

Targeted Dietary Modulation of Gut Microbiota in Crohn's Disease: From Mechanisms to Engineered Solutions

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Abstract. Crohn's disease (CD) is a chronic inflammatory bowel disease of complex etiology, and current treatment methods have limitations. Diet, a basic environmental factor affecting gut microbiota, faces intervention and translation challenges. From a food science and engineering perspective, a systematic literature review is used in this study to evaluate targeted dietary intervention evidence in Crohn's disease management, assess clinical translation challenges, and explore engineering-based solutions. The findings indicate that existing intervention strategies are challenging to implement in practical settings. People react in different ways, traditional oral formulations have delivery problems, and lack of enough strong clinical data. The research indicates that overcoming these challenges requires the creation of an innovative framework that integrates "precision nutrition" and "smart delivery." Future research should focus on utilizing individualized data to inform protocol design, particularly in the development of delivery methods like micro-nano encapsulation that rely on multi-trigger mechanisms. This method aims to create a consistent, efficient, and precise way to deliver active ingredients to lesions in the colon. This will help dietary therapies become more predictable and controllable therapeutic tools.

Keywords: Crohn's disease, Gut microbiota, Targeted intervention, Dietary strategies, Microbiome modulation.

1. Introduction

Crohn's disease (CD) is a chronic inflammatory bowel illness with multiple origins, its recurrent nature often causing long-term distress to patients. This illness has been happening more and more around the world in the last few years. For instance, reported incidence rates reveal that there are roughly 21 cases per 100,000 individuals in North America and 16 cases per 100,000 persons in Europe. It puts a lot of stress [1]. The results suggest that it's hard to put existing intervention tactics into practice in the real world. This is largely because people react differently, there are restrictions on how typical oral formulations may be given, and there isn't enough high-quality clinical data. And they still have a lot of challenges to cope with, like uneven therapeutic responses, substantial side effects, high prices, and the fact that it is hard to accomplish complete mucosal healing [2]. Because of this, there is a clear clinical need for non-drug supplementary therapy options that are safer, easy to administer, and treat the disease in its early stages.

In the last few years, studies on the microbiome have found that an imbalance is a major cause of Crohn's disease. Patients often have less diverse gut bacteria, fewer helpful bacteria, and changes in how bacteria break down food. This state of imbalance establishes a self-perpetuating vicious cycle characterized by intestinal epithelial barrier dysfunction and abnormal immunological activation [1]. Diet is a significant environmental factor affecting the composition and function of gut microbiota. Consequently, targeting microbial communities through dietary nutritional processes to disrupt this infectious cycle has become a highly attractive area of research [3]. Strategies like complete enteral nutrition have shown promise in clinical practice, but ongoing issues with individual variability and treatment stability indicate a significant translational gap between theory and practice [2,4-6].

This research examines the efficacy of various dietary interventions aimed at the gut microbiota in managing Crohn's disease. It wants to look at the evidence and how current treatments work in a systematic way. From an engineering standpoint, it examines the technical factors that contribute to variability in clinical outcomes. In the end, it suggests a way to move forward that combines the newest food delivery engineering technology with ideas about nutrition that are very precise. The

goal of this method is to provide theoretical support and help with strategic planning for the next generation of microbiome-modulating intervention products that are very effective, stable, and aimed at specific groups.

2. Current Status of Dietary Management for Crohn's Disease

2.1. Crohn's Disease Overview

People with Crohn's disease have a unique dysbiosis in their gut microbiota. This imbalance is the biological basis and therapeutic target of all dietary changes. A lot of research shows that alpha diversity in patients' gut microbiota has dropped significantly, which means that the microbial community's richness and balance have been disturbed throughout the body. The microbial composition often shows a drop in important good bacteria that help keep the intestinal barrier strong or have anti-inflammatory properties. For example, *Faecalibacterium prausnitzii*, a kind of bacteria that makes short-chain fatty acids (SCFAs). On the other hand, some types of microbes that live in pro-inflammatory microenvironments may grow too much [1].

This imbalance isn't just a side effect of being sick; it actively changes the gut's physical barrier function by changing the chemicals in it. This changes how energy is used and how tight junction proteins are made in intestinal epithelial cells. The imbalanced microbiota and its parts also usually turn on the host's mucosal immune system. This makes the body make too many chemicals that cause inflammation and keep it going in that area. The gut's physical properties and nutritional niche are affected by the inflammatory environment that exists during disease activity. The characteristics of this environment are like lower pH, more oxidative stress, and the presence of immune cells, etc. This naturally raises the quantity of bacteria that may live in places where there is inflammation. This makes dysbiosis and inflammation worse in a cycle.

One of the most promising approaches to break the cycle of disease and change it is to actively change the makeup of the gut microbiota through dietary changes from the outside. This will restore its ecological balance and good metabolic functions. At the moment, there are three basic strategies to manage this imbalance: standardized nutritional support, adjustments to specific eating patterns, and direct probiotic supplementation. The robustness of medical data and the fundamental processes of action vary significantly among various approaches.

2.2. Exclusive Enteral Nutrition

Exclusive enteral nutrition (EEN) is the first-line therapy for developing cure in children with active Crohn's disease. Its mode of action goes beyond simple food additives and intestinal rest, focusing on the substantial and quick alteration of the makeup of the gut microbiota in order to establish an environment suitable to barrier repair [1].

The Crohn's Disease Elimination Diet (CDED) has received lots of scientific attention because of its relatively uniform three-phase intervention approach. Clinical findings show that CDED causes significant recovery rates in both adult and kid patients. Short-term remission rates in children can reach 82% when paired with partial enteral nutrition, but 6-week remission rates in adults are around 76.7%, with good safety reported [7,8]. Deep examinations reveal distinct effects of CDED in gut microbiota and metabolites in children and adult patients: pediatric patients frequently exhibit stronger beneficial chemical changes and faster clinical responses, potentially linked to greater immune system and microbiota change; whereas adult responses show more personal variety, possibly due to long-established stable health structures and lifestyle habits [7, 8].

In contrast, other dietary approaches such as the low-FODMAP diet (low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet), low-carbohydrate diets, or strict restrictions on red meat/processed meat consumption processed meat, while widely adopted among patients, have received cautious evaluations in systematic reviews: except for a few protocols like the CDED, most solid food dietary interventions show either unclear efficacy or no significant difference from controls in inducing or maintaining remission in Crohn's disease [2]. For instance, the low-

FODMAP diet may only provide symptomatic relief for patients with overlapping irritable bowel syndrome-like symptoms, rather than targeting intestinal inflammation itself. Meanwhile, specialized studies on healthy dietary patterns like the Mediterranean diet in Crohn's disease remain extremely limited, with weak evidence supporting their efficacy. Also, a future study found that the Crohn's Disease Therapeutic Dietary Intervention (CD-TDI) protocol, a modified Mediterranean diet-based approach aimed at reducing infection and regulate metabolism, had the potential to improve patients' inflammatory markers while promoting beneficial gut microbiota. This is a model for future dietary improvements, however its findings require additional validation through controlled studies [9].

2.3. Prebiotic and Probiotic Supplements

Prebiotics, as insoluble food components, are thought to manage the gut microbiota by selectively raising the growth of beneficial bacteria like bifidobacteria and lactobacilli. However, the evidence for the benefits in Crohn's disease is poor and inconsistent. A Cochrane study from 2024 found inadequate evidence to support prebiotics for producing or keeping remission in ulcerative colitis, with even less evidence for Crohn's disease [3]. This shows that prebiotic efficacy may vary by condition, requiring more rigorous research.

Direct probiotic use, on the other hand, has more theoretical impact, but high-level evidence-based medical studies do not support its routine usage in causing or maintaining remission in Crohn's disease. Multiple systematic reviews and meta-analyses have consistently shown lack of proof to support probiotic efficacy in initiating or maintaining remission in Crohn's disease [10-12]. This lack of efficacy is due in part to the high strain- and formulation-specificity of treatment responses. For example, many complicated probiotic formulations suggested a possible trend in avoiding postoperative recurrence in small studies, but these findings were difficult to confirm. The certain strains may reduce active diarrhea symptoms, they have little effect on overall disease activity indices [10-12]. This means probiotic effects vary greatly based on strain combinations, intervention techniques, and disease stage.

In addition, the strength of data for probiotics varies greatly between Crohn's disease and ulcerative colitis. Probiotics may grow and have regulatory functions more easily in ulcerative colitis, when lesions are mainly limited to the colon's mucosal layer. In contrast, Crohn's disease's transmural and pan-intestinal active nature causes significant damage of the intestinal barrier and a wide range of lesion sites. This poses basic delivery issues for dietary probiotics, making it difficult for them to survive, colonize, and reach their target areas. This helps to explain the limited research supporting their usage [10-12].

2.4. Holistic Modulation of Dietary Patterns

In conclusion, present dietary treatments aimed at the gut microbiota provide a unique evidence gradient and translation bottleneck environment. Total enteral nutrition and the Crohn's disease elimination diet (CDED) are backed by a large body of clinical research data, particularly because CDED efficacy differences between populations (children vs. adults) give information for exact groups. Yet, a great deal of other solid food dietary patterns and standard prebiotic/probiotic products are still in the early stages of research or inquiry [8].

The European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recently released a position paper, which explicitly states that there is currently lacking high-level evidence to support regular precision or divided dietary advice for patients with confirmed inflammatory bowel disease [13]. This truly reflects the practical limitations experienced through the move from factual to scientific, personalized approaches in this field. Such barriers are caused not only because biological diversity but also by the technical limits of current intervention delivery systems.

3. Challenges in Clinical Translation

Translating previous nutritional concepts into stable, generally applicable treatments has presented a number of issues because of biological heterogeneity, delivery technology limitations, and a lack of evidence.

3.1. Heterogeneity in Individual Responses

The main problem with using nutritional strategies on a regular basis is that different people achieve different results. The host-microbiome interaction system is very complicated, and many things can affect it, like the patient's unique genetic background, basic gut microbiota structure, biologic status, disease type, and age. The different ways that microbes respond to energy in pediatric and adult CDAD treatments show how age affects the results of an intervention [8,13]. Also, people's long-term habits, eating habits, and underlying health problems make it challenging to predict how they will react.

Due to inherent biological variability, it is nearly impossible to establish a singular, global, uniform "one-size-fits-all" approach. This variability is the main reason why clinical trials often get different results and it's hard to come to a clear conclusion. This difference is especially clear in probiotic research, where different strains, groups of patients, and stages of illness respond in very different ways. This shows how important it is to be very clear [10-12].

3.2. Bottlenecks in Delivery Technologies

Present intervention techniques encounter considerable technological limitations, especially regarding active biological agents like probiotics. The bad physical conditions of the upper digestive tract (gastric acid and bile) break down oral probiotics a lot, which makes them very hard to absorb. Pills and powders, which are common forms of supplements, don't release their active ingredients in a targeted way or stay in the colon for a long time. Active chemicals often run out too soon in places where they shouldn't be used, which can be uncomfortable.

The central inflammation, the broken intestinal barrier, and different lesion areas that are common in Crohn's disease all make it hard for probiotics to grow and work [10-12]. Even drug delivery systems made just for targeting the colon often don't work right when they only use physiological signals like pH or time to activate. This is especially bad because Crohn's disease patients have a lot of differences between them, and their digestive factors change all the time. This often leads to early or incomplete release and targeting failure [5].

3.3. Gaps in the Evidence Base and Translational Pathway

The most important problem in this field is that there is not enough high-quality, evidence-based medical data. Many dietary intervention studies have disadvantages, such as limited samples, short intervention periods, and significant differences in trial designs. Further, subjective symptom scores, rather than objective hard objectives such as oral healing or histological remission, are frequently used as major evaluation measures. The ESPGHAN position statement also observes that present research struggles to clearly define between "treatment failure" and "poor patient compliance," the latter of which is especially common in nutritional interventions with significant degrees of freedom [13].

This evidence gap not only keeps international clinical guidelines from making definitive recommendations for the majority of dietary therapy, but also limits physicians and nutritionists authoritative, unified scientific support for delivering precise, specific dietary advice. As a result, systematic execution and outcome evaluation of these initiatives remain limited. The probiotics sector reflects this situation: despite a large number of studies, the majority are of poor quality, with diverse conclusions, and fail to offer compelling evidence for strong recommendations [10-12].

4. Future Development Direction

To methodically solve these challenges and transition dietary interventions from an optional, empirical health management approach to a predictable, controllable targeted therapeutic strategy, two core paradigms must be developed and combined within the future: precision nutrition based on deep marker analysis and food engineering solutions that revolutionize delivery efficacy.

4.1. Precision Nutrition

The main goal of precision nutrition is to ensure that everyone receives the right treatment for them. But at this point, it's important to first build a scientific evidence base. The main goal is to stop doing small-scale exploratory studies and start doing large-scale, long-term controlled experiments with strong designs that look at big populations and objective negative outcomes.

The main goal of research should be to identify and confirm biomarkers that can predict how certain dietary treatments will work. Some examples are baseline gut microbiota richness patterns that are linked to the effectiveness of total enteral nutrition, specific metabolite profiles that are linked to CDED response, and genetic differences in fatty acid metabolism [7,8]. In the probiotics market, future research must also look for patient groups that are likely to respond to certain strains or formulations (based on gut microbiome features, antibody markers, and so on) [10-12].

It is also vital to design and use objective, easy-to-use tools to see how well people keep to their diets. These tools could be digital health technology or biomarker-based detection. People can use these methods to find out how well any nutrition program really works and get clinical practice results closer to the optimal standards. This is still one of the weaker elements of the study as it is now.

4.2. Intelligent Delivery Systems

To make sure that certain solutions get to the right people, it is important to use safe engineering methods. Adaptive delivery systems are a huge step in solving problems with giving out probiotics and other regular oral drugs. The best approach to do this is to put probiotics in biocompatible materials like chitosan and alginate on a micro- and nanosize. This makes it keep living for the probiotics to travel through the stomach and intestines [4].

The also very important thing is making delivery systems that can be turned on in many ways. One way is to use both microbial enzymatic hydrolysis and pH responsiveness at the same time. These machines are better at reacting to changes in a person's body, which keeps active substances from getting into the gut. Because of it, people are much more sure that the delivery and therapy will work better [5].

Synthetic biology can also be used to make probiotics that are stronger at withstanding bile and acid, that can fight inflammation, or that can produce helpful compounds. This is more than just protecting the body; it can also help living things live and spread, and it can even make medicine work better [6]. Lastly, personalized manufacturing platforms like 3D printing can manufacture compounds with different amounts, release rates, and even shapes to fit a person's individual dietary demands. Then give the carrying things to a certain person according to a plan [5].

5. Conclusion

This review shows that nutritional therapies like EEN and CDED work well, but they are hard to use in real life. These include a lot of differences between people, delivery technology that isn't fully developed, and a lack of strong clinical data. To solve these problems, future research needs to focus on how to deeply combine precision medicine and engineering technologies and use multi-omics data and artificial intelligence to create personalized nutrition plans.

The full model suggested in this study shows how to move dietary interventions from extra health measures to engineered "curative nutrition products." This shows how important it is for different fields to work together. But a lot of engineered solutions are still being worked on, so they need to be fully tested for their long-term safety, effectiveness, and costs of scaling up. In the future, researchers

should focus on rigorous precision nutrition studies to build high-level knowledge, work together to solve real-world problems by making personalized products, and finally promote scientific, specific CD nutritional management methods.

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