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STRENGTHENING OF INTESTINAL BARRIER INTEGRITY AND PROTEIN ANABOLISM DURING COMBINED APPLICATION OF CHITOSAN AND WHEY POWDER: AN EVIDENCE-BASED NARRATIVE REVIEW AND PRACTICAL IMPLICATIONS

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Abstract. The intestinal barrier is a dynamic multilayer system that separates the host from luminal antigens, microorganisms, and toxic metabolites, while enabling selective absorption of nutrients and water. Barrier disruption (often summarized as increased permeability) is increasingly linked to inflammatory and metabolic disorders in humans and to impaired productivity, feed efficiency, and welfare in poultry and other livestock.

Within this context, nutrition-based strategies that simultaneously stabilize epithelial tight junctions and support efficient protein accretion are of high translational value. Chitosan (a cationic deacetylated derivative of chitin) and whey-derived products (rich in indispensable amino acids, including leucine and other branched-chain amino acids) are widely discussed as affordable functional ingredients. This review synthesizes mechanistic and applied evidence on how chitosan and whey powder may modulate mucosal immunity, oxidative stress responses, microbiota ecology, and the mTORC1-dependent anabolic program, with a particular focus on tight-junction proteins (occludin, claudins, ZO-1) and inflammation-sensitive barrier regulation.

Controlled animal studies indicate that chitosan oligosaccharides can improve intestinal development and barrier markers and attenuate inflammatory and oxidative stress signaling in early-life broilers.

Whey powder and whey protein concentrates have also demonstrated improvements in growth performance, nutrient digestibility, and gut microbial profiles when applied within appropriate inclusion levels.

Finally, regional (CIS) reports, including experimental data from Uzbekistan, suggest that combined chitosan–whey premixes may beneficially influence selected biochemical indices and growth dynamics in broiler production systems.

Keywords: chitosan; chitosan oligosaccharide; whey powder; tight junction; intestinal permeability; microbiota; mTORC1; branched-chain amino acids; broiler chicken; protein accretion.

Introduction

Maintaining intestinal barrier integrity is a central prerequisite for metabolic homeostasis, immunological tolerance, and efficient nutrient utilization. The barrier must reconcile two competing tasks: strict limitation of microbial translocation and toxins, and high-capacity absorption of water and nutrients. A large body of work has established that barrier failure is not merely a passive consequence of disease; it can actively shape inflammatory signaling and systemic immune responses [1,2]. In animal production, early-life barrier immaturity and environmental stressors (diet transitions, crowding, heat stress, pathogen exposure) can precipitate low-grade inflammation, reduced digestive efficiency, and poorer growth outcomes.

From a nutritional perspective, two mechanistic levers are especially relevant: (i) restoration of epithelial tight-junction competence and anti-oxidant defenses, and (ii) optimization of post-absorptive anabolic signaling for protein deposition. Chitosan and its oligosaccharide derivatives have been extensively studied as functional

polysaccharides with antimicrobial, immunomodulatory, and anti-inflammatory activity [8,9]. Whey-derived products, in turn, provide a dense supply of essential amino acids—particularly leucine—capable of activating the mTORC1 axis and supporting protein synthesis [4–6]. The combined use of chitosan and whey powder therefore represents a rational functional strategy to couple mucosal stabilization with anabolic support.

Main Part

Barrier architecture and biomarkers. The intestinal barrier is commonly conceptualized as the mucus layer, the epithelial monolayer with intercellular junctional complexes, and the underlying mucosal immune system. Tight junctions—formed by claudins, occludin, and scaffold proteins such as ZO-1—are critical regulators of paracellular permeability and are dynamically remodeled by cytokines, oxidative stress, and microbial metabolites [1–3]. Common experimental readouts include transepithelial electrical resistance (TEER), permeability tracers, expression of tight-junction proteins, villus/crypt morphometry in animals, and systemic proxies of barrier disruption [3,13].

Inflammation–oxidative stress coupling. Barrier disruption is strongly amplified by pro-inflammatory cytokines and reactive oxygen species, creating a positive feedback loop: epithelial stress weakens junctional complexes, increased permeability augments immune activation, and the resulting cytokine milieu further destabilizes the epithelial interface [1,13]. Nutritional interventions that support antioxidant pathways (e.g., Nrf2-regulated enzymes) and dampen excessive innate immune activation are therefore expected to improve both local barrier integrity and systemic metabolic resilience.

Protein accretion and the leucine–mTORC1 axis. Whey proteins are rapidly digested, produce a pronounced postprandial rise in essential amino acids, and are relatively leucine-rich. Leucine acts as a key nutrient signal for mTORC1 activation,

stimulating translation initiation and muscle protein synthesis in humans and animal models [4,5].

Comparative studies show that whey can stimulate muscle protein synthesis more rapidly than slower proteins such as casein, and that leucine supplementation can partially rescue anabolic responses when protein dose is limited [5,6,12]. In livestock, improved amino acid delivery to peripheral tissues depends on intact intestinal digestion–absorption, highlighting the relevance of barrier-first strategies.

Methodology

Study design. This manuscript is a narrative review with an evidence-based emphasis on mechanistic plausibility and applicability to nutrition practice. Search strategy. Publications were identified via structured keyword searches in PubMed and open-access full-text repositories, complemented by manual backward citation tracking. Core search terms included: “intestinal barrier”, “tight junction”, “permeability”, “chitosan”, “chitosan oligosaccharide”, “whey powder”, “whey protein concentrate”, “leucine”, “BCAA”, and “mTORC1”, combined with “broiler”, “poultry”, and “growth performance”. Selection criteria.

Priority was given to peer-reviewed reviews (for conceptual frameworks), mechanistic studies linking interventions to tight junction or oxidative-stress pathways, and controlled animal trials reporting gut morphology, barrier markers, and/or performance outcomes. In addition, regional (CIS) publications and research reports relevant to chitosan–whey applications in broiler production were included when sufficient methodological information was available [14–19].

Analysis

Mechanistic rationale for chitosan. Chitosan is a cationic polymer capable of interacting with negatively charged microbial membranes and mucosal surfaces. Across animal nutrition studies, chitosan and chitooligosaccharides have been associated with

reduced pathogen pressure, modulation of intestinal microbiota, and improvements in mucosal morphology and immune indices [8,9].

A controlled early-life broiler trial in Poultry Science reported that dietary chitosan oligosaccharide supplementation promoted intestinal development and altered expression of tight-junction genes (including occludin and ZO-1), while reducing pro-inflammatory signaling and improving antioxidant enzyme activity [7].

Such findings align with the broader concept that barrier stabilization can be mediated through concurrent attenuation of inflammatory cascades and support of redox homeostasis [1,3,13].

Mechanistic rationale for whey-derived products. Whey powder and whey protein concentrates provide high-quality protein, bioactive peptides, and a high concentration of essential amino acids. Beyond their anabolic potential, whey-derived peptides may influence gut ecology through effects on luminal substrates and microbial fermentation patterns. In broilers, randomized feeding trials have shown that inclusion of dry whey powder or whey protein concentrate can improve growth and feed efficiency, enhance apparent ileal digestibility, and shift cecal microbiota composition [10].

Additional work in broilers has linked whey protein concentrate inclusion to changes in intestinal tract parameters and oxidative status markers [11].

Why a combined chitosan–whey approach may be synergistic. Conceptually, chitosan may improve the “upstream” conditions for effective nutrient utilization by reducing inflammatory tone and supporting epithelial repair, whereas whey provides the “downstream” substrate and signaling (leucine/BCAA) necessary for efficient protein accretion. A stable barrier limits endotoxin exposure and inflammation-driven catabolism, which can otherwise blunt anabolic signaling. In humans, studies demonstrate that whey protein ingestion robustly stimulates muscle protein synthesis and that leucine can act as a potent trigger for mTORC1 activation [4–6,12].

Translationally, this supports the hypothesis that barrier-stabilizing feed additives may amplify the benefits of high-quality protein inputs—especially during early growth phases or under stress conditions that threaten gut integrity [1,3].

Regional (CIS) context and practical observations. Clinical and gastroenterological literature from the CIS region emphasizes epithelial protection, mucosal healing, and barrier preservation as core therapeutic concepts in gastrointestinal disorders [14–16].

In parallel, experimental reports from Uzbekistan describe the use of chitosan and whey powder premixes in broiler feeding systems, with observed improvements in growth dynamics and selected biochemical indicators, supporting the feasibility of implementing such functional strategies under local production conditions [17–19].

While these reports require further confirmation in larger multi-center trials with standardized barrier biomarkers, they provide context-specific signals that justify continued research and controlled optimization.

Results

Synthesis of evidence. Across the reviewed sources, several convergent patterns emerge. First, barrier integrity is tightly linked to inflammatory and oxidative stress signaling, and interventions that reduce these stressors tend to preserve or restore tight-junction competence [1,3,13].

Second, chitosan oligosaccharides have repeatedly demonstrated improvements in early-life intestinal development and barrier-related gene expression in poultry models [7,8].

Third, whey products can enhance growth performance and nutrient digestibility in broilers and activate anabolic signaling pathways through their essential amino acid profile—particularly leucine—supporting efficient protein synthesis [4,5,10–12].

Finally, the combined rationale suggests that simultaneous stabilization of the gut barrier and optimization of protein supply may deliver additive or synergistic outcomes, although direct head-to-head combination trials with robust barrier endpoints remain scarce in the open literature and represent a priority for future research.

Table 1. Mechanistic summary and practical interpretation of chitosan and whey powder interventions.

Intervention	Primary mechanisms	Barrier-related outcomes	Model / evidence type	Practical notes
Chitosan / COS	Antimicrobial and immunomodulatory effects; antioxidant support [8,9]	Improved villus development; altered occludin/ZO-1 expression; reduced inflammation in broilers [7]	Controlled poultry trial and reviews	Dose and molecular weight matter; assess tolerance and diet matrix
Whey powder / WPC	High-quality protein; leucine-driven mTORC1 activation [4–6,12]	Improved digestibility and microbiota shifts; indirect support of barrier via reduced catabolism [10,11]	Broiler feeding trials; human mechanistic studies	Inclusion levels should match protein targets and lactose tolerance
Combined strategy	Barrier-first stabilization plus anabolic substrate/signaling	Hypothesized additive benefits; limited direct combination trials [17–19]	Regional trials and translational rationale	Prioritize trials with standardized permeability and tight-junction markers

Conclusion

Chitosan and whey powder represent complementary nutritional tools that target two interdependent determinants of performance and health: intestinal barrier integrity and protein accretion. The international literature consistently supports the centrality of tight-junction regulation and oxidative–inflammatory control in maintaining barrier function [1–3,13].

Poultry studies further indicate that chitosan oligosaccharides can improve early intestinal development and barrier-related gene expression [7–9].

Whey products provide a practical source of highly bioavailable protein and leucine-rich amino acids that activate the mTORC1 pathway and support efficient protein synthesis [4–6,10–12].

For publication-ready translation, future studies should (i) test chitosan–whey combinations against single-component controls, (ii) quantify standardized barrier endpoints (permeability assays, tight-junction protein abundance, inflammatory and antioxidant markers), and (iii) link these endpoints to performance, carcass composition, and economic outcomes under real production conditions. Such work will help define evidence-based inclusion levels and clarify whether synergy exists beyond the sum of individual effects.

Declarations

Conflict of interest: The authors declare no conflict of interest.

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References

1. Turner J.R. Intestinal mucosal barrier function in health and disease // Nature Reviews Immunology. – 2009. – Vol. 9, No. 11. – P. 799–809. – DOI: 10.1038/nri2653.

2. Peterson L.W., Artis D. Intestinal epithelial cells: regulators of barrier function and immune homeostasis // Nature Reviews Immunology. – 2014. – Vol. 14, No. 3. – P. 141–153. – DOI: 10.1038/nri3608.

3. Schoultz I., Keita Å.V. The intestinal barrier and current techniques for the assessment of gut permeability // Cells. – 2020. – Vol. 9, No. 8. – Article 1909. – DOI: 10.3390/cells9081909.

4. Dodd K.M., Tee A.R. Leucine and mTORC1: a complex relationship // American Journal of Physiology – Endocrinology and Metabolism. – 2012. – Vol. 302, No. 11. – P. E1329–E1342. – DOI: 10.1152/ajpendo.00525.2011.

5. Churchward-Venne T.A., Burd N.A., Mitchell C.J., et al. Supplementation of a suboptimal protein dose with leucine or essential amino acids: effects on myofibrillar protein synthesis at rest and following resistance exercise // The Journal of Physiology. – 2012. – Vol. 590. – DOI: 10.1113/jphysiol.2012.228833.

6. Tang J.E., Moore D.R., Kujbida G.W., Tarnopolsky M.A., Phillips S.M. Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men // Journal of Applied Physiology. – 2009. – Vol. 107, No. 3. – P. 987–992. – DOI: 10.1152/japplphysiol.00076.2009.

7. Lan R., Wu F., Wang Y., et al. Chitosan oligosaccharide improves intestinal function by promoting intestinal development, alleviating intestinal inflammatory response, and enhancing antioxidant capacity in broilers aged d 1 to 14 // Poultry Science. – 2023. – Vol. 103, No. 2. – Article 103381. – DOI: 10.1016/j.psj.2023.103381.

8. Świątkiewicz S., Świątkiewicz M., Arczewska-Włosek A., Józefiak D. Chitosan and its oligosaccharide derivatives (chito-oligosaccharides) as feed supplements in poultry and swine nutrition // Journal of Animal Physiology and Animal Nutrition. – 2015. – Vol. 99, No. 1. – P. 1–12. – DOI: 10.1111/jpn.12222.

9. Khambualai O., Yamauchi K., Tangtaweewipat S., Cheva-Isarakul B. Growth performance and intestinal histology in broiler chickens fed with dietary chitosan // British Poultry Science. – 2009. – Vol. 50, No. 5. – P. 592–598. – DOI: 10.1080/00071660903247182.

10. Pineda-Quiroga C., Camarinha-Silva A., Borda-Molina D., et al. Feeding broilers with dry whey powder and whey protein concentrate affected productive performance,

ileal digestibility of nutrients and cecal microbiota community // Animal. – 2018. – Vol. 12, No. 4. – P. 692–700. – DOI: 10.1017/S1751731117002208.

11. Szczurek W., Szymczyk B., Arczewska-Włosek A., Józefiak D., Alloui M.N. The effects of dietary whey protein concentrate level on performance, selected intestinal tract and blood parameters, and thiobarbituric acid reactive substances in the liver and breast meat of broiler chickens // Journal of Animal and Feed Sciences. – 2013. – Vol. 22, No. 4. – P. 342–353. – DOI: 10.22358/jafs/65923/2013.

12. Kanda A., Nakayama K., Sanbongi C., et al. Effects of whey, caseinate, or milk protein ingestion on muscle protein synthesis after exercise // Nutrients. – 2016. – Vol. 8, No. 6. – Article 339. – DOI: 10.3390/nu8060339.

13. Dmytriv T.R., Oduor C.I., Lehman J., et al. Intestinal barrier permeability: the influence of gut microbiota in health and disease // Frontiers in Physiology. – 2024. – Article 1380713. – DOI: 10.3389/fphys.2024.1380713.

14. Trukhan D.I., Chusova I.G. Epithelial protective therapy: possible potential and experience of use in diseases of the digestive tract // Terapiya (Therapy). – 2020. – No. 8. – P. 174–185. – DOI: 10.18565/therapy.2020.8.174-185.

15. Simanenkov V.I., et al. Comprehensive recommendations for diagnosis and treatment of chronic gastritis and gastroduodenitis // Terapevticheskii arkhiv. – 2022. – Vol. 94, No. 8. – P. 961–973. – DOI: 10.26442/00403660.2022.08.201676.

16. Maev I.V., et al. Inflammatory bowel diseases: transformation of representations. A review // Terapevticheskii arkhiv. – 2023. – Vol. 95, No. 12. – P. 1064–1074. – DOI: 10.26442/00403660.2023.12.202507.

17. Holbayevich R. F. et al. Explanation on the physiological and biochemical indicators of broiler chicks fed with chitosan and whey powder //Academia Repository. – 2024. – T. 5. – №. 2. – C. 184-187.

18. Xolbayevich R. F. et al. Effect of chitosan and whey powder on the productivity of broiler chickens //Emerging Frontiers Library for The American Journal of Interdisciplinary Innovations and Research. – 2025. – Т. 7. – №. 06. – С. 10-12.

19. Komilov Oyatullo Meliboy ugli,Rakhmonov Farkhod Kholbayevich. EFFECT OF A WHEY POWDER AND CHITOSAN MIXTURE ON NUTRIENT ABSORPTION IN INTESTINAL EPITHELIAL CELLS. Ijai 2025, 5 (11), 2096-2099.

20. Li J., Cheng Y., Chen Y., Qu H., Zhao Y., Wen C., Zhou Y. Dietary chitooligosaccharide inclusion as an alternative to antibiotics improves intestinal morphology, barrier function, antioxidant capacity, and immunity of broilers at early age // Animals. – 2019. – Vol. 9, No. 8. – Article 493. – DOI: 10.3390/ani9080493.