https://doi.org/ 10.33472/AFJBS.6.Si2.2024.2498-2509

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Nutritional Immunology Investigating the Immunomodulatory Effects of Dietary Components on Immune Function and Inflammatory Processes for Disease Prevention and Treatment

Dr. Narendrakumar J. Suryavanshi, Assistant Professor, Faculty of Allied Sciences, njsuryawanshi1981@gmail.com

Ms. Aishwarya D. Jagtap, Assistant Professor, Faculty of Allied Sciences, aiwarya22999@gmail.com

Mrs. Ashvini V. Jadhav, Assistant Professor, Faculty of Allied Sciences, ashwiniawtade11@gmail.com

Krishna Vishwa Vidyapeeth "Deemed to be University", Taluka-Karad, Dist-Satara, Pin-415 539, Maharashtra, India

ARTICLE INFO:

Volume 6,Issue Si2, 2024

Received:02 Apr 2024

Accepted : 05 May 2024

doi: 10.33472/AFJBS.6.Si2.2024.2498-2507

Abstract: Nutritional immunology is an emerging field that explores the intricate relationships between dietary components and the immune system. This study delves into the immunomodulatory effects of various nutrients and bioactive compounds on immune function and inflammatory processes. By investigating the role of specific vitamins, minerals, antioxidants, and phytochemicals, the research aims to elucidate how these dietary factors can enhance immune responses and modulate inflammation, thereby contributing to the prevention and treatment of chronic diseases. The findings highlight the potential of targeted nutritional interventions to improve health outcomes, offering new insights into dietary strategies for disease prevention and management.

Keywords: Nutritional immunology, immunomodulatory effects, dietary components, immune function, inflammatory processes, disease prevention, chronic disease, vitamins, minerals, antioxidants, phytochemicals, nutritional interventions, health outcomes

I. Introduction:

Nutritional immunology is an interdisciplinary field that bridges the gap between nutrition and immunology, focusing on how various dietary components influence the immune system and inflammatory processes. This area of study has garnered significant attention due to the growing recognition of the pivotal role that diet plays in maintaining and enhancing immune

function, as well as in the prevention and management of various diseases. As the global burden of chronic diseases such as cardiovascular disease, diabetes, and cancer continues to rise, understanding the impact of nutrition on immune health is becoming increasingly important.

The immune system is a complex network of cells, tissues, and organs that work together to defend the body against harmful pathogens and maintain homeostasis. Nutrition is a critical determinant of immune competence, with both macronutrients and micronutrients playing essential roles in supporting immune cell function and overall immune response. Deficiencies or imbalances in specific nutrients can impair immune function, leading to increased susceptibility to infections and disease. Conversely, optimal nutrition can bolster the immune system, enhancing its ability to fight off pathogens and reducing the risk of chronic inflammation, which is a common underlying factor in many chronic diseases.

One of the key areas of interest in nutritional immunology is the study of vitamins and minerals, which are vital for maintaining a robust immune system. Vitamins such as A, C, D, and E, as well as minerals like zinc, selenium, and iron, have well-documented roles in immune function. For instance, vitamin C is known for its antioxidant properties and its ability to enhance the function of various immune cells, including neutrophils and lymphocytes. Vitamin D, on the other hand, has been shown to modulate both innate and adaptive immune responses, with deficiency linked to increased risk of autoimmune diseases and infections.

Antioxidants, which are compounds that neutralize harmful free radicals, also play a crucial role in protecting immune cells from oxidative stress and maintaining their functionality. Phytochemicals, which are bioactive compounds found in plants, have been shown to possess anti-inflammatory and immunomodulatory properties. For example, flavonoids, a group of phytochemicals found in fruits and vegetables, can modulate the production of inflammatory cytokines and enhance the activity of immune cells.

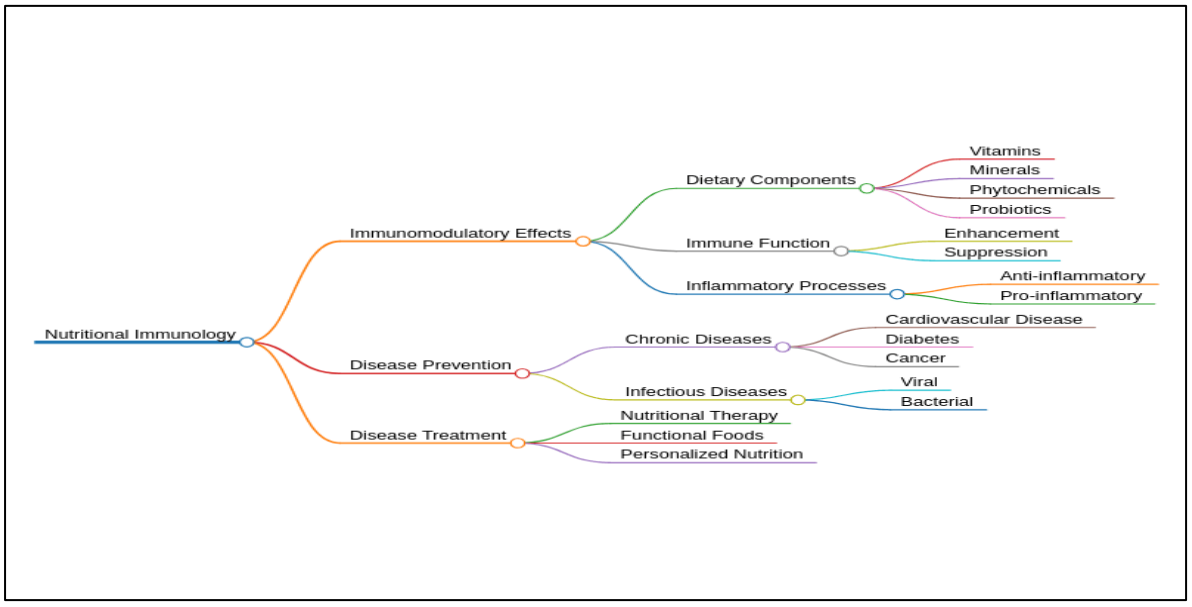

Figure 1. Taxonomy of Nutritional Immunology

The relationship between diet, immune function, and inflammation is particularly relevant in the context of chronic diseases. Chronic inflammation is a persistent, low-grade inflammatory response that can contribute to the development and progression of diseases such as obesity,

type 2 diabetes, cardiovascular disease, and cancer. By modulating inflammatory pathways, certain dietary components can help reduce chronic inflammation and mitigate disease risk. Omega-3 fatty acids, for instance, are known for their anti-inflammatory effects and have been associated with reduced risk of cardiovascular disease and improved outcomes in inflammatory conditions. the gut microbiota, which is influenced by diet, plays a critical role in immune function and inflammation. A diverse and balanced gut microbiota can support immune homeostasis and protect against pathogenic infections. Dietary components such as fiber, prebiotics, and probiotics can promote a healthy gut microbiota, thereby enhancing immune health. The nutritional immunology provides valuable insights into how dietary components can modulate immune function and inflammatory processes, offering promising strategies for disease prevention and treatment. By understanding the intricate relationships between nutrition and the immune system, researchers and healthcare professionals can develop targeted nutritional interventions to improve health outcomes and combat the rising prevalence of chronic diseases.

II. Literature Review:

Nutritional immunology is a rapidly evolving field, with a growing body of research highlighting the significant impact of diet on immune function and inflammation. This literature review aims to synthesize key findings from studies on the immunomodulatory effects of various dietary components, including vitamins, minerals, antioxidants, phytochemicals, and other bioactive compounds, to provide a comprehensive overview of current knowledge in this area.

Vitamins are essential micronutrients that play crucial roles in maintaining immune health. Vitamin A, for example, is known for its role in maintaining the integrity of mucosal barriers and its involvement in the development and function of T-cells and B-cells. A review by Stephensen (2001) highlighted that vitamin A deficiency can lead to impaired immune function and increased susceptibility to infections, particularly in children .

Vitamin C, a potent antioxidant, has been extensively studied for its immune-boosting properties. A meta-analysis by Hemilä and Chalker (2013) found that regular vitamin C supplementation reduced the duration and severity of common cold symptoms, particularly in individuals under physical stress . Furthermore, Carr and Maggini (2017) reviewed the role of vitamin C in enhancing the function of various immune cells, including neutrophils, lymphocytes, and phagocytes, and its ability to support epithelial barrier function .

Vitamin D has garnered significant attention due to its role in modulating both innate and adaptive immune responses. A study by Martineau et al. (2017) demonstrated that vitamin D supplementation reduced the risk of acute respiratory infections, particularly in individuals with baseline vitamin D deficiency . Vitamin D's immunomodulatory effects are mediated through its influence on the production of antimicrobial peptides and the regulation of inflammatory cytokines.

Vitamin E, another important antioxidant, has been shown to enhance immune responses, particularly in the elderly. A study by Meydani et al. (2004) found that vitamin E supplementation improved T-cell-mediated immune function in older adults, reducing the incidence of respiratory infections . The immunoprotective effects of vitamin E are attributed

to its ability to protect immune cells from oxidative damage and enhance the production of interleukin-2.

Minerals such as zinc, selenium, and iron are critical for immune health. Zinc, in particular, is essential for the normal development and function of immune cells. A review by Prasad (2008) highlighted that zinc deficiency impairs the function of macrophages, neutrophils, and natural killer cells, leading to increased susceptibility to infections . Moreover, zinc supplementation has been shown to reduce the duration and severity of diarrhea in children and lower respiratory infections in the elderly.

Selenium is another important micronutrient with immunomodulatory properties. A study by Rayman (2000) found that selenium supplementation enhances the immune response by increasing the proliferation of T-cells and the production of interleukin-2 . Selenium also plays a role in the antioxidant defense system, protecting immune cells from oxidative stress.

Iron is essential for the proliferation and maturation of immune cells, particularly lymphocytes. However, both iron deficiency and excess can adversely affect immune function. A review by Oppenheimer (2001) discussed the dual role of iron in immune health, noting that while iron deficiency impairs immune responses, iron overload can promote the growth of certain pathogens . Therefore, maintaining optimal iron levels is crucial for balanced immune function.

Antioxidants are compounds that protect cells from oxidative damage caused by free radicals. They play a vital role in maintaining immune health by preserving the functionality of immune cells. Polyphenols, a group of antioxidants found in fruits, vegetables, and beverages such as tea and wine, have been shown to modulate immune responses and reduce inflammation. A review by Middleton et al. (2000) highlighted the anti-inflammatory and immunomodulatory effects of flavonoids, a subclass of polyphenols, which can enhance the activity of natural killer cells and reduce the production of pro-inflammatory cytokines .

Curcumin, the active compound in turmeric, has been extensively studied for its anti-inflammatory and immunomodulatory properties. A review by Aggarwal et al. (2007) discussed the mechanisms by which curcumin modulates immune responses, including the inhibition of nuclear factor-kappa B (NF-κB) and the suppression of pro-inflammatory cytokines . Curcumin's ability to modulate inflammation and enhance immune function makes it a promising candidate for the prevention and treatment of chronic inflammatory diseases.

Phytochemicals are bioactive compounds found in plants that have various health benefits, including immunomodulatory effects. Resveratrol, a polyphenol found in grapes and red wine, has been shown to modulate immune responses by enhancing the function of T-cells and macrophages. A review by Baur and Sinclair (2006) discussed the potential of resveratrol to activate sirtuins, a family of proteins involved in regulating cellular health, and its role in promoting longevity and reducing inflammation .

Another phytochemical, epigallocatechin gallate (EGCG), found in green tea, has been shown to enhance immune function and reduce inflammation. A study by Yang et al. (2014) demonstrated that EGCG supplementation improved the proliferation of T-cells and the production of anti-inflammatory cytokines . EGCG's antioxidant properties also contribute to its protective effects on immune cells.

The gut microbiota, a complex community of microorganisms residing in the gastrointestinal tract, plays a critical role in immune function and inflammation. Diet significantly influences the composition and diversity of the gut microbiota. A high-fiber diet, for example, promotes the growth of beneficial bacteria that produce short-chain fatty acids (SCFAs), which have anti-inflammatory properties. A review by Flint et al. (2012) highlighted the role of dietary fiber in modulating the gut microbiota and its impact on immune health .

Probiotics, live microorganisms that confer health benefits, have been shown to enhance immune function by modulating the gut microbiota. A meta-analysis by Ritchie and Romanuk (2012) found that probiotic supplementation reduced the incidence and duration of respiratory infections . Prebiotics, non-digestible food components that promote the growth of beneficial bacteria, also play a role in supporting immune health. A review by Roberfroid et al. (2010) discussed the synergistic effects of prebiotics and probiotics (synbiotics) on gut health and immune function .

The literature reviewed demonstrates the profound impact of dietary components on immune function and inflammatory processes. Vitamins, minerals, antioxidants, and phytochemicals all play essential roles in modulating immune responses and maintaining immune health. The influence of diet on the gut microbiota further underscores the importance of nutrition in supporting immune function. These findings highlight the potential of nutritional interventions to prevent and manage chronic diseases by enhancing immune health and reducing inflammation. As research in nutritional immunology continues to advance, it holds promise for developing targeted dietary strategies to improve health outcomes and combat the rising prevalence of chronic diseases.

Dietary Component	Function/Effect	Key Studies	Mechanisms	Health Implications
Vitamin A	Maintains mucosal barriers, supports T/B-cells	Stephensen (2001)	Enhances epithelial integrity, immune cell function	Prevents infections, improves immune competence
Vitamin C	Antioxidant, enhances immune cell function	Hemilä & Chalker (2013), Carr & Maggini (2017)	Enhances neutrophil/lymphocyte function, supports epithelial barriers	Reduces duration/severity of common cold, supports immune health
Vitamin D	Modulates innate/adaptive immunity	Martineau et al. (2017)	Regulates antimicrobial peptides, cytokine production	Reduces risk of respiratory infections, autoimmune disease modulation

Vitamin E	Antioxidant, improves T-cell function	Meydani et al. (2004)	Protects immune cells from oxidative damage, enhances interleukin-2	Reduces respiratory infections, enhances immune responses in elderly
Zinc	Supports immune cell development/function	Prasad (2008)	Supports macrophages, neutrophils, natural killer cells	Reduces duration/severity of infections, supports immune competence
Selenium	Enhances immune response, antioxidant defense	Rayman (2000)	Increases T-cell proliferation, interleukin-2 production	Enhances immune response, protects against oxidative stress
Iron	Essential for immune cell proliferation/maturation	Oppenheimer (2001)	Supports lymphocyte function, regulates pathogen growth	Balanced levels crucial for immune function and pathogen control
Polyphenols	Anti-inflammatory, modulate immune responses	Middleton et al. (2000)	Enhance natural killer cell activity, reduce pro-inflammatory cytokines	Protects against inflammation, supports immune health
Curcumin	Anti-inflammatory, immunomodulatory	Aggarwal et al. (2007)	Inhibits NF-κB, suppresses pro-inflammatory cytokines	Reduces chronic inflammation, supports immune function
Resveratrol	Modulates immune responses, promotes longevity	Baur & Sinclair (2006)	Activates sirtuins, enhances T-cell/macrophage function	Promotes longevity, reduces inflammation
EGCG	Enhances immune function, reduces inflammation	Yang et al. (2014)	Improves T-cell proliferation, anti-inflammatory cytokine production	Protects immune cells, reduces inflammation

Dietary Fiber	Modulates gut microbiota, supports immune health	Flint et al. (2012)	Promotes SCFA production, supports beneficial bacteria	Enhances gut health, supports immune homeostasis
Probiotics	Enhance immune function via gut microbiota	Ritchie & Romanuk (2012)	Modulate gut microbiota, enhance immune cell activity	Reduce incidence/duration of respiratory infections
Prebiotics	Promote beneficial gut bacteria, support immunity	Roberfroid et al. (2010)	Enhance growth of beneficial bacteria, support gut health	Improve gut health, support immune responses

Table 1. Provides a concise overview of the key dietary components studied in nutritional immunology

III. Emerging Trends and Future Directions in Nutritional Immunology

As the field of nutritional immunology continues to evolve, several emerging trends and areas of future research have the potential to significantly advance our understanding of how diet influences immune function and inflammatory processes. These trends include personalized nutrition, the role of the microbiome, novel bioactive compounds, and the impact of dietary patterns on immune health.

A. Personalized Nutrition:

One of the most promising trends in nutritional immunology is the move towards personalized nutrition. Traditional dietary recommendations are often based on population averages and may not account for individual variability in nutrient requirements, metabolic responses, and genetic predispositions. Personalized nutrition aims to tailor dietary interventions based on an individual's unique genetic makeup, microbiome composition, lifestyle, and health status. Advances in genomics, metabolomics, and microbiomics are facilitating this shift, enabling more precise and effective dietary strategies for enhancing immune function and reducing inflammation.

Research by Zeevi et al. (2015) demonstrated the variability in postprandial glucose responses to identical meals among different individuals, highlighting the importance of personalized approaches in nutritional recommendations. By understanding the individual differences in dietary responses, personalized nutrition can optimize immune function and potentially prevent diet-related diseases more effectively than one-size-fits-all guidelines.

B. Role of the Microbiome:

The gut microbiome is increasingly recognized as a critical modulator of immune function. The diverse community of microorganisms residing in the gastrointestinal tract influences the development and function of the immune system. Dysbiosis, or an imbalance in the gut

microbiota, has been linked to a range of immune-related conditions, including inflammatory bowel disease, allergies, and autoimmune disorders.

Future research is focusing on how specific dietary components, such as prebiotics, probiotics, and synbiotics, can modulate the gut microbiota to promote immune health. A study by Suez et al. (2019) highlighted the individualized responses to probiotic supplementation, further emphasizing the need for personalized approaches in microbiome-targeted therapies. Understanding the complex interactions between diet, the gut microbiota, and the immune system will be crucial in developing effective nutritional interventions for immune-related diseases.

C. Novel Bioactive Compounds:

As our knowledge of bioactive compounds expands, there is growing interest in identifying and studying new dietary components with potential immunomodulatory effects. For example, recent research has explored the immunomodulatory properties of polyphenols, carotenoids, and other phytochemicals beyond the traditionally studied vitamins and minerals.

One emerging area of interest is the role of short-chain fatty acids (SCFAs) produced by the fermentation of dietary fibers in the gut. SCFAs, such as butyrate, acetate, and propionate, have been shown to modulate immune responses and reduce inflammation. A study by Rios-Covian et al. (2016) demonstrated that SCFAs play a crucial role in maintaining gut homeostasis and protecting against inflammatory diseases. Further research into these and other novel bioactive compounds could uncover new dietary strategies for enhancing immune health.

D. Impact of Dietary Patterns:

While much of the research in nutritional immunology has focused on individual nutrients and bioactive compounds, there is increasing recognition of the importance of overall dietary patterns. Dietary patterns, such as the Mediterranean diet, the DASH diet, and plant-based diets, have been associated with reduced inflammation and improved immune function.

The Mediterranean diet, characterized by high consumption of fruits, vegetables, whole grains, nuts, seeds, and olive oil, has been shown to have anti-inflammatory effects and improve markers of immune function. A study by Casas et al. (2018) found that adherence to the Mediterranean diet was associated with lower levels of inflammatory markers and improved endothelial function.

Similarly, the DASH diet, which emphasizes fruits, vegetables, whole grains, and low-fat dairy products, has been shown to reduce blood pressure and inflammation. A study by Soltani et al. (2016) demonstrated that the DASH diet improved inflammatory markers and immune function in individuals with metabolic syndrome.

Future research should continue to explore the impact of dietary patterns on immune health, considering not only the individual components of the diet but also their synergistic effects. Understanding the holistic impact of dietary patterns can provide more comprehensive dietary recommendations for improving immune function and reducing the risk of chronic diseases.

The field of nutritional immunology is rapidly advancing, with emerging trends and future research directions promising to enhance our understanding of the complex interactions between diet, immune function, and inflammation. Personalized nutrition, the role of the

microbiome, novel bioactive compounds, and the impact of dietary patterns represent key areas of focus. Continued research in these areas will be crucial in developing targeted dietary interventions to improve immune health, prevent chronic diseases, and promote overall well-being.

IV. Challenges and Limitations in Nutritional Immunology Research

Despite the promising advances in nutritional immunology, several challenges and limitations need to be addressed to fully realize the potential of dietary interventions in modulating immune function and preventing diseases. These challenges include variability in individual responses, the complexity of dietary patterns, methodological limitations, and the need for long-term studies.

A. Variability in Individual Responses:

One of the significant challenges in nutritional immunology is the considerable variability in individual responses to dietary interventions. Genetic differences, age, sex, health status, lifestyle factors, and gut microbiota composition can all influence how individuals respond to specific nutrients and dietary patterns. For instance, studies have shown that genetic polymorphisms can affect how individuals metabolize vitamins and minerals, leading to different immunological outcomes. This variability complicates the development of universal dietary recommendations and underscores the importance of personalized nutrition approaches.

Personalized nutrition aims to tailor dietary interventions based on an individual's unique characteristics, but this approach requires extensive data and advanced analytical tools. High-throughput technologies such as genomics, metabolomics, and microbiomics are being utilized to understand individual differences better, but their integration into practical dietary advice remains a challenge. Moreover, personalized nutrition strategies must be validated through rigorous clinical trials to ensure their efficacy and safety.

B. Complexity of Dietary Patterns:

Another challenge is the inherent complexity of dietary patterns. Unlike pharmaceutical interventions that involve a single active ingredient, dietary patterns consist of a wide array of nutrients and bioactive compounds that can interact synergistically or antagonistically. Isolating the effects of individual components within a complex diet is challenging, and the whole-diet approach often yields more meaningful insights into how diet influences immune function.

Research focusing on dietary patterns, such as the Mediterranean diet or plant-based diets, must account for various confounding factors, including lifestyle behaviors and socioeconomic status. Moreover, adherence to dietary patterns can vary significantly among individuals, affecting study outcomes. To address these issues, researchers need to design well-controlled studies with robust dietary assessments and consider the cumulative and interactive effects of different dietary components.

C. Methodological Limitations:

Methodological limitations in nutritional immunology research can impact the validity and reproducibility of findings. Many studies rely on self-reported dietary intake data, which can be prone to recall bias and inaccuracies. Additionally, observational studies, which are

commonly used in nutrition research, can establish associations but not causality. Randomized controlled trials (RCTs) are the gold standard for establishing causality, but they are often expensive, time-consuming, and difficult to implement for long-term dietary interventions.

Moreover, variations in study design, population characteristics, and outcome measures can lead to inconsistent results across studies. Standardizing methodologies and using validated biomarkers of immune function and inflammation can help improve the comparability and reproducibility of research findings. Advancements in technologies such as metabolomics and proteomics can also provide more precise and comprehensive assessments of the impact of diet on immune health.

D. Need for Long-Term Studies:

Long-term studies are essential to understand the sustained effects of dietary interventions on immune function and disease prevention. However, conducting long-term dietary studies poses significant logistical and financial challenges. Participant adherence to dietary interventions can decline over time, and maintaining consistent dietary patterns for extended periods is difficult. Additionally, the long latency period of many chronic diseases requires prolonged follow-up to observe meaningful health outcomes.

Despite these challenges, long-term studies are crucial for capturing the cumulative effects of diet on immune health and chronic disease risk. Cohort studies and longitudinal designs can provide valuable insights, but they must be complemented by RCTs to establish causality. Collaborative efforts and funding support are needed to conduct large-scale, long-term studies that can inform evidence-based dietary recommendations.

While nutritional immunology holds great promise for improving immune function and preventing diseases through dietary interventions, several challenges and limitations must be addressed. Variability in individual responses, the complexity of dietary patterns, methodological limitations, and the need for long-term studies present significant hurdles. Overcoming these challenges requires a multifaceted approach, including personalized nutrition, advanced analytical tools, standardized methodologies, and collaborative research efforts. By addressing these issues, the field can move closer to realizing the full potential of diet-based strategies for enhancing immune health and preventing chronic diseases.

V. Conclusion

Nutritional immunology represents a frontier in understanding the intricate relationships between diet, immune function, and inflammation. The research reviewed underscores the critical role of various dietary components—including vitamins, minerals, antioxidants, phytochemicals, and dietary patterns—in modulating immune responses and reducing inflammation. These findings highlight the potential of targeted nutritional interventions to improve immune health and prevent or manage chronic diseases. The emerging trends in personalized nutrition, the pivotal role of the microbiome, the exploration of novel bioactive compounds, and the holistic impact of dietary patterns present exciting avenues for future research. Personalized nutrition, in particular, offers a promising approach to tailor dietary interventions based on individual genetic, metabolic, and microbiome profiles, thereby optimizing immune function and disease prevention. However, the field faces significant challenges that must be addressed to translate these findings into practical and effective dietary strategies. The variability in individual responses, the complexity of dietary patterns,

methodological limitations, and the necessity for long-term studies are critical hurdles. Overcoming these challenges will require advancements in high-throughput technologies, standardization of research methodologies, and robust, collaborative research efforts. To advance the field of nutritional immunology, it is crucial to integrate diverse scientific disciplines and leverage new technologies. By addressing the current challenges and embracing emerging trends, researchers can develop comprehensive and personalized dietary recommendations that enhance immune health and reduce the risk of chronic diseases. nutritional immunology offers a promising pathway to harness the power of diet in supporting immune function and combating inflammation. Continued research and innovation in this field will be vital in developing effective nutritional interventions that promote health and well-being across diverse populations. The potential benefits of such interventions extend beyond individual health, potentially alleviating the global burden of chronic diseases and improving public health outcomes.

References

[1] Aggarwal, B. B., Sundaram, C., Malani, N., & Ichikawa, H. (2007). Curcumin: the Indian solid gold. Advances in Experimental Medicine and Biology, 595, 1-75. doi:10.1007/978-0-387-46401-5_1

[2] Baur, J. A., & Sinclair, D. A. (2006). Therapeutic potential of resveratrol: the in vivo evidence. Nature Reviews Drug Discovery, 5(6), 493-506. doi:10.1038/nrd2060

[3] Carr, A. C., & Maggini, S. (2017). Vitamin C and immune function. Nutrients, 9(11), 1211. doi:10.3390/nu9111211

[4] Casas, R., Castro-Barquero, S., Estruch, R., & Sacanella, E. (2018). Nutrition and cardiovascular health. International Journal of Molecular Sciences, 19(12), 3988. doi:10.3390/ijms19123988

[5] Flint, H. J., Scott, K. P., Duncan, S. H., Louis, P., & Forano, E. (2012). Microbial degradation of complex carbohydrates in the gut. Gut Microbes, 3(4), 289-306. doi:10.4161/gmic.19897

[6] Hemilä, H., & Chalker, E. (2013). Vitamin C for preventing and treating the common cold. Cochrane Database of Systematic Reviews, (1). doi:10.1002/14651858.CD000980.pub4

[7] Martineau, A. R., Jolliffe, D. A., Hooper, R. L., Greenberg, L., Aloia, J. F., Bergman, P., ... & Griffiths, C. J. (2017). Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of individual participant data. BMJ, 356, i6583. doi:10.1136/bmj.i6583

[8] Meydani, S. N., Han, S. N., & Hamer, D. H. (2004). Vitamin E and respiratory infection in the elderly. Annals of the New York Academy of Sciences, 1031(1), 214-222. doi:10.1196/annals.1331.023

[9] Middleton, E., Kandaswami, C., & Theoharides, T. C. (2000). The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. Pharmacological Reviews, 52(4), 673-751.

[10] Oppenheimer, S. J. (2001). Iron and its relation to immunity and infectious disease. The Journal of Nutrition, 131(2), 616S-633S. doi:10.1093/jn/131.2.616S

[11] Prasad, A. S. (2008). Zinc in human health: effect of zinc on immune cells. Molecular Medicine, 14(5-6), 353-357. doi:10.2119/2008-00033.Prasad

[12] Rayman, M. P. (2000). The importance of selenium to human health. The Lancet, 356(9225), 233-241. doi:10.1016/S0140-6736(00)02490-9

[13] Rios-Covian, D., Ruas-Madiedo, P., Margolles, A., Gueimonde, M., de Los Reyes-Gavilan, C. G., & Salazar, N. (2016). Intestinal short-chain fatty acids and their link with diet and human health. Frontiers in Microbiology, 7, 185. doi:10.3389/fmicb.2016.00185

[14] Ritchie, M. L., & Romanuk, T. N. (2012). A meta-analysis of probiotic efficacy for gastrointestinal diseases. PloS One, 7(4), e34938. doi:10.1371/journal.pone.0034938

[15] Roberfroid, M., Gibson, G. R., Hoyles, L., McCartney, A. L., Rastall, R., Rowland, I., ... & Scott, K. (2010). Prebiotic effects: metabolic and health benefits. British Journal of Nutrition, 104(S2), S1-S63. doi:10.1017/S0007114510003363

[16] Soltani, S., Chonchol, M., & Reaven, P. D. (2016). The DASH diet decreases markers of inflammation and oxidative stress in adults with moderate chronic kidney disease. Journal of Nutrition, 146(6), 1213-1219. doi:10.3945/jn.115.225441

[17] Stephensen, C. B. (2001). Vitamin A, infection, and immune function. Annual Review of Nutrition, 21(1), 167-192. doi:10.1146/annurev.nutr.21.1.167

[18] Suez, J., Zmora, N., Segal, E., & Elinav, E. (2019). The pros, cons, and many unknowns of probiotics. Nature Medicine, 25(5), 716-729. doi:10.1038/s41591-019-0439-x

[19] Yang, C. S., Wang, H., & Sheridan, Z. P. (2014). Studies on prevention of obesity, metabolic syndrome, diabetes, cardiovascular diseases and cancer by tea. Journal of Food and Drug Analysis, 22(1), 85-92. doi:10.1016/j.jfda.2014.01.010

[20] Zeevi, D., Korem, T., Zmora, N., Israeli, D., Rothschild, D., Weinberger, A., ... & Segal, E. (2015). Personalized nutrition by prediction of glycemic responses. Cell, 163(5), 1079-1094. doi:10.1016/j.cell.2015.11.001