



## Editorial

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# Special issue: molecular nutrition and chronic diseases

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“Let food be thy medicine and medicine be thy food”—the ancient adage proposed by Greek philosopher Hippocrates of Kos thousands of years ago already acknowledged the importance of the beneficial and health-promoting effects of food nutrients on the body (Mafra et al., 2021). Recent epidemiological and large-scale community studies have also reported that unhealthy diets or eating habits may contribute heavily to the burden of chronic, non-communicable diseases, such as obesity, type 2 diabetes mellitus (T2DM), hypertension, cardiovascular disease (CVD), cancer, neurodegenerative diseases, arthritis, chronic kidney disease (CKD), and chronic obstructive pulmonary disease (COPD) (Jayedi et al., 2020; Gao et al., 2022). Emerging evidence highlights that a diet rich in fruits and vegetables can prevent various chronic diseases (Chen et al., 2022). Food bioactive compounds including vitamins, phytochemicals, and dietary fibers are responsible for these nutraceutical benefits (Boeing et al., 2012). Recently, phytochemicals such as polyphenols, phytosterols, and carotenoids have gained increasing attention due to their potential health benefits to alleviate chronic diseases (van Breda and de Kok, 2018). Understanding the role of phytochemicals in health promotion and preventing chronic diseases can inform dietary recommendations and the development of functional foods. Therefore, it is crucial to investigate the health benefits of phytochemicals derived from commonly consumed foods for the prevention and management of chronic diseases.

Molecular nutrition is one of the most attractive research topics in this field, as it investigates the molecular mechanisms by which food nutrients and bioactive compounds interact with the body at the cellular and molecular levels (Zempleni and Daniel, 2003). This discipline focuses on understanding how specific dietary components, such as vitamins, minerals, phytochemicals, and macronutrients, affect biological processes and influence gene expression, metabolism, and overall health (Norheim et al., 2012). Over the past few decades, numerous researchers have found that the dietary intake of vegetables, fruits, grains, and legumes rich in bioactive compounds such as flavonoids, anthocyanins, and procyanidins can help combat and prevent various chronic conditions and diseases (Gao et al., 2022). However, the precise and detailed molecular mechanisms of food bioactive compounds against chronic diseases remain largely unknown. Recently, molecular nutrition research has been positioned at the center of the field of food and nutritional science. By focusing on the molecular mechanisms underlying the effects of phytochemicals, this special issue provides valuable data for researchers, healthcare professionals and individuals seeking evidence-based dietary guidance. In addition, it helps to identify knowledge gaps and proposes future directions for molecular nutrition research to further investigate the health benefits of phytochemicals.

Our research group is committed to investigating the health-promoting effects of food bioactive compounds from various food resources. Our previous efforts have deepened our understanding of the molecular mechanisms of food bioactive compounds beyond their regular biological activities. For example, we developed a novel strategy for the isolation of anthocyanins from multiple berry fruits using a combination of high-speed countercurrent chromatography (HSCCC)

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and high-performance liquid chromatography (HPLC) techniques, and identified a novel  $\alpha$ -glucosidase inhibitor, pelargonidin-3-*O*-rutinoside (Xu et al., 2019). On the one hand, we are devoted to investigating the detailed molecular mechanisms of food bioactive compounds, including pelargonidin-3-*O*-glucoside, procyanidin B2, andrographolide, and malvidin-3-*O*-glucoside, in metabolic diseases such as non-alcoholic fatty liver disease (NAFLD), obesity, and diabetes (Su et al., 2018, 2020a, 2020b; Xie et al., 2020; Xu et al., 2021). On the other hand, we are interested in understanding the molecular mechanisms of food toxicants, such as ethyl carbamate and acrylamide-induced toxicity (Li et al., 2019; Xu et al., 2022). The above studies have established new foundations and methodologies for the research of molecular nutrition and chronic diseases. To further expand these research efforts, we dedicate this special issue to the latest advances made by peer researchers.

This issue contains original and previously unpublished works in the research fields of molecular nutrition and chronic diseases. The topics include, but are not limited to: (1) new methods for the identification and characterization of food-derived functional ingredients and their bioactivity screening and verification; (2) the bioavailability, absorption, and metabolism of food-derived functional ingredients studied using novel *in vitro* and *in vivo* models; (3) the nutritional efficacy, responses, and molecular mechanisms of food bioactive compounds on chronic diseases through the regulation of gene expression and signal transduction; (4) state-of-the-art multi-omics approaches to elucidate the regulatory mechanism of food bioactive compounds on chronic diseases.

Several studies incorporated into this special issue shed new light on the impact of food bioactive compounds on chronic diseases. Among these, Rahman et al. (2023) performed a systematic and comprehensive review of the potential neuroprotective effects of tea tree oil extracted from *Melaleuca alternifolia*. The authors highlight that tea tree oil has promising neuroprotective properties due to its ability to inhibit neuroinflammation, regulate neuropeptides and growth factors, and modulate gene expression. They suggest that further research is needed to fully understand the mechanisms behind these effects and to determine the optimal dosage and administration of tea tree oil for neuroprotection.

Anthocyanins are a subgroup of flavonoids with a diphenylpropane skeleton formed by two benzene rings. More than 20 different anthocyanidins have been described in total, with six of them being the most frequently reported bioactive compounds: cyanidin, delphinidin, pelargonidin, malvidin, peonidin, and petunidin (Xie et al., 2018). Shen et al. (2023) uncovered the effects and mechanisms of diacylated anthocyanins from purple sweet potato (diacylated AF-PSPs) on hyperglycemia and hyperuricemia induced by a high-fructose/high-fat diet. The major findings of their study are that diacylated AF-PSPs can effectively regulate glucose and uric acid metabolism, improve renal function, and reduce inflammation in mice with diet-induced hyperglycemia and hyperuricemia. The researchers also identified several molecular pathways involved in these effects, including adenosine 5'-monophosphate (AMP)-activated protein kinase (AMPK) signaling, glucose transporter type 4 (GLUT4) expression, and peroxisome proliferator-activated receptor  $\alpha$  (PPAR $\alpha$ ) activation. Their results suggest that diacylated AF-PSPs may be a promising dietary supplement or functional food ingredient for the prevention or treatment of metabolic disorders.

In addition to studying the health-promoting and therapeutic effects of food bioactive compounds, we cannot neglect the research on their bioavailability, absorption, or metabolism. Wang et al. (2023) investigated the antioxidant activity of blueberry anthocyanins extracted from "Brightwell" rabbiteye blueberries in mice. The results showed that the anthocyanin extracts have significant antioxidant effects in various tissues, including the plasma, eyeball, intestine, liver, and adipose tissues; they increased total antioxidant capacity and superoxide dismutase activity while decreasing malondialdehyde levels. These data suggest that consuming blueberry anthocyanin extracts may have potential health benefits due to their antioxidant properties.

Previous research has indicated that oxidative stress plays a pivotal role in various chronic diseases (Forman and Zhang, 2021). Food bioactive compounds with antioxidant capacity have been proposed as potential therapeutic agents to counteract oxidative stress associated with chronic diseases by regulating redox signaling and function (Mafra et al., 2021). However, the underlying molecular mechanisms of food bioactive compounds in regulating oxidative stress are still elusive. In this special issue, Zhang et al.

(2023) report that scutellarin (SCU) has a hepatoprotective effect in acute alcoholic liver injury by regulating oxidative stress and inflammation pathways. Specifically, SCU inhibits oxidative stress by regulating the nuclear factor erythroid 2-related factor 2 (Nrf2)/heme oxygenase-1 (HO-1) pathway and controls inflammation by regulating the protein kinase B (AKT), p38 mitogen-activated protein kinase (MAPK)/nuclear factor- $\kappa$ B (NF- $\kappa$ B) pathways. Their results indicate that SCU may have potential as a natural bioactive ingredient in herbal medicine for preventing or treating alcohol-induced liver injury. Yu et al. (2023) suggest that andrographolide can protect against atrial fibrillation by alleviating oxidative stress injury and promoting impaired mitochondrial bioenergetics. It does so by activating the translocation of Nrf2 to the nucleus and upregulating HO-1 to promote mitochondrial bioenergetics. Andrographolide also inhibits atrial myocyte apoptosis and myolysis through regulating the processes of mitochondrial fission and fusion, improving mitochondrial energy metabolism, and reducing the incidence of atrial fibrillation.

Polysaccharides are polymeric carbohydrates composed of long chains of monosaccharide units joined by glycosidic linkages, and they are the most abundant carbohydrates found in food. Increasing evidence indicates that polysaccharides derived from food have potential health benefits (Sun et al., 2021; Ma et al., 2022), although the molecular mechanisms of food polysaccharides are largely unknown. In the current issue, Zhao et al. (2023) present that *Astragalus* polysaccharide can regulate certain gut microbiota associated with immune and inflammatory response, short-chain fatty acid (SCFA) production, and endotoxin levels in rats with syndrome of dampness stagnancy due to spleen deficiency (DSSD). Additionally, *Astragalus* polysaccharide modulates the gut microbiota-mediated Toll-like receptor 4 (TLR4)/NF- $\kappa$ B pathway and inflammatory cytokine levels to attenuate immune disorders in rats with DSSD syndrome. These findings suggest that *Astragalus* polysaccharide may have potential applications in the treatment of human immune disorders. Ethyl carbamate is an emerging food toxicant that may contribute to the pathogenesis of chronic diseases (Gowd et al., 2018). Food bioactive compounds have the potential to provide protection against ethyl carbamate-induced toxicity (Chen et al., 2016). Bao et al. (2023) claims that wax

apple polysaccharide (WAP) has antioxidant properties and can protect human hepatocytes from oxidative damage caused by ethyl carbamate. Their study also characterizes the chemical properties of WAP, such as its molecular weight, monosaccharide composition, linkages, functional groups, and internal chemical bonds. The authors conclude that WAP has great potential as a natural compound for preventing or treating liver diseases caused by ethyl carbamate-induced oxidative stress.

In summary, this special issue presents a collection of studies that all explore the molecular nutrition and health benefits of food bioactive compounds in the context of chronic diseases. It is indisputable that food bioactive compounds have great value in the prevention or treatment of chronic diseases. The included studies provide valuable insights into the potential roles of these compounds in preventing and managing chronic diseases and contribute to our understanding of the molecular mechanisms by which food bioactive compounds exert their beneficial effects.

Recently, the field of molecular nutrition has attracted increasing interest, and with the emergence and application of novel technologies such as multi-omics and artificial intelligence (AI), we can expect further advancements in our understanding of how food bioactive compounds prevent chronic diseases at the molecular level. In addition, this new knowledge will pave the way for the development of practical approaches that utilize food as medicine for the prevention and treatment of chronic illnesses. We hope that this special issue inspires further research and promotes the development of functional foods, dietary guidelines, as well as precision and personalized nutrition strategies for the prevention and treatment of chronic diseases.

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### Author contributions

Wei CHEN conceived and edited the draft of manuscript. Hongming SU performed the literature review, and conceived and completed the draft of the manuscript. Both authors have reviewed and approved the final manuscript.

### Compliance with ethics guidelines

Wei CHEN and Hongming SU declare that they have no conflict of interest.

This article does not contain any studies with human or animal subjects performed by any of the authors.

## References

- Bao T, Karim N, Ke HH, et al., 2023. Polysaccharide isolated from wax apple suppresses ethyl carbamate-induced oxidative damage in human hepatocytes. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 24(7):574-586. <https://doi.org/10.1631/jzus.B2200629>
- Boeing H, Bechthold A, Bub A, et al., 2012. Critical review: vegetables and fruit in the prevention of chronic diseases. *Eur J Nutr*, 51(6):637-663. <https://doi.org/10.1007/s00394-012-0380-y>
- Chen W, Xu Y, Zhang LX, et al., 2016. Blackberry subjected to *in vitro* gastrointestinal digestion affords protection against Ethyl Carbamate-induced cytotoxicity. *Food Chem*, 212:620-627. <https://doi.org/10.1016/j.foodchem.2016.06.031>
- Chen X, Li HY, Zhang B, et al., 2022. The synergistic and antagonistic antioxidant interactions of dietary phytochemical combinations. *Crit Rev Food Sci Nutr*, 62(20):5658-5677. <https://doi.org/10.1080/10408398.2021.1888693>
- Forman HJ, Zhang HQ, 2021. Targeting oxidative stress in disease: promise and limitations of antioxidant therapy. *Nat Rev Drug Discov*, 20(9):689-709. <https://doi.org/10.1038/s41573-021-00233-1>
- Gao L, Gou N, Yao MJ, et al., 2022. Food-derived natural compounds in the management of chronic diseases via Wnt signaling pathway. *Crit Rev Food Sci Nutr*, 62(17):4769-4799. <https://doi.org/10.1080/10408398.2021.1879001>
- Gowd V, Su HM, Karlovsky P, et al., 2018. Ethyl carbamate: an emerging food and environmental toxicant. *Food Chem*, 248:312-321. <https://doi.org/10.1016/j.foodchem.2017.12.072>
- Jayedi A, Soltani S, Abdolshahi A, et al., 2020. Healthy and unhealthy dietary patterns and the risk of chronic disease: an umbrella review of meta-analyses of prospective cohort studies. *Br J Nutr*, 124(11):1133-1144. <https://doi.org/10.1017/S0007114520002330>
- Li YT, Ye X, Zheng XD, et al., 2019. Transcription factor EB (TFEB)-mediated autophagy protects against ethyl carbamate-induced cytotoxicity. *J Hazard Mater*, 364:281-292. <https://doi.org/10.1016/j.jhazmat.2018.10.037>
- Ma GX, Du HJ, Hu QH, et al., 2022. Health benefits of edible mushroom polysaccharides and associated gut microbiota regulation. *Crit Rev Food Sci Nutr*, 62(24):6646-6663. <https://doi.org/10.1080/10408398.2021.1903385>
- Mafra D, Borges NA, Lindholm B, et al., 2021. Food as medicine: targeting the uraemic phenotype in chronic kidney disease. *Nat Rev Nephrol*, 17(3):153-171. <https://doi.org/10.1038/s41581-020-00345-8>
- Norheim F, Gjelstad I, Hjorth M, et al., 2012. Molecular nutrition research: the modern way of performing nutritional science. *Nutrients*, 4(12):1898-1944. <https://doi.org/10.3390/nu4121898>
- Rahman MA, Sultana A, Khan MF, et al., 2023. Tea tree oil, a vibrant source of neuroprotection via neuroinflammation inhibition: a critical insight into repurposing *Melaleuca alternifolia* by unfolding its characteristics. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 24(7):554-573. <https://doi.org/10.1631/jzus.B2300168>
- Shen LH, Yang Y, Zhang JL, et al., 2023. Diacylated anthocyanins from purple sweet potato (*Ipomoea batatas* L.) attenuate hyperglycemia and hyperuricemia in mice induced by a high-fructose/high-fat diet. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 24(7):587-601. <https://doi.org/10.1631/jzus.B2200587>
- Su HM, Li YT, Hu DW, et al., 2018. Procyanidin B2 ameliorates free fatty acids-induced hepatic steatosis through regulating TFEB-mediated lysosomal pathway and redox state. *Free Radical Biol Med*, 126:269-286. <https://doi.org/10.1016/j.freeradbiomed.2018.08.024>
- Su HM, Mo JL, Ni JD, et al., 2020a. Andrographolide exerts antihyperglycemic effect through strengthening intestinal barrier function and increasing microbial composition of *Akkermansia muciniphila*. *Oxid Med Cell Longev*, 2020:6538930. <https://doi.org/10.1155/2020/6538930>
- Su HM, Xie LH, Xu Y, et al., 2020b. Pelargonidin-3-O-glucoside derived from wild raspberry exerts antihyperglycemic effect by inducing autophagy and modulating gut microbiota. *J Agric Food Chem*, 68(46):13025-13037. <https://doi.org/10.1021/acs.jafc.9b03338>
- Sun Y, Zhang ZP, Cheng L, et al., 2021. Polysaccharides confer benefits in immune regulation and multiple sclerosis by interacting with gut microbiota. *Food Res Int*, 149:110675. <https://doi.org/10.1016/j.foodres.2021.110675>
- van Breda SGJ, de Kok TCM, 2018. Smart combinations of bioactive compounds in fruits and vegetables may guide new strategies for personalized prevention of chronic diseases. *Mol Nutr Food Res*, 62(1):1700597. <https://doi.org/10.1002/mnfr.201700597>
- Wang J, Zhao XY, Zheng JW, et al., 2023. In vivo antioxidant activity of rabbiteye blueberry (*Vaccinium ashei* cv. 'Brightwell') anthocyanin extracts. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 24(7):602-616. <https://doi.org/10.1631/jzus.B2200590>
- Xie LH, Su HM, Sun CD, et al., 2018. Recent advances in understanding the anti-obesity activity of anthocyanins and their biosynthesis in microorganisms. *Trends Food Sci Technol*, 72:13-24. <https://doi.org/10.1016/j.tifs.2017.12.002>
- Xie LH, Mo JL, Ni JD, et al., 2020. Structure-based design of human pancreatic amylase inhibitors from the natural anthocyanin database for type 2 diabetes. *Food Funct*, 11(4):2910-2923. <https://doi.org/10.1039/c9fo02885d>
- Xu Y, Xie LH, Xie JH, et al., 2019. Pelargonidin-3-O-rutinoside as a novel  $\alpha$ -glucosidase inhibitor for improving postprandial hyperglycemia. *Chem Commun*, 55(1):39-42. <https://doi.org/10.1039/c8cc07985d>

- Xu Y, Ke HH, Li YT, et al., 2021. Malvidin-3-O-glucoside from blueberry ameliorates nonalcoholic fatty liver disease by regulating transcription factor EB-mediated lysosomal function and activating the Nrf2/ARE signaling pathway. *J Agric Food Chem*, 69(16):4663-4673. <https://doi.org/10.1021/acs.jafc.0c06695>
- Xu Y, Li YT, Li JX, et al., 2022. Ethyl carbamate triggers ferroptosis in liver through inhibiting GSH synthesis and suppressing Nrf2 activation. *Redox Biol*, 53:102349. <https://doi.org/10.1016/j.redox.2022.102349>
- Yu PC, Cao JR, Sun HX, et al., 2023. Andrographolide protects against atrial fibrillation by alleviating oxidative stress injury and promoting impaired mitochondrial bioenergetics. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 24(7):632-649. <https://doi.org/10.1631/jzus.B2300086>
- Zempleni J, Daniel H, 2003. *Molecular Nutrition*. CABI Publishing, Wallingford, New England, USA.
- Zhang X, Dong ZC, Fan H, et al., 2023. Scutellarin prevents acute alcohol-induced liver injury via inhibiting oxidative stress by regulating the Nrf2/HO-1 pathway and inhibiting inflammation by regulating the AKT, p38 MAPK/NF- $\kappa$ B pathways. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 24(7):617-631. <https://doi.org/10.1631/jzus.B2200612>
- Zhao WX, Duan CC, Liu YL, et al., 2023. Modulating effects of *Astragalus* polysaccharides on immune disorders via gut microbiota and the TLR4/NF- $\kappa$ B pathway in rats with syndrome of dampness stagnancy due to spleen deficiency. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 24(7):650-662. <https://doi.org/10.1631/jzus.B2200491>

## Introducing Guest Editor-in-Chief and Guest Editor

### Guest Editor-in-Chief



Dr. Wei CHEN, Professor of Food Science, Director of the Institute of Food Science, Zhejiang University, China. He was selected as the “Chang Jiang Scholars Program,” and won the Outstanding Youth Fund of Zhejiang Province, the Qianjiang Talents Program of Zhejiang Province, and the 151 Talents Program of Zhejiang Province. As a program leader, he has won China Industry-University-Research Institute Collaboration Award. He has published more than 110 peer-reviewed papers as the corresponding author in SCI journals with H index of 41, has obtained 21 granted national invention patents, and was nominated as World’s Top 2% Scientists in 2022.

### Guest Editor



Dr. Hongming SU is a Postdoctoral Associate at the Department of Food Science and Nutrition of University of Minnesota-Twin Cities, USA. He earned his Ph.D. in Food Science at Zhejiang University in 2020. His research is mainly focused on two fields: understanding the novel role and mechanism of adipose tissue in the regulation of energy metabolism in obesity, and dietary interventions to prevent metabolic diseases. He has published more than 20 peer-reviewed papers that have been cited over 1000 times over the past few years. He was granted the Young Investigator Award (2022) by the American Diabetes Association (ADA).