

Supplemental Micronutrients, Tight Junctions and Epithelial Barrier Function: A Narrative Review

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Abstract

This narrative review examines the role of supplemental micronutrients in modulating tight junctions and epithelial barrier function. Tight junctions are critical components of epithelial barriers in various tissues, including the gastrointestinal tract, respiratory system and skin, regulating the paracellular transport of ions, solutes and immune cells. Emerging evidence suggests that micronutrients, such as vitamins (e.g., vitamin D, vitamin A and vitamin C), minerals (e.g., zinc, selenium) and polyphenols, play crucial roles in maintaining the integrity and function of tight junctions. This review explores the mechanisms through which micronutrients influence tight junction dynamics, barrier integrity and immune responses, highlighting their potential therapeutic implications in conditions characterized by epithelial barrier dysfunction, such as inflammatory bowel disease, allergic disorders and skin diseases. Understanding the interplay between supplemental micronutrients and tight junctions can inform strategies for optimizing epithelial barrier function and promoting overall health and wellbeing.

Keywords: Tight junctions • Supplemental micronutrients • Polyphenols • Allergic disorders • Paracellular transport

Introduction

In recent years, there has been a growing interest in understanding the intricate relationship between nutrition and gut health. The epithelial barrier, formed by tight junctions, plays a crucial role in maintaining intestinal integrity and preventing the translocation of harmful substances into systemic circulation. Various factors, including diet, have been implicated in modulating tight junction function. In this narrative review, we delve into the role of supplemental micronutrients in supporting tight junctions and epithelial barrier function. The intestinal epithelium serves as a selectively permeable barrier that regulates the absorption of nutrients while preventing the entry of pathogens, toxins and antigens into the bloodstream. Tight junctions, specialized protein complexes located at the apical end of epithelial cells, play a pivotal role in maintaining the integrity of this barrier. These junctions form a seal between adjacent cells, controlling the paracellular transport of ions, water and macromolecules. Disruption of tight junctions can lead to increased intestinal permeability, commonly referred to as "leaky gut," which has been implicated in the pathogenesis of various gastrointestinal disorders, autoimmune diseases and metabolic disorders. Therefore, strategies aimed at preserving or restoring tight junction integrity are of significant interest in maintaining overall health and well-being [1].

Literature Review

Emerging evidence suggests that certain micronutrients play a crucial role in modulating tight junction function and epithelial barrier integrity. Here, we explore the impact of several key micronutrients on tight junctions:

Vitamin C: Vitamin C, also known as ascorbic acid, is a powerful antioxidant with immunomodulatory properties. Studies have shown that

vitamin C can enhance tight junction integrity and reduce barrier dysfunction in various experimental models of gastrointestinal injury. Moreover, vitamin C supplementation has been associated with improved clinical outcomes in conditions characterized by mucosal inflammation and oxidative stress.

Vitamin D: Beyond its well-known role in calcium homeostasis and bone health, vitamin D has been shown to exert protective effects on the intestinal barrier. Vitamin D receptors are present in intestinal epithelial cells, where they regulate the expression of tight junction proteins. Studies have demonstrated that vitamin D deficiency is associated with increased intestinal permeability and inflammation, while supplementation with vitamin D can enhance tight junction integrity and reduce barrier dysfunction [2].

Zinc: Zinc is an essential micronutrient involved in numerous cellular processes, including the maintenance of epithelial barrier function. Zinc deficiency has been linked to impaired tight junction assembly and increased intestinal permeability. Supplemental zinc has been shown to strengthen tight junctions, enhance barrier function and protect against intestinal injury caused by various insults.

Magnesium: Magnesium is an essential mineral involved in numerous physiological processes, including muscle contraction, nerve function and protein synthesis. Emerging evidence suggests that magnesium deficiency may compromise tight junction integrity and increase intestinal permeability. Supplemental magnesium has been shown to enhance epithelial barrier function and reduce inflammation in preclinical studies.

Polyphenols: Polyphenols, abundant in fruits, vegetables, tea and red wine, possess potent antioxidant and anti-inflammatory properties. Certain polyphenols, such as Epigallocatechin Gallate (EGCG) from green tea and resveratrol from red wine, have been shown to strengthen tight junctions and preserve epithelial barrier function. These effects are attributed to their ability to modulate signalling pathways involved in inflammation, oxidative stress and cellular junction dynamics.

Probiotics and prebiotics: Probiotics are live microorganisms that confer health benefits when consumed in adequate amounts, while prebiotics are nondigestible carbohydrates that selectively stimulate the growth and activity of beneficial gut bacteria. Both probiotics and prebiotics have been shown to modulate tight junction function and enhance epithelial barrier integrity through their effects on gut microbiota composition, immune regulation and metabolite production [3].

Curcumin: Curcumin, a bioactive compound found in turmeric,

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exhibits potent anti-inflammatory and antioxidant properties. Studies have demonstrated that curcumin can strengthen tight junctions, reduce intestinal permeability and alleviate mucosal inflammation in various experimental models. These effects are mediated through multiple mechanisms, including the inhibition of pro-inflammatory cytokines and Nuclear Factor-kappa B (NF- κ B) signaling pathways.

Omega-3 fatty acids: The omega-3 polyunsaturated fatty acids, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA), found in fish oil, have anti-inflammatory properties and have been implicated in preserving epithelial barrier integrity. Omega-3 fatty acids modulate tight junction assembly and function through various mechanisms, including the regulation of inflammatory signaling pathways and lipid raft dynamics within the cell membrane [2,3].

Glutamine: Glutamine is a conditionally essential amino acid that serves as a fuel source for rapidly dividing cells, including enterocytes. Glutamine plays a critical role in maintaining intestinal barrier function by promoting tight junction assembly, stimulating mucin production and enhancing epithelial cell proliferation. Supplementation with glutamine has been shown to reduce intestinal permeability and improve clinical outcomes in conditions associated with mucosal injury [4].

Vitamin A: Vitamin A and its derivatives, such as retinoic acid, are essential for epithelial cell differentiation and mucosal immunity. Vitamin A deficiency has been associated with epithelial barrier dysfunction and increased susceptibility to mucosal injury. Retinoic acid has been shown to regulate the expression of tight junction proteins and enhance barrier integrity in experimental models of intestinal inflammation.

Vitamin E: As a potent antioxidant, vitamin E protects cell membranes from oxidative damage and inflammation. Vitamin E deficiency has been linked to increased intestinal permeability and mucosal injury. Supplementation with vitamin E has been shown to preserve tight junction integrity, reduce oxidative stress and mitigate barrier dysfunction in various experimental models.

Discussion

The findings discussed in this review have significant clinical implications for the management and prevention of gastrointestinal disorders characterized by epithelial barrier dysfunction. Nutritional interventions targeting tight junctions and epithelial barrier function may offer a promising adjunctive approach to conventional therapies. However, further research is needed to elucidate the optimal dosing, timing and duration of micronutrient supplementation in different clinical contexts.

The accumulating evidence on the role of supplemental micronutrients in supporting tight junctions and epithelial barrier function has important clinical implications for the management of gastrointestinal disorders and other systemic conditions associated with barrier dysfunction. Incorporating micronutrient supplementation into clinical practice may offer a safe and effective adjunctive approach to conventional therapies, particularly in patients with compromised gut barrier function. However, several challenges and unanswered questions remain regarding the optimal selection, dosing and duration of micronutrient supplementation in different patient populations. Future research efforts should focus on addressing these gaps through well-designed clinical trials with rigorous methodology and standardized outcome measures. Additionally, mechanistic studies are needed to elucidate the specific molecular pathways by which micronutrients modulate tight junction function and barrier integrity [5,6].

Conclusion

In conclusion, the narrative review highlights the intricate relationship

between supplemental micronutrients, tight junctions and epithelial barrier function. Tight junctions serve as crucial regulators of paracellular transport and immune surveillance in various epithelial tissues, playing a pivotal role in maintaining barrier integrity. Emerging evidence suggests that micronutrients, including vitamins, minerals and polyphenols, exert significant influences on tight junction dynamics and epithelial barrier function. By modulating tight junction protein expression, distribution and function, these micronutrients contribute to the maintenance of barrier integrity and immune homeostasis. The findings underscore the therapeutic potential of supplemental micronutrients in conditions characterized by epithelial barrier dysfunction, such as inflammatory bowel disease, allergic disorders and skin diseases. Moving forward, further research is warranted to elucidate the precise mechanisms underlying the interactions between micronutrients and tight junctions, as well as their implications for human health and disease. By integrating targeted nutritional interventions aimed at supporting tight junction integrity, clinicians and researchers can potentially improve therapeutic strategies for managing epithelial barrier-related disorders and promoting overall wellbeing.

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Conflict of Interest

There are no conflicts of interest by author.

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