 19.02), low-density lipoprotein (LDL) (MD: 10.26 mg/dL, 95% CI: 6.14 to 14.38), homocysteine (WMD: -1.30 micromol/L, 95% CI: -1.61 to -0.98), dimethylglycine (DMG) (MD: 21.33 micromol/L, 95% CI: 13.87 to 28.80), and methionine (MD: 2.06 micromol/L, 95% CI: 0.23 to 3.88). Moreover, our analysis indicated that betaine supplementation did not affect serum concentrations of triglyceride (TG), high-density lipoprotein (HDL), fasting blood glucose (FBG), C-reactive protein (CRP), liver enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT)], and blood pressure. Our subgroup analysis suggested that a maximum dose of 4 g/d might have homocysteine-lowering effects without any adverse effect on lipid profiles reported with doses of ≥ 4 g/d. In conclusion, the present systematic review and meta-analysis supports the advantage of a lower dose of betaine supplementation (< 4 g/d) on homocysteine concentrations without the lipid-augmenting effect observed with a higher dosage.

KEYWORDS

Betaine supplementation; cardiovascular disease; homocysteine; lipid profile; meta-analysis

Introduction

It is well known that cardiovascular disease (CVD) is the leading cause of mortality worldwide (Mc Namara, Alzubaidi, and Jackson 2019). Research has demonstrated that several risk factors such as abdominal obesity, dyslipidemia, and hypertension are strongly linked to CVD (Cercato and Fonseca 2019). Additionally, it has been ascertained that higher fasting concentrations of homocysteine ($> 15 \mu\text{mol/L}$) are associated with elevated inflammatory markers, triglycerides, and blood glucose, which increase the likelihood of CVD (Guthikonda and Haynes 2006). Nutritional strategies to lessen the occurrence of CVD have sustained substantial interest for several decades. For instance, an inverse relationship between betaine (trimethylglycine) supplementation and homocysteine concentrations has previously been demonstrated (Cho et al. 2006; Velzing-Aarts et al. 2005). The homocysteine-lowering property of betaine is likely due to an increase in betaine-dependent methylation of

homocysteine into methionine (McRae 2013). A considerable amount of literature has reported the effects of betaine supplementation on CVD patients and healthy individuals. For instance, the meta-analysis of McRae (2013) indicated that 4 to 6 g/d of betaine supplementation lowered plasma concentrations of homocysteine by 11.8% in healthy individuals (McRae 2013). In regards to other CVD markers, betaine supplementation has previously failed to significantly modulate serum cholesterol and low-density lipoprotein (LDL) concentrations in some investigations (Atkinson et al. 2009; Steenge, Verhoef, and Katan 2003). More strikingly, other investigations reported that betaine supplementation significantly increased total cholesterol and LDL concentrations in obese and healthy individuals (Schwab et al. 2011; Schwab et al. 2002). Conversely, healthy individuals who supplemented with > 360 mg/d of betaine had significantly lower concentrations of homocysteine and inflammatory markers' concentrations [C-reactive protein (CRP) and tumor necrosis factor- α (TNF- α)] (Detopoulou et al. 2008).

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Supplemental data for this article can be accessed at <https://doi.org/10.1080/10408398.2021.1902938>.

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The effects of oral magnesium supplementation on glycaemic control in patients with type 2 diabetes: a systematic review and dose-response meta-analysis of controlled clinical trials

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(Submitted 23 October 2020 – Final revision received 10 December 2021 – Accepted 27 December 2021 – First published online 20 January 2022)

Abstract

The current systematic review and meta-analysis were conducted to evaluate the effects of oral Mg supplementation on glycaemic control in type 2 diabetes mellitus (T2DM) patients. Related articles were found by searching the PubMed, SCOPUS, Embase and Web of Science databases (from inception to 30 February 2020). A one-stage robust error meta-regression model based on inverse variance weighted least squares regression and cluster robust error variances was used for the dose–response analysis between Mg supplementation and duration of intervention and glycaemic control factors. Eighteen eligible randomised clinical trials were included in our final analysis. The dose–response testing indicated that the estimated mean difference in HbA1c at 500 mg/d was -0.73% (95 % CI: -1.25% , -0.22%) suggesting modest improvement in HbA1c with strong evidence (P value: 0.004). And in fasting blood sugar (FBS) at 360 mg/d was -7.11 mg/dl (95 % CI: -14.03 mg/dl , -0.19 mg/dl) suggesting minimal amelioration in FBS with weak evidence (P value: 0.092) against the model hypothesis at this sample size. The estimated mean difference in FBS and HbA1c at 24 weeks was -15.58 mg/dl (95 % CI: -24.67 mg/dl , -6.49 mg/dl) and -0.48 mg/dl (95 % CI: -0.77 mg/dl , -0.19 mg/dl), respectively, suggesting modest improvement in FBS (P value: 0.034) and HbA1c (P value: 0.001) with strong evidence against the model hypothesis at this sample size. Oral Mg supplementation could have an effect on glycaemic control in T2DM patients. However, the clinical trials so far are not sufficient to make guidelines for clinical practice.

Key words: Magnesium supplementation; Glycaemic control; Type 2 diabetes; Meta-analysis

Diabetes is a well-known public health issue with an increasing prevalence worldwide. The scientific community has estimated that 592 million people will be diagnosed with diabetes by 2030⁽¹⁾. In type 2 diabetes mellitus (T2DM), raised blood sugar levels known as hyperglycaemia^(2,3) can lead to various chronic complications, including CVD, kidney disease, retinopathy,

neuropathy and amputation^(2–4). Patients with diabetes are three times more likely to be hospitalised than healthy subjects. Higher risk of early death and shorter life expectancy have been observed in T2DM patients^(5,6). One of the essential goals in the treatment of T2DM is the control of glycaemic parameters⁽⁷⁾.

Abbreviations: FBS, fasting blood sugar; HOMA-IR, homeostatic model assessment of insulin resistance; RCT, randomised clinical trials; T2DM, type 2 diabetes mellitus.

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Betaine supplementation fails to improve body composition: a systematic review and meta-analysis

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(Submitted 18 December 2020 – Final revision received 20 September 2021 – Accepted 1 October 2021 – First published online 7 October 2021)

Abstract

Previous studies evaluating the effects of betaine supplementation on body composition offer contradictory findings. This systematic review and meta-analysis assessed the effects of betaine supplementation on body composition indices (body mass (BM), BMI, body fat percentage (BFP), fat mass (FM), fat-free mass (FFM)), and dietary intakes. Studies examining the effects of betaine supplementation on body composition and dietary intakes published up to August 2021 were identified through PubMed, the Cochrane Library, Web of Science, Embase, SCOPUS and Ovid databases. Betaine supplementation failed to significantly affect BM ((weighted mean difference (WMD): -0.40 kg, 95% CI -1.46, 0.64), $P=0.447$), BMI ((WMD: -0.05 kg/m², 95% CI -0.36, 0.25), $P=0.719$), BFP ((WMD: 0.26%, 95% CI -0.82, 1.36), $P=0.663$), FM ((WMD: -0.57 kg, 95% CI -2.14, 0.99), $P=0.473$) and FFM ((WMD: 0.61 kg, 95% CI -1.27, 2.49), $P=0.527$). Subgroup analyses based on participant's age (< 40 and > 40 years), sex, BMI, trial duration (< 8 and ≥ 8 weeks), betaine supplementation dosage (< 4 and ≥ 4 g) and health status (healthy or unhealthy) demonstrated similar results. Other than a potential negligible increase in protein intake (WMD: 3.56 g, 95% CI 0.24, 6.88, $P=0.035$), no changes in dietary intakes were observed following betaine supplementation compared with control. The present systematic review and meta-analysis does not show any beneficial effects of betaine supplementation on body composition indices (BM, BMI, FM and FFM).

Key words: **Betaine supplementation: Body composition: Fat mass: Fat-free mass: Meta-analysis**

Betaine is a non-toxic and chemically stable compound that is extensively distributed in nature⁽¹⁾. It was initially identified in the juice of sugar beets (*B. Vulgaris*) and has subsequently been observed in other organisms⁽²⁾. Foods containing betaine include wheat products, spinach, beets and liver, among others⁽³⁾. However, the precise amount of dietary betaine depends both on the food source and cooking method⁽³⁾. Dietary betaine intake influences betaine content in kidneys, liver and brain which seem to be the primary destinations of ingested betaine⁽⁴⁾. Intakes of 9–15 g of betaine appear to be safe

in humans⁽⁴⁾. Besides dietary intake, betaine can be made from choline in the human body⁽⁵⁾. Previous studies indicate that betaine supplementation may improve cardiovascular risk and inflammatory status^(5,6).

While 'betaine' technically refers to a class of related molecules, the term is most commonly used to describe a glycine molecule with three additional methyl groups, termed trimethylglycine⁽⁴⁾. Reports have shown that both choline and betaine supplements can combat obesity in animals, including rats⁽⁷⁾, pigs^(8,9) and chickens⁽¹⁰⁾. Moreover, human studies have reported that higher betaine

Abbreviations: BFP, body fat percentage; BM, body mass; FFM, fat-free mass; FM, fat mass; RCT, randomised controlled trials; WMD, weighted mean difference.

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The Effects of Magnesium Supplementation on Blood Pressure and Obesity Measure Among Type 2 Diabetes Patient: a Systematic Review and Meta-analysis of Randomized Controlled Trials

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Received: 16 December 2019 / Accepted: 15 April 2020
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Abstract

In this study, we aimed to systematically review the literature to evaluate the effects of magnesium (Mg) supplementation on blood pressure (BP) and obesity measure among patients with type 2 diabetes mellitus (T2DM). Major electronic databases of Web of Science, the Cochrane library, PubMed, and Scopus were searched completely from the inception until 15 October 2019 to identify randomized clinical trials (RCTs) pertaining to the topic of interest. All outcomes were pooled using a random-effects model and expressed as weighted mean differences (WMD) with 95% confidential intervals (CI). Heterogeneity, sensitivity analysis, and publication bias were also assessed using standard methods. The pooled analysis of five RCTs showed that Mg supplementation did not affect body weight (WMD: -0.01 kg, 95% CI: -0.36 to 0.33), BMI (WMD: -0.07, 95% CI: -0.18 to 0.04), and waist circumference (WMD: 0.12, 95% CI: -1.24 to 1.48) in T2DM patients compared to the control groups of the patients who received placebo. However, pooling seven RCTs together showed significant reduction of systolic blood pressure (WMD: -5.78 mmHg, 95% CI: -11.37 to -0.19) and diastolic blood pressure (WMD: -2.50 mmHg, 95% CI: -4.58 to -0.41) in T2DM patients. Furthermore, subgroup analysis by dose of intervention, intervention duration, and type of intervention suggested that Mg supplementation for > 12 weeks, in doses higher than 300 mg/day or inorganic forms, could significantly decrease both systolic and diastolic BP in T2DM patients. Based on the findings, Mg supplementation has beneficial effects on BP in type 2 diabetes patients independent of body weight status. However, further investigations are needed to provide more reliable evidences.

Keywords Magnesium supplementation · Blood pressure · Obesity · Type 2 diabetes mellitus

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Effect of green coffee bean extract supplementation on liver function and inflammatory biomarkers: A meta-analysis of randomized clinical trials

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ABSTRACT

Inflammation is considered a major contributor to non-alcoholic fatty liver disease (NAFLD) and several chronic diseases such as, cardiovascular disease and type two diabetes. Green coffee bean extract (GCBE) supplementation has been suggested to enhancing antioxidant capacity in people with obesity but results across studies are mixed. We conducted a meta-analysis of randomized controlled trials of GCBE supplementation in overweight/obese with normal liver function and NAFLD adults with ALT, AST, γ -GTP, ALP, LDH, CRP, IL-6, and TNF- α as outcomes by searching PubMed and other databases. Eight studies were included, totaling 330 participants randomized to GCBE supplementation or placebo ranging from 50 mg/day to 1200 mg/day for 8–12 weeks. GCBE supplementation resulted in lower levels of TNF- α (mean difference = 1.37 pg/mL [95% CI = 0.97–1.76]; $p < 0.00001$). No significant difference was found in the remaining markers. In conclusion, GCBE supplementation attenuated TNF- α , a circulating inflammatory marker mediator which may be linked with lower systemic inflammation. However, potential cellular and molecular mechanisms by which GCBE exerts this positive effect warrants further investigations in human model studies.

1. Introduction

The liver is one of the most important organs involved in metabolism and synthesis, and uses 25% of cardiac output, more than any other organ in the body [1,2]. It also has a wide range of functions such as, breaking down toxins into low-risk substances, producing and secreting bile, storing glycogen, and metabolizing drugs [3]. These liver functions can be disrupted by damage caused by liver diseases and/or drug use [2, 3].

In light of increases in liver disease such as hepatocellular carcinoma (HCC), fatty liver, and liver cirrhosis, nonalcoholic fatty liver disease (NAFLD) is one of the most common liver diseases worldwide with a prevalence of 25.24% [4]. It is proposed that by the year 2020, the main cause of liver transplantation will be nonalcoholic steatohepatitis (NASH), which is a type of NAFLD which includes fibrosis and inflammation [5,6]. One suggested method for reducing the risk of developing liver disease is weight loss by modifying dietary intake and lifestyle [7, 8].

Coffee is one of the most common beverages in the world. Green

coffee in particular, is the bean of the Coffee fruit that has not yet been roasted, meaning it is able to maintain more bioactive phytochemicals than common roasted coffee beans [9]. Further, green coffee beans are rich in a polyphenol called chlorogenic acid (CGA) [10]. CGA is a natural chemical compound which is the ester of caffeic acid and quinic acid [11]. Studies have found that CGA can exert several functions such as, anti-cancer, anti-inflammatory, anti-lipidemic, anti-hypertensive, and anti-diabetic [12]. Due to these proposed qualities, and the association between coffee compounds and decreased levels of liver enzymes, several lines of evidence suggest that coffee constituents can also lower the likelihood of chronic diseases such as type 2 diabetes (T2D) and cardiovascular disease (CVD), as well as liver diseases [13–15].

Liver health can be evaluated by assessing several biomarkers. There are some enzymatic biomarkers (aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT)) as well as three pro-inflammatory markers such as, high-sensitive C-reactive protein (hs-CRP), IL-6, and TNF- α have been shown to indicate liver function and health [16]. Mechanistically, IL-6 elevates in the early phase of inflammation, which will induce the production of CRP.

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<https://doi.org/10.1016/j.ctcp.2021.101349>

Received 16 August 2020; Received in revised form 4 February 2021; Accepted 27 February 2021

Available online 4 March 2021

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Review Article

The effects of L-carnitine supplementation on lipid concentrations in patients with type 2 diabetes: A systematic review and meta-analysis of randomized clinical trials

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Article info

Article History:

Received: 14 December 2019

Accepted: 27 July 2020

epublished: 7 September 2020

Keywords:

L-Carnitine

Lipid Profile

Meta-Analysis

Randomized Controlled Trials

Abstract

This meta-analysis was performed to assess the effect of L-carnitine supplementation on lipid profile. A systematic search were conducted in PubMed and Scopus to identify randomized clinical trials (RCTs) which evaluated the effects of L-carnitine on lipid profile. Pooled effect sizes were measured using random-effect model (DerSimonian-Laird). Meta-analysis showed that L-carnitine supplementation significantly reduced total cholesterol (TC) (weighted mean difference [WMD]: -8.17 mg/dL; 95% CI, -14.68 to -1.65, $I^2=52.2\%$, $P=0.041$). Baseline level of TC was a source of heterogeneity, with a greater effect in studies with a baseline level of more than 200 mg/d (WMD: -11.93 mg/dL; 95% CI, -20.80 to -3.05). L-carnitine also significantly decreased low-density lipoprotein-cholesterol (LDL-C) (WMD: -5.22 mg/dL; 95% CI, -9.54 to -0.91, $I^2=66.7\%$, $P=0.010$), and LDL-C level <100 mg/dL, trial duration, and L-carnitine dosage were potential sources of heterogeneity. L-carnitine supplementation appeared to have no significant effect on high-density lipoprotein-cholesterol (HDL-C) (WMD: -0.51 mg/dL; 95% CI, -2.45 to 1.44) and triglyceride (TG) (WMD: 2.80 mg/dL; 95% CI, -8.09 to 13.69). This meta-analysis revealed that L-carnitine may have favorable effects on lipid profile, especially LDL-C and TC. However, further RCTs are needed to confirm the veracity of these results, particularly among hyperlipidemic patients.

Introduction

Diabetes mellitus is a common human metabolic diseases in all countries, and of all incidences of diabetes; type 2 diabetes is the most common, comprising about 90% of patients.¹ Type 2 diabetes is a major health concern and often occurs concurrently with dyslipidemia in individuals at high risk of cardiovascular disease.² Indeed, dyslipidemia, which is defined as abnormal level of serum lipids including decreased level of high-density lipoprotein-cholesterol (HDL-C), and elevated level of plasma triglyceride, cholesterol, and low-density lipoprotein-cholesterol (LDL-C) particles, is a key risk factor for cardiovascular disease in people with diabetes.^{3,4} Several other factors unrelated to glycemia or insulin resistance like chronic kidney disease, hyperthyroidism and genetic disorders of lipoproteins, may influence lipid profile. Unhealthy diet including high fat and low

fiber diets, elevated weigh, lack of glycemic control, and smoking also are associated with increased risk of dyslipidemia in type 2 diabetes. Accumulating evidence has suggested potentially beneficial effects of functional foods for dyslipidemia, which subsequently could ameliorate the long-term diabetes-related complications, including macro- and microvascular diseases.⁵

L-carnitine (3-hydroxy-4-N-trimethylammonio-butanoate) is a water-soluble, unbound, amine that plays an important role in transportation of long-chain fatty acids into the mitochondria, therein facilitating an increase in fatty acids metabolism.⁶⁻⁸ L-carnitine is synthesized endogenously from lysine and methionine or can be obtained from animal products, such as milk and meat.⁹ Moreover, L-carnitine might change glucose catabolism because it acts as a carrier of acetate from mitochondria to the cytoplasm, which results in reducing the acetyl



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Effect of L-Carnitine Supplementation on Lipid Profiles of Patients with Liver Disease: A Systematic Review and Meta-Analysis

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ABSTRACT: Results of previous studies regarding the effect of L-carnitine on lipid profiles in the patients with liver diseases are contradictory. This meta-analysis was performed to assess the effect of L-carnitine on serum levels of low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), and total cholesterol (TC) in overweight patients with liver diseases. A systematic search was carried out using the Web of Science, PubMed, Scopus, and Cochrane library databases to identify articles published before April 2019 investigating the effects of L-carnitine supplementation on patients with liver disease. There was no language or time limitation for the studies. A meta-analysis was carried out using both the random and fixed effects model where appropriate, and I^2 index were used to evaluate heterogeneity. These results indicated that L-carnitine supplementation significantly reduces blood levels of TC and TG in patients with liver disease, whereas carnitine had no effect on the levels of HDL and LDL. The reducing effect of L-carnitine on both TC and TG was found following long-term carnitine supplementation (≥ 24 weeks), supplementation with doses less than or equal to 2,000 mg/d, and in patients with chronic hepatitis C. This meta-analysis indicates the beneficial effect of L-carnitine on TC and TG in overweight patients with liver disease, particularly patients with chronic hepatitis C, in both long-term and low doses.

Keywords: high-density lipoprotein, L-carnitine, low-density lipoprotein, total cholesterol, triglyceride

INTRODUCTION

It is well known that the liver plays an important role in lipogenesis, gluconeogenesis, and cholesterol metabolism (Ponziani et al., 2015). Over the last decade, it has been shown that metabolic syndrome and obesity promote pathophysiological changes that can cause liver damage and ultimately lead to liver disease, such as non-alcoholic fatty liver disease (NAFLD), the most common liver disease in Western societies (Bechmann et al., 2012). Lipid accumulation and oxidation of fatty acids play an important role in damage, repair, and regeneration of the liver due to autosomal induction and production of reactive oxygen species (ROS) (Bechmann et al., 2012). Dyslipidemia is prevalent amongst people with NAFLD and has an important role in the development of cardiovascular

disease, which is the leading cause of mortality for these patients (Speliotis et al., 2018). Dyslipidemia in patients with NAFLD is typically characterized by increased levels of low-density lipoproteins (LDL) and hypertriglyceridemia, and decreased levels of high-density lipoproteins (HDL) (Speliotis et al., 2018). Furthermore, it has been shown that treatment with interferon alpha (IFN α) in combination with ribavirin in patients infected with hepatitis C virus influences lipid metabolism (Malaguarnera et al., 1995). These therapies reduce serum HDL levels and increase triglyceride (TG) levels and, consequently, the amount of fat in the liver (Naeem et al., 2001).

Exercise and diet are the first-line approaches for managing dyslipidemia (Alipour et al., 2018). When these approaches are insufficient, the first-line pharmacologic approach for managing dyslipidemia is treatment with sta-

Received 16 January 2020; Accepted 15 February 2020; Published online 30 June 2020

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META ANALYSIS AND SYSTEMATIC REVIEW

Effect of L-carnitine on liver enzymes and biochemical factors in hepatic encephalopathy: A systematic review and meta-analysis

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Key words

albumin, ammonia, bilirubin, hepatic encephalopathy, L-carnitine, meta-analysis.

Accepted for publication 15 June 2019.

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Declaration of conflict of interest: The authors declare that no conflict of interest exists.

Author contribution: A. A. and R. C. designed the study. S. K. and O. A. reviewed and selected the articles. S. K. and M. A. extracted needed data from articles. A. A. and R. M. performed data analysis and interpretation. R. C. drafted the manuscript.

Financial support: There are no financial or other competing interests for principal investigators, patients included, or any member of the trial.

Abstract

Background and Aims: We aimed to investigate the effect of L-carnitine on biochemical factors including ammonia, bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase (AST), blood urea nitrogen (BUN), and creatinine (Cr) in patients with hepatic encephalopathy (HE).

Methods: A systematic search was carried out in Web of Science, PubMed, Scopus, and Cochrane Library databases to find articles related to the effect of L-carnitine supplementation in patients with HE, up to 7 February 2019. There was no language and time limitation. Meta-analyses were carried out using both the random and fixed effects models where appropriate, and I^2 index was used to evaluate the heterogeneity.

Results: Search yielded 3462 publications. Nine randomized clinical trials with 779 patients were eligible. L-carnitine supplementation significantly reduced blood levels of ammonia. Furthermore, our results indicated that L-carnitine supplementation significantly reduced blood levels of bilirubin, AST, BUN, and Cr in patients with HE. Subgroup analysis demonstrated that L-carnitine significantly reduced ammonia in patients with all the ages, long and short duration of the supplementation, doses less or higher than 4000 mg/day, any route of treatment (intravenous or oral), and in patients with any grade of the symptoms of HE. Moreover, we found that L-carnitine significantly increased circulating levels of albumin in HE patients.

Conclusions: Present systematic review and meta-analysis revealed that L-carnitine supplementation significantly reduced blood levels of ammonia, bilirubin, AST, BUN, and Cr in HE patients. Moreover, we found that L-carnitine significantly increased circulating levels of albumin. However, further large-scale randomized clinical trials are needed.

Introduction

Hepatic encephalopathy (HE) is a neuropsychiatric complication with various symptoms including lethargy, confusion, and behavioral abnormalities that occurs commonly in acute liver failure or chronic liver disease.¹ Recent studies have indicated that over 30% of patient with hepatic cirrhosis will eventually develop HE and even a higher percentage of them are at risk of developing minimal degrees of HE.² Severity of the symptoms of HE ranges from minimal HE with no detectable alterations in personality or behavior to severe HE with marked confusion, amnesia, and coma.³ In hepatic failure, gut neurotoxins, which enter the systemic circulation, cause neurological damages.⁴ One of the neurotoxins whose levels increase in the blood is ammonia, which directly and indirectly changes the neuronal function.⁴ Moreover, most hepatic failure cases have abnormal circulating levels of

alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, and albumin that indicate the presence of concomitant coagulopathy, inflammation, and infection.⁵ In addition, it has been reported that kidney disease occurs approximately in 25% of the patients with liver diseases,⁶ and thus, assessment of kidney function is important in these patients.

Carnitine is an essential nutrient that plays a vital role in energy metabolism.⁷ It is synthesized from two essential amino acids, lysine and methionine.⁸ Carnitine transports long-chain fatty acids into the inner mitochondrial compartment and thus is essential for beta-oxidation.⁸ It has been reported that carnitine deficiency occurs in various disorders, such as renal disease treated by hemodialysis, diabetes mellitus, malnutrition, cirrhosis, and endocrine disorders.^{6,7} Therefore, recently, the supplementation of carnitine has become the subject of many investigations. Numerous studies have assessed the effect of L-carnitine supplementation in HE. A

Effect of Curcumin Supplementation on Liver Function Enzymes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Received May 2, 2019; Accepted April 18, 2020

Communicated By: Prof. Hsin-Ling Yang, PhD

Results of the previous studies assessed the effect of curcumin/turmeric on liver function are controversial. We conducted a systematic review and meta-analysis to examine the efficacy of curcumin/turmeric supplementation on liver function. A systematic search was carried out in PubMed, Cochrane Library, Web of Science, Embase, SCOPUS and Google scholar until March 15, 2018, to retrieve the randomized controlled trials which examined the effects of curcumin/turmeric on alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase and gamma glutamyl transferase. Meta-analyses were carried out using a random effects model where heterogeneity was significant or $I^2 > 50\%$. The search yielded 1946 citations. 16 randomized controlled trials with 1238 patients were eligible. Results indicated that curcumin/turmeric supplementation significantly reduced serum levels of aspartate aminotransferase and alanine aminotransferase. Curcumin/turmeric supplementation with doses more than 500 mg/day appeared to have beneficial reducing effects on aspartate aminotransferase and alanine aminotransferase. Furthermore, the beneficial effects of curcumin/turmeric supplementation were observed in less than 12 weeks supplementation. Present meta-analysis indicated the beneficial effects of curcumin/turmeric supplementation on liver function. Therefore, curcumin can be considered as a therapeutic component to reduce liver injuries in subjects who are at risk of liver damages.

Keywords: Alanine aminotransferase, Aspartate aminotransferase, Curcumin, Liver function enzymes, Meta-analysis, Systematic Review, Turmeric

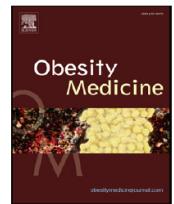
Abbreviations Used: Alkaline phosphatase, ALP; Alanine aminotransferase, ALT; Aspartate aminotransferase, AST; Catalase, CAT; Confidence interval, CI; Gamma-glutamyl transferase, GGT; Glutathione peroxidase, GPx; Glutathione reductase, GR; Glutathione S-transferase, GST; Heme oxygenase-1, HO-1; Interleukin-8, IL-8; Non-alcoholic fatty liver disease, NAFLD; Randomized controlled trials, RCTs; Reactive nitrogen species, RNS; Reactive oxygen species, ROS; Superoxide dismutase, SOD; Weighted mean difference, WMD

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INTRODUCTION

Most common biochemical factors assessed for the detection of liver diseases are serum concentrations of ALP, AST, ALT and GGT. Any chronic or acute injury to the liver, results in an elevated serum level of aminotransferases, including AST and ALT (Giannini et al., 2005). Both enzymes catalyze the transfer of α -amino groups to generate required products for gluconeogenesis and citric acid cycle (Cohen and Kaplan, 1979). Another enzyme is GGT, which

is present in both hepatocytes and biliary epithelial cells. An elevated serum level of GGT can be observed in non-hepatic diseases, and in hepatic diseases related with bile duct damage and fibrosis (Giannini et al., 2001). In addition, ALP is an enzyme that is present on the surface of bile duct epithelia, and its serum concentrations rises due to the bile duct obstruction (Fishman, 1990). Serum levels of these enzymes are considered as indicators for liver function; thus, abnormalities of these biochemical factors may represent liver damage or alteration in bile flow.



Review

Effect of calcium and vitamin D co-supplementation on lipid profile of overweight/obese subjects: A systematic review and meta-analysis of the randomized clinical trials

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ARTICLE INFO

Keywords:

Calcium
Vitamin D
Co-supplementation
LDL-C
HDL-C
Meta-analysis

ABSTRACT

Background: Results of the studies assessed the effect of calcium and vitamin D co-supplementation on lipid profiles are contradictory. Due to the inconsistent results found in the literature, we performed a systematic review and meta-analysis of randomized clinical trials (RCTs) to assess the effect of calcium and vitamin D co-supplementation on lipids concentrations.

Methods: A systematic search was carried out in Web of Science, PubMed, Scopus and Cochrane library without any language and time restriction up to March 2019, to retrieve the randomized controlled trials (RCTs) which examined the effect of calcium and vitamin D co-supplementation on lipids concentrations in overweight/obese subjects. Meta-analyses were carried out using a random effects model. I² index was used to evaluate the heterogeneity.

Results: Initial search yielded 1847 publications. Seven RCTs with 414 patients were eligible. Results show that lower doses of vitamin D and calcium significantly reduced TG and TC levels. Furthermore, we found that this co-supplementation increased the blood concentrations of HDL-C. The effect of calcium and vitamin D co-supplementation on increasing HDL-C was significant in equal or less than 8 weeks supplementation and in higher doses of vitamin D and calcium. In addition, we found that this co-supplementation significantly reduced LDL-C in equal or less than 8 weeks supplementation.

Conclusion: Present systematic review and meta-analysis indicated the beneficial effects of calcium and vitamin D co-supplementation on lipid profile of overweight/obese subjects. We found that the lower doses and short-term supplementation could have more beneficial effects.

1. Introduction

Recently, it has been shown that in overweight people with low calcium and dairy consumption, the risk of developing a metabolic syndrome was much higher than those who were overweight, but had higher calcium and dairy consumption (Pereira et al., 2002). This findings suggest that adequate calcium intake, as well as having a healthy diet and adequate physical activity, can have a significant effect on the predisposition to a healthier metabolic profile (Eriksson and Lindgarde, 1991). From a physiological point of view, the metabolic syndrome and its potential relationship with calcium or dairy consumption are the focus of attention recently. Previous studies have

shown that a low calcium diet increases the calcium content of the adipocyte (Zemel et al., 2000). One of the consequences of increasing levels of calcium in the adipose tissue is the increase in lipogenesis, which can explain the results of previous studies that demonstrated the relationship between low calcium intake and low lipid oxidation (Melanson et al., 2003). These findings were confirmed by the studies that indicated a relationship between calcium intake and lipoprotein levels. It has been reported that low calcium intake was associated with increased levels of low-density lipoprotein (LDL) and a reduction in high-density lipoprotein (HDL) levels (Jacqmain et al., 2003). As well as calcium, the association of vitamin D with metabolic syndrome has been also well-defined. Several studies have shown that vitamin D plays

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Effect of Calcium-Vitamin D Co-Supplementation on Insulin, Insulin Sensitivity, and Glycemia: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

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Key words

vitamin D, calcium, glucose, insulin, systematic review, meta-analysis

received 17.01.2019

accepted 27.03.2019

Bibliography

DOI <https://doi.org/10.1055/a-0887-0205>

Horm Metab Res 2019; 51: 288–295

© Georg Thieme Verlag KG Stuttgart · New York

ISSN 0018-5043

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Supplementary Material for this article is available online at <http://www.thieme-connect.de/products>

ABSTRACT

We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to assess the effect of calcium-vitamin D co-supplementation on insulin, insulin sensitivity, and glycemia. A systematic search was carried out in Web of Science, PubMed, EMBASE, Scopus, and Cochrane library without any language and time restriction up to 12 August 2018, to retrieve the RCTs, which examined the effect of calcium and vitamin D co-supplementation on fasting blood glucose (FBG), insulin, HOMA-B, HOMA-IR, and QUICKI. Meta-analyses were carried out using a random effects model, and I² indexes were used to evaluate the heterogeneity. Search yielded 2225 publications. Twelve RCTs with 4395 patients were eligible. Results demonstrated that calcium and vitamin D co-supplementation had significantly reducing effects on FBG, HOMA-IR and circulating levels of insulin. As the subgroup analysis demonstrated, short-term (≤ 12 weeks) calcium and vitamin D co-supplementation had a significant reducing effect on FBG. However, beneficial effects of calcium and vitamin D co-supplementation on circulating level of insulin and HOMA-IR were seen in both short-term and long-term (> 12 weeks) supplementations. Furthermore, we found that high doses of vitamin D and calcium co-supplementation (vitamin D ≥ 2000 mg/day and calcium ≥ 1000 mg/day) had significantly reducing effects on FBG, HOMA-IR and insulin. Present meta-analysis indicated the beneficial effects of high-dose and short-term combined vitamin D and calcium supplementation on insulin, insulin resistance and glycemia; however, further large-scale RCTs with adequate and multiple dosing schedules are needed.

Introduction

Insulin resistance is present in most patients with glucose intolerance or non-insulin-dependent diabetes mellitus (NIDDM), and in 25% of normal-weight subjects with normal glucose tolerance [1]. In these situations, glucose intolerance can just be prevented when the β -cell is able to increase and maintain insulin secretion [1]. Failure to achieve this goal results in instability of glucose homeosta-

sis, which is associated with many diseases [1]. An elevated blood level of glucose, insulin deficiency, and insulin resistance are the characteristic features of type 2 diabetes mellitus (DM) [2]. Type 2 DM has become a major problem for global health whose prevalence is expected to increase to 366 million by 2030 worldwide [3]. As one of the main causes of disability in 2015 [4], diabetes causes many social and economic problems and increases health costs