

Editorial

Dietary Intake of Phytochemicals, Gut Microbiota, and Appetite Control

Emad A. S. Al-Dujaili 

Centre for Cardiovascular Science, Faculty of Medicine and Veterinary Medicine, Queen's Medical Research Institute, University of Edinburgh, Edinburgh EH16 4TJ, UK; ealduja1@exseed.ed.ac.uk

1. Introduction

It has recently become apparent that plant phytochemicals can yield multiple benefits for human health, including optimizing physiological functions; modulating immune responses, inflammation, depression and anxiety, and the gut microbiota [1–5]; influencing cognitive function and Alzheimer disease [6]; enhancing stress adaptation; and impacting body system pathophysiology [7–9]. A prominent example is the probiotic and prebiotic activity of the major active constituent of phytochemicals, which modulate molecular pathways related to various body functions [10], including appetite control, which may manipulate the gut–brain axis to treat obesity [11,12], in addition to their antitumor and chemo-preventive activities [13,14]. Therefore, it is now recognized that gut health is essential for general health and wellbeing. The microbial content of the gut includes various colonies of beneficial bacteria and other microorganisms that have been found to influence the health status of the human body. Poor and fast-food diets and chronic stress cause constant gut inflammation-related compromised immunity and the development of various mood disorders through the gut–brain axis [9,12]. Thus, healthy, balanced, and gut friendly foods are important to maintain good health as well as minimizing stress [15]. Liu and colleagues [16] showed that dietary polyphenols exert various activities on aging hallmarks, including genomic instability, telomere attrition, epigenetic alterations, impaired macroautophagy, mitochondrial dysfunction, cellular senescence, altered intercellular communication, chronic inflammation, and dysbiosis [16].

At present, the growing interest in natural products is also driven by consumer demands, industry advancements, and the increasing prevalence of non-communicable diseases in aging populations [7–9]. As people seek safe and effective alternatives, the potential of natural products and functional foods in promoting health and wellness has gained momentum [7,17]. Functional foods and supplements rich in antioxidants polyphenols have been found to reduce the risk of chronic diseases, such as coronary heart disease, stroke, type 2 diabetes, obesity, and some cancers [18–20]. The pleiotropic effects of these polyphenols are evident regarding their role in redox modulation and inflammatory processes, molecular signaling, stem cell proliferation and differentiation, metabolism regulation, and hormonal imbalance, as well as their potential effects in cancer and neurodegenerative diseases [15,21]. The biological actions of diet and its active natural components have been mainly attributed to their multiple actions affecting various cellular and hormonal pathways [22]. For example, the mechanisms by which natural products could exert their antihypertensive effect have shown a multiplicity of actions (increased NO production, inhibition of renin release and ACE activity, angiotensin receptor and calcium channel blockade, antioxidant and anti-inflammatory activities, and opioid agonistic effects) [11,23,24].



Received: 23 July 2025

Accepted: 11 August 2025

Published: 15 August 2025

Citation: Al-Dujaili, E.A.S. Dietary Intake of Phytochemicals, Gut Microbiota, and Appetite Control. *Nutrients* **2025**, *17*, 2646. <https://doi.org/10.3390/nu17162646>

Copyright: © 2025 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

2. Phytochemicals and Gut Microbiota Contributions from Reviews and Original Research

This Special Issue presents recent high-quality research in the field of appetite regulation, the gut microbiota, and the probiotic actions of phytochemicals, focusing on the investigation of gut-related mechanisms in relation to functional foods, including gut hormones, gastrointestinal motility, gut–brain communication, and the roles of diet and the microbiome. The authors and co-authors have published several articles on the subject, and some of their contributions have been listed among the list of contributions [1–4]. This Special Issue comprises the following five articles, including two research papers, two reviews, and one systematic review: One of the research papers investigated the effect of the short-term intake of elderberry juice rich in anthocyanin on fecal microbiota and reported an augmentation of the fecal microbiota and an improvement in glucose tolerance and fat oxidation [5]. The other research article is a clinical trial that compared the effects of high-protein versus high-carbohydrate diets on the gut microbiome, concluding that manipulating the impact of diet, microbiome, and metabolic health might require prolonged dietary intervention to generate a significant modification of the gut ecosystem to support diabetes T2 risk reduction [6]. Among the two reviews, one of them focused on postbiotics as adjuvant therapy in cancer care, concluding that postbiotics tend to have poor bioavailability. However, the use of symbiotics (a mixture of prebiotics and probiotics) would be expected to produce better homogeneous bioavailability [7]. The other review explored the significance of gut microbiota in diabetes pathogenesis and management, suggesting that interventions focusing on the gut microbiota of diabetic patients may have the potential as a promising approach to diabetes management [8]. The last article is a systematic review and meta-analysis exploring the effect of polyphenol supplementation on memory functioning in overweight and obese adults. It concluded that there was a potential positive effect of chronic supplementation with polyphenols on immediate retrieval in participants aged over 60 years, and that obesity is a risk factor for cognitive impairment [9].

3. Future Gut–Brain Axis Interactions

The gut–brain axis (GBA) is a bidirectional communication network between the gastrointestinal tract and the brain, which is modulated by gut microbiota and the related biomarkers. Malnutrition disrupts GBA homeostasis, exacerbating GBA dysfunction through gut dysbiosis, impaired neuroactive metabolite production, and systemic inflammation. Nutraceuticals, including probiotics, prebiotics, symbiotics, postbiotics, and paraprobiotics, offer a promising approach to improving GBA homeostasis by modulating the gut microbiota composition and related neuroactive metabolites [25]. A recent review aimed to elucidate the interplay between gut microbiota-derived biomarkers and GBA dysfunction in malnutrition, evaluating the potential of nutraceuticals in combating malnutrition [26]. Furthermore, it explored the future of personalized nutraceutical interventions tailored to individual genetic and microbiome profiles, providing a targeted approach to optimizing health outcomes. The integration of nutraceuticals into GBA health management could transform malnutrition treatment and improve cognitive and metabolic health.

4. Summary and Conclusions

In summary, understanding the importance of gut microbiomes has recently become vital for health, wellbeing, and disease. There has been considerable interest in research investigating the impact of gut microbiomes on metabolic diseases. The microbial content of the gut includes various colonies of beneficial bacteria and other microorganisms which have been found to determine the health status of the human body. Gut microbiota and phytochemical-rich diets can modulate the gut–brain axis, which plays a bidirec-

tional homeostatic role between gut and brain functions. Dysbiosis and poor-quality diets cause a multitude of diseases, including cancer, neurodegenerative diseases, and non-communicable diseases, particularly in aging populations. Future and ongoing research studies should focus on the gut–brain axis and appetite control.

Conflicts of Interest: The author declares no conflicts of interest.

List of Contributions:

1. Al-Dujaili, E.A.S.; Casey, C.; Stockton, A. Antioxidant Properties and Beneficial Cardiovascular Effects of a Natural Extract of Pomegranate in Healthy Volunteers: A Randomized Preliminary Single-Blind Controlled Study. *Antioxidants* **2022**, *11*, 2124. <https://doi.org/10.3390/antiox1112124>.
2. Stockton, A.; Al-Dujaili, E.A.S.; McDougall, G.J.; Davidson, I.; Drummond, S.; Wyness, L. Effect of Pomegranate Extract Consumption on Cardiovascular Disease Risk Factors, Stress Hormones, and Quality of Life in Human Volunteers: An Exploratory Randomised, Double-Blind, Placebo-Controlled Trial". *EC Nutr.* **2015**, *2*, 396–411.
3. Stockton, A.; Al-Dujaili, E.A.S. Effect of Pomegranate Extract Consumption on Satiety Parameters in Healthy Volunteers: A Preliminary Randomized Study. *Foods* **2022**, *11*, 2639. <https://doi.org/10.3390/foods11172639>.
4. Bajes, H. and Al-Dujaili, E. Probiotics and Biotechnology Advances in Reducing and Preventing Colorectal Cancer; Minireview. *Jordan J. Pharm. Sci.* **2019**, *12*, 39–49.
5. Teets, C.; Ghanem, N.; Ma, G.; Minj, J.; Perkins-Veazie, P.; Johnson, S.A.; Etter, A.J.; Carbonero, F.G.; Solverson, P.M. A One-Week Elderberry Juice Intervention Augments the Fecal Microbiota and Suggests Improvement in Glucose Tolerance and Fat Oxidation in a Randomized Controlled Trial. *Nutrients* **2024**, *16*, 3555. <https://doi.org/10.3390/nu16203555>.
6. Faraj, S.; Sequeira-Bisson, I.R.; Lu, L.; Miles-Chan, J.L.; Hoggard, M.; Barnett, D.; Parry-Strong, A.; Foster, M.; Krebs, J.D.; Poppitt, S.D.; et al. Effect of a Higher-Protein Nut versus Higher-Carbohydrate Cereal Enriched Diet on the Gut Microbiomes of Chinese Participants with Overweight and Normoglycaemia or Prediabetes in the Tu Ora Study. *Nutrients* **2024**, *16*, 1971. <https://doi.org/10.3390/nu16121971>.
7. Balendra, V.; Rosenfeld, R.; Amoroso, C.; Castagnone, C.; Rossino, M.G.; Garrone, O.; Ghidini, M. Postbiotics as Adjuvant Therapy in Cancer Care. *Nutrients* **2024**, *16*, 2400. <https://doi.org/10.3390/nu16152400>.
8. Młynarska, E.; Wasiak, J.; Gajewska, A.; Steć, G.; Jasińska, J.; Rysz, J.; Franczyk, B. Exploring the Significance of Gut Microbiota in Diabetes Pathogenesis and Management—A Narrative Review. *Nutrients* **2024**, *16*, 1938. <https://doi.org/10.3390/nu16121938>.
9. Farag, S.; Tsang, C.; Al-Dujaili, E.A.S.; Murphy, P.N. Effect of Polyphenol Supplementation on Memory Functioning in Overweight and Obese Adults: A Systematic Review and Meta-Analysis. *Nutrients* **2024**, *16*, 474. <https://doi.org/10.3390/nu16040474>.

References

1. Santhiravel, S.; Bekhit, A.E.A.; Mendis, E.; Jacobs, J.L.; Dunshea, F.R.; Rajapakse, N.; Ponnampalam, E.N. The Impact of Plant Phytochemicals on the Gut Microbiota of Humans for a Balanced Life. *Int. J. Mol. Sci.* **2022**, *23*, 8124. [[CrossRef](#)] [[PubMed](#)] [[PubMed Central](#)]
2. Giampazolias, E.; da Costa, M.P.; Lam, K.C.; Lim, K.H.J.; Cardoso, A.; Piot, C.; Chakravarty, P.; Blasche, S.; Patel, S.; Biram, A.; et al. Vitamin D regulates microbiome-dependent cancer immunity. *Science* **2024**, *384*, 428–437. [[CrossRef](#)]
3. Yahfoufi, N.; Alsadi, N.; Jambi, M.; Matar, C. The Immunomodulatory and Anti-Inflammatory Role of Polyphenols. *Nutrients* **2018**, *10*, 1618. [[CrossRef](#)] [[PubMed](#)] [[PubMed Central](#)]
4. Peirce, J.M.; Alviña, K. The role of inflammation and the gut microbiome in depression and anxiety. *J. Neurosci. Res.* **2019**, *97*, 1223–1241. [[CrossRef](#)]
5. Cerullo, M.; Armeli, F.; Mengoni, B.; Menin, M.; Crudeli, M.L.; Businaro, R. Curcumin Modulation of the Gut–Brain Axis for Neuroinflammation and Metabolic Disorders Prevention and Treatment. *Nutrients* **2025**, *17*, 1430. [[CrossRef](#)]
6. Ciccone, L.; Nencetti, S.; Rossello, A.; Orlandini, E. Pomegranate: A Source of Multifunctional Bioactive Compounds Potentially Beneficial in Alzheimer’s Disease. *Pharmaceuticals* **2023**, *16*, 1036. [[CrossRef](#)]

7. Noce, A.; Di Daniele, N. Aging, Natural Bioactive Compounds and Non-Communicable Chronic Degenerative Diseases. *Nutrients* **2025**, *17*, 1442. [[CrossRef](#)] [[PubMed](#)]
8. Alami, M.; Boumezough, K.; Khalil, A.; Ramchoun, M.; Boulbaroud, S.; Fulop, T.; Morvaridzadeh, M.; Berrougui, H. The Modulatory Bioeffects of Pomegranate (*Punica granatum* L.) Polyphenols on Metabolic Disorders: Understanding Their Preventive Role against Metabolic Syndrome. *Nutrients* **2023**, *15*, 4879. [[CrossRef](#)] [[PubMed](#)]
9. Fekete, M.; Lehocski, A.; Kryczyk-Poprawa, A.; Zábó, V.; Varga, J.T.; Bálint, M.; Fazekas-Pongor, V.; Csíró, T.; Rzaşa-Duran, E.; Varga, P. Functional Foods in Modern Nutrition Science: Mechanisms, Evidence, and Public Health Implications. *Nutrients* **2025**, *17*, 2153. [[CrossRef](#)] [[PubMed](#)]
10. Yin, R.; Kuo, H.C.; Hudlikar, R.; Sargsyan, D.; Li, S.; Wang, L.; Wu, R.; Kong, A.N. Gut microbiota, dietary phytochemicals and benefits to human health. *Curr. Pharmacol. Rep.* **2019**, *5*, 332–344. [[CrossRef](#)] [[PubMed](#)] [[PubMed Central](#)]
11. Mahboob, A.; Samuel, S.M.; Mohamed, A.; Wani, M.Y.; Ghorbel, S.; Miled, N.; Büsselberg, D.; Chaari, A. Role of flavonoids in controlling obesity: Molecular targets and mechanisms. *Front. Nutr.* **2023**, *10*, 1177897. [[CrossRef](#)]
12. Régnier, M.; Van Hul, M.; Knauf, C.; Cani, P.D. Gut microbiome, endocrine control of gut barrier function and metabolic diseases. *J. Endocrinol.* **2021**, *248*, R67–R82. [[CrossRef](#)]
13. Russo, V.; Continella, A.; Drago, C.; Gentile, A.; La Malfa, S.; Leotta, C.G.; Pulvirenti, L.; Ruberto, G.; Pitari, G.M.; Siracusa, L. Secondary metabolic profiles and anticancer actions from fruit extracts of immature pomegranates. *PLoS ONE* **2021**, *16*, e0255831. [[CrossRef](#)]
14. Maaz, M.; Sultan, M.T.; Khalid, M.U.; Raza, H.; Imran, M.; Hussain, M.; Al Abdulmonem, W.; Alsagaby, S.A.; Abdelgawad, M.A.; Ghoneim, M.M.; et al. A Comprehensive Review on the Molecular Mechanism of Lycopene in Cancer Therapy. *Food Sci. Nutr.* **2025**, *13*, e70608. [[CrossRef](#)]
15. Tako, E. Emerging Dietary Bioactives in Health and Disease. *Nutrients* **2023**, *15*, 1956. [[CrossRef](#)]
16. Liu, Y.; Fang, M.; Tu, X.; Mo, X.; Zhang, L.; Yang, B.; Wang, F.; Kim, Y.-B.; Huang, C.; Chen, L.; et al. Dietary Polyphenols as Anti-Aging Agents: Targeting the Hallmarks of Aging. *Nutrients* **2024**, *16*, 3305. [[CrossRef](#)] [[PubMed](#)]
17. Valero-Cases, E.; Cerdá-Bernad, D.; Pastor, J.J.; Frutos, M.J. Non-Dairy Fermented Beverages as Potential Carriers to Ensure Probiotics, Prebiotics, and Bioactive Compounds Arrival to the Gut and Their Health Benefits. *Nutrients* **2020**, *12*, 1666. [[CrossRef](#)] [[PubMed](#)]
18. Al-Samydai, A.; Qaraleh, M.A.; Alshaer, W.; Al-Halaseh, L.K.; Issa, R.; Alshaikh, F.; Abu-Rumman, A.; Al-Ali, H.; Al-Dujaili, E.A.S. Preparation, Characterization, Wound Healing, and Cytotoxicity Assay of PEGylated Nanophytosomes Loaded with 6-Gingerol. *Nutrients* **2022**, *14*, 5170. [[CrossRef](#)]
19. Nani, A.; Murtaza, B.; Sayed Khan, A.; Khan, N.A.; Hichami, A. Antioxidant and Anti-Inflammatory Potential of Polyphenols Contained in Mediterranean Diet in Obesity: Molecular Mechanisms. *Molecules* **2021**, *26*, 985. [[CrossRef](#)] [[PubMed](#)]
20. Wang, Y.; Haskell-Ramsay, C.; Gallegos, J.L.; Lodge, J.K. Effects of chronic consumption of specific fruit (berries, cherries and citrus) on cognitive health: A systematic review and meta-analysis of randomised controlled trials. *Eur. J. Clin. Nutr.* **2022**, *77*, 7–22. [[CrossRef](#)]
21. Behl, T.; Bungau, S.; Kumar, K.; Zengin, G.; Khan, F.; Kumar, A.; Kaur, R.; Venkatachalam, T.; Tit, D.M.; Vesa, C.M.; et al. Pleotropic Effects of Polyphenols in Cardiovascular System. *Biomed. Pharmacother.* **2020**, *130*, 110714. [[CrossRef](#)]
22. Sochacka, K.; Lachowicz-Wiśniewska, S. Phytotherapy and the Role of Bioactive Compounds in Modulating Mechanisms of Overweight and Obesity Comorbid with Depressive Symptoms—A Scoping Review of Mechanisms of Action. *Molecules* **2025**, *30*, 2827. [[CrossRef](#)]
23. Shaik Mohamed Sayed, U.F.; Moshawih, S.; Goh, H.P.; Kifli, N.; Gupta, G.; Singh, S.K.; Chellappan, D.K.; Dua, K.; Hermansyah, A.; Ser, H.L.; et al. Natural products as novel anti-obesity agents: Insights into mechanisms of action and potential for therapeutic management. *Front. Pharmacol.* **2023**, *14*, 1182937. [[CrossRef](#)] [[PubMed](#)]
24. Lu, S.; Zhao, Q.; Guan, Y.; Sun, Z.; Li, W.; Guo, S. The communication mechanism of the gut-brain axis and its effect on central nervous system diseases: A systematic review. *Biomed. Pharmacother.* **2024**, *178*, 117207. [[CrossRef](#)] [[PubMed](#)]
25. Fekete, M.; Lehocski, A.; Major, D.; Fazekas-Pongor, V.; Csíró, T.; Tarantini, S.; Csizmadia, Z.; Varga, J.T. Exploring the Influence of Gut–Brain Axis Modulation on Cognitive Health: A Comprehensive Review of Prebiotics, Probiotics, and Symbiotics. *Nutrients* **2024**, *16*, 789. [[CrossRef](#)] [[PubMed](#)]
26. Liu, L.; Qi, W.; Zhang, N.; Zhang, J.; Liu, S.; Wang, H.; Jiang, L.; Sun, Y. Nutraceuticals for Gut-Brain Axis Health: A Novel Approach to Combat Malnutrition and Future Personalized Nutraceutical Interventions. *Nutrients* **2025**, *17*, 1551. [[CrossRef](#)] [[PubMed](#)] [[PubMed Central](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.