DOI: https://doi.org/10.61841/s3gwnr60 Publication URL: https://nnpub.org/index.php/MHS/article/view/2007

THE ROLE OF DIETARY SUPPLEMENTS IN INFLAMMATORY BOWEL DISEASE : A SYSTEMATIC REVIEW

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ABSTRACT

Background: *The microbiome is an important contributor to a variety of fundamental aspects of human health, including host metabolism, infection, and the immune response. Gut dysbiosis has been inditified as a contributor to the errant immune response in disease such as inflammatory bowel disease.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 58 articles, whereas the results of our search on SagePub brought up 177 articles. The results of the search conducted for the last year of 2013 yielded a total 39 articles for PubMed and 9 articles for SagePub. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.*

Conclusion: *In summary, most substances reviewed showed a positive effect on patients with IBD and their clinical symptoms. Fibers have also shown similar results. Those fibers, such as fructans, psyllium, oat bran, and barley foodstuff have relieved some gastrointestinal symptoms that have been associated with IBD, this has improved patient's quality of life. The fatty acids reviewed have proved to be effective in decreasing corticosteroid use among may IBD patients. Probiotics have shown some promising results; however, more testing is required to provide definite results. Lastly, low FODMAP diets have also shown a very positive effect in decreasing uncomfortable gastrointestinal symptoms.*

Keyword: *Dietary supplements, Inflammatory bowel disease, efficac*

INTRODUCTION

The microbiome is a key contributor to various fundamental aspects of human health, including host metabolism, infection, and the immune response. It is composed of 1000–1500 species of bacteria as well as fungi and viruses, whose diversity is important for the maintenance of the metabolic system and maturation of intestinal immunity. An imbalance of these gut microbial communities has been shown to disrupt host immunity and has been linked to intestinal disease. While we are only beginning to understand the complexity of interactions between the microbiome and the host immune system, it has been shown that gut dysbiosis is one of the key contributors to errant host immune responses in a variety of immune-mediated inflammatory diseases (IMIDs). As such, there is strong rationale to suspect demonstrable therapeutic potential with prebiotic and probiotic usage in inflammatory bowel disease (IBD), a chronic relapsing intestinal disease without medical cure, and other IMIDs. With growing supporting evidence, the interest in probiotics and prebiotics, as well as additional supplements, to modulate disease has dramatically grown. While the importance of supplements to correct certain aspects of IBD, such as mineral deficiencies, is well-established, the role of other dietary supplements in affecting the overall disease course is less clear.[1,2]

The incidence of IBD—including both Crohn's disease (CD), which can affect any part of the gastrointestinal tract, and ulcerative colitis (UC), which is restricted to the colon—is increasing worldwide. Recent literature increasingly supports the use of prebiotics, probiotics, and other supplements to treat gut dysbiosis. Despite this, however, there are few clear guidelines advocating for their use as a treatment for IBD, and results in clinical trials have generally been equivocal. In fact, the American Gastroenterology Association (AGA) practice guidelines on the role of probiotics in management of gastrointestinal disorders do not recommend their use outside of a clinical trial as a result of knowledge gaps caused by low sample sizes as well as study design and treatment heterogeneity.[3,4]

The role of diet in the pathogenesis of Inflammatory Bowel Diseases (IBD) remains an open topic despite the advances in our understanding of the gastrointestinal (patho)physiology microbiology and mucosal immunology. A shift from a more "aboriginal" food to the highly refined and processed western diet and the associated change in gut microbiome as contributing environmental factors has been suggested by many nutritional studies. In IBD patients, they are aimed at eliminating food triggers and improving nutrition, and include supplementation of vitamins and other micro- and macronutrients. Nutritional interventions are an integral part of clinical practice, although evidence from clinical studies is relatively uncommon and frequently suffers from inadequate design and/or small numbers of patients. In some instances, e.g. vitamin D_3, supplementation with doses far exceeding the recommended daily allowances has been proposed. The mechanisms responsible for nutritional deficiencies are not always clear and could be related to decreased intake, malabsorption, or excess losses. Increased metabolic demand related to the active inflammatory process should also be taken into consideration. Micronutrient and vitamin deficiencies are relatively common among IBD patients, especially in Crohn's Disease with active small bowel disease, or patients undergoing intestinal resection.[4]

However, there is still much to extract and extrapolate from these IBD studies. In this review, we examine the data from the literatures surrounding probiotics, prebiotics, and other dietary supplements in IBD patients.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we review published literature of studies to identify studies that reported efficacy of dietary supplements used by patients with inflammatory bowel disease. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "dietary supplements", "inflammatory bowel diseaese" and "efficacy" as keywords.The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *("dietary supplements"[MeSH Terms] OR ("dietary"[All Fields] AND "supplements"[All Fields]) OR "dietary*

supplements"[All Fields]) AND ("inflammatory bowel diseases"[MeSH Terms] OR ("inflammatory"[All Fields] AND "bowel"[All Fields] AND "diseases"[All Fields]) OR "inflammatory bowel diseases"[All Fields] OR ("inflammatory"[All Fields] AND "bowel"[All Fields] AND "disease"[All Fields]) OR "inflammatory bowel disease"[All Fields]) AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields]) AND ("role"[MeSH Terms] OR "role"[All Fields]) AND ("functional"[All Fields] OR "functionals"[All Fields] OR "functionalities"[All Fields] OR "functionality"[All Fields] OR "functionalization"[All Fields] OR "functionalizations"[All Fields] OR "functionalize"[All Fields] OR "functionalized"[All Fields] OR "functionalizes"[All Fields] OR "functionalizing"[All Fields] OR "functionally"[All Fields] OR "functionals"[All Fields] OR "functioned"[All Fields] OR "functioning"[All Fields] OR "functionings"[All Fields] OR "functions"[All Fields] OR "physiology"[MeSH Subheading] OR "physiology"[All Fields] OR "function"[All Fields] OR "physiology"[MeSH Terms]) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

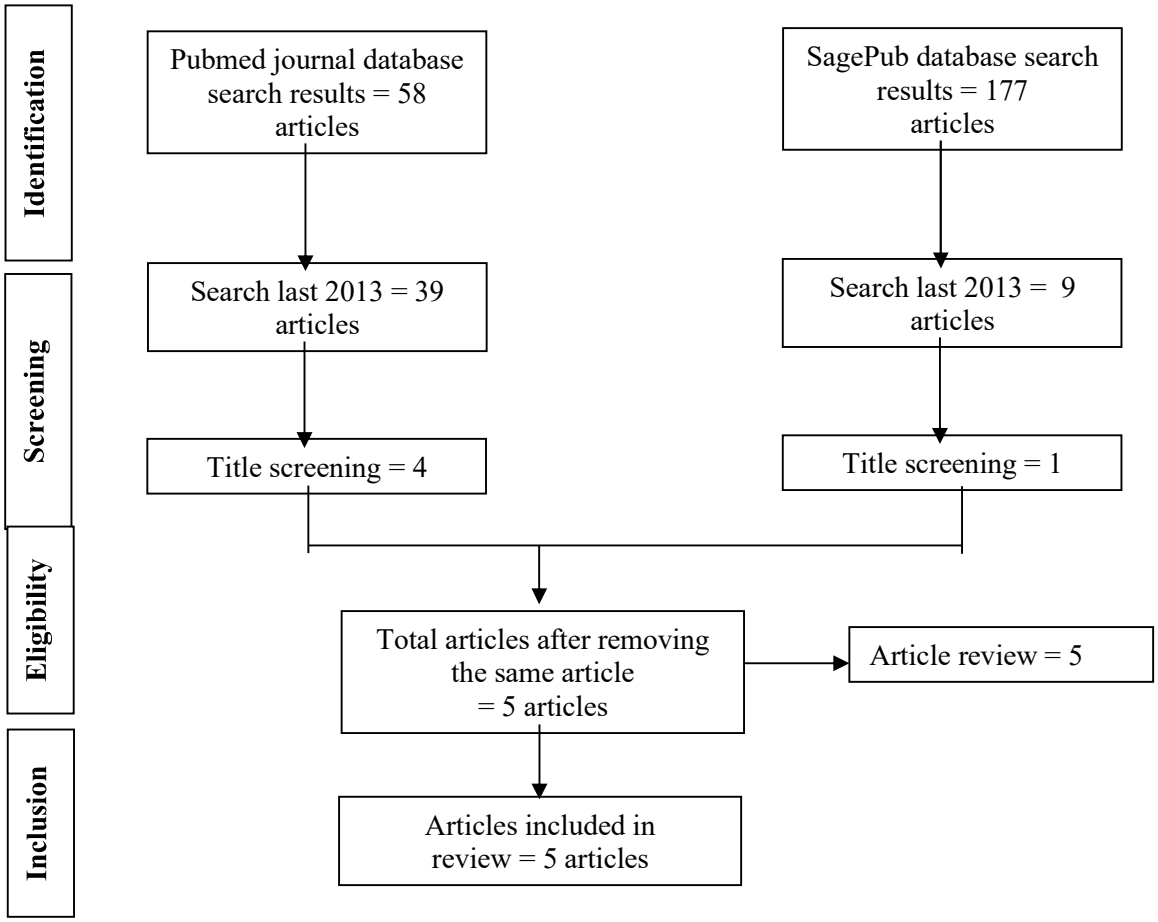

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll

determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 58 articles, whereas the results of our search on SagePub brought up 177 articles. The results of the search conducted for the last year of 2013 yielded a total 39 articles for PubMed and 9 articles for SagePub. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.

Stan, et al[5] (2019) showed that the environmental factors associated with the genetic predisposition of the individual can lead to the appearance of chronic autoimmune diseases, among them the inflammatory bowel diseases. Intestinal inflammation is the common symptom of these diseases and is associated with increased production of reactive oxygen and nitrogen species, and induction of oxidative stress. The therapeutic properties of *T. occidentalis* MT were best noted in orally administered medium and high doses, which succeeded in inhibiting the inflammatory process induced by TNBS in the intestine, most probably based on its rich contents of flavonoids and phenolic compounds. These data can contribute to the formulation of therapeutic products based on *T. occidentalis* that could patients who have an inflammatory bowel disease.

Kedia, et al[6] (2017) showed that low dose oral curcumin for 8 wk is not effective in inducing clinical remission or response in patients with mild to moderate UC. A multicenter collaborative trial using newer formulations of curcumin with higher bioavailability and a dose defining study design is required to conclusively answer this research question.

Faghfoori, et al[7] (2014) showed that the consumption of GBF along with routine medication in attenuates the inflammation and appears to be an effective and safe treatment in UC. On the other hand, it can prolong the remission course with an improvement in clinical signs in these patients. The present study was designed as a pilot study and the results may provide a basis for more future clinical trials to obtain the details of molecular and biological anti-inflammatory mechanism of GBF action. Further studies are required to examine the effect of GBF on different inflammatory factors.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Stan et al, 2019[5]	Romania	Randomized controlled trial	100 samples	The characterization of the tincture included common phytochemical screening assays for antioxidant capacity measurement, cell viability assays on Caco-2 colon cells, and in vivo assessment of antioxidant and anti-inflammatory effects by histopathological and ultrastructural analysis of the intestinal mucosa, measurement of reduced glutathione, lipid peroxidation, and gene expression of the inflammation markers (interleukin-6 and tumor necrosis factor-α) in intestine after oral administration to an experimental mouse model of colon inflammation (colitis) developed by intrarectal administration of 2,4,6-trinitrobenzenesulfonic acid (TNBS). This study proved that administration of 25 or 50 mg *T. occidentalis* MT/kg of body weight/day by gavage for 7 days succeeded in inhibiting the inflammatory process

				induced by TNBS in the intestine, most probably because of its rich contents of flavonoids and phenolic compounds. These data could contribute to the formulation of therapeutic products based on *T. occidentalis* that could come to the aid of IBD patients.
Kedia et al, 2017[6]	India	Randomized double blind placebo controlled trial study	300	Of 300 patients with UC, 62 patients (curcumin: 29, placebo: 33) fulfilled the inclusion criteria and were randomized at baseline. Of these, 21 patients did not complete the trial, 41 patients (curcumin: 16, placebo: 25) finally completed 8 wk. There was no significant difference in rates of clinical remission (31.3% *vs* 27.3%, *P* = 0.75), clinical response (20.7% *vs* 36.4%, *P* = 0.18), mucosal healing (34.5% *vs* 30.3%, *P* = 0.72), and treatment failure (25% *vs* 18.5%, *P* = 0.59) between curcumin and placebo at 8 wk.
Faghfoori et al, 2014[7]	Iran	Randomized controlled study	46	The mean serum CRP in the GBF group decreased significantly (P=0.017) compared with the baseline. Although the frequency of clinical signs including the number of episodes diarrhea, degree of visible blood in stool, degree of abdominal pain or cramping, nausea, vomiting, and anorexia decreased in the GBF group but it was statistically significant only in the case of abdominal pain and cramping. However, this reduction was only significant in the case of abdominal pain and cramping (P=0.016)
Prossomariti et al, 2017[8]	Italy	Randomized controlled study	20	Twenty long-standing UC patients in stable clinical remission and with fecal calprotectin (FC) > 150 µg/g were enrolled (T0) and supplemented with EPA-FFA 2 g/daily for 90 days (T3). Endoscopic and histologic disease activities were measured by Mayo and Geboes scores, respectively. HES1, KLF4, STAT3, IL-10 and SOCS3 levels were determined using western blotting and

				qRT-PCR, while phospho-STAT3 levels were assessed by western blotting. Goblet cells were stained by Alcian blue. Microbiota analyses were performed on both fecal and colonic samples. Nineteen patients completed the study; seventeen (89.5%) were compliant. EPA-FFA treatment reduced FC levels at T3. Patients with FC > 150 µg/g at T3 (n = 2) were assumed as non-responders. EPA-FFA improved endoscopic and histological inflammation and induced *IL-10, SOCS3*, HES1 and KLF4 in compliant and responder patients. Importantly, long-term UC-driven microbiota composition was partially redressed by EPA-FFA.
Pedersen et al, 2017[9]	Denmark	Randomised controlled study	89	Eighty-nine patients, 67 (75%) women, median age 40, range 20-70 years were randomised: 44 to LFD group and 45 to ND, from which 78 patients completed the study period and were included in the final analysis (37 LFD and 41 ND). There was a significantly larger proportion of responders in the LFD group (n = 30, 81%) than in the ND group (n = 19, 46%); (OR = 5.30; 95%CI: 1.81-15.55, P < 0.01). At week 6, the LFD group showed a significantly lower median IBS-SSS (median 115; inter-quartile range [IQR] 33-169) than ND group (median 170, IQR 91-288), P = 0.02. Furthermore, the LFD group had a significantly greater increase in SIBDQ (median 60, IQR 51-65) than the ND group (median 50, IQR 39-60), P < 0.01.

Prossomariti, et al[8] (2017) showed that long-term UC-driven microbiota composition was partially redressed by EPA-FFA. In conclusion, EPA-FFA supplementation reduced mucosal inflammation, promoted goblet cells differentiation and modulated intestinal microbiota composition in long-standing UC patients.

Pedersen, et al[9] (2017) showed that LFD intervention has a beneficial effect among IBD patients in remission with IBS-like symptoms, as the results from this study show amelioration of symptoms and improvement in the quality of life. Based on these results a dietician-assisted LFD could be recommended in the short-term for IBD patients in remission who are experiencing IBS-like symptoms.

DISCUSSION

This systematic review involved a total of 555 patients who received combined heart surgery and lung tumor resection in 6 observational studies. Inflammatory bowel disease (IBD) is a life-long problem around the world. It has been defined by the Center of Disease Control (CDC) as chronic inflammation of the gastrointestinal tract, and includes Crohn's disease and ulcerative colitis/ IBD has been grossly divided into two subtypes—ulcerative colitis (UC) and Crohn's disease (CD). While the disease presents similar clinical features in both subtypes, there are some differing characteristics which are essential for proper treatment. Yangyang and Rodriguez have listed the following symptoms: diarrhea, constipation, pain or rectal bleeding, bowel movement urgency, tenesmus, abdominal cramping, and nausea or vomiting.[10]

Probiotics are a very common topic of discussion among today's health professionals. Often, they are prescribed at the same time as antibiotics to ensure replacement of intestinal microflora after ingesting somewhat harmful, but necessary antibiotics. However, there has been some recent interest in probiotics for the improvement of IBD symptoms and to alter the course of the disease. Probiotics are, generally, defined as food ingredients made from live bacteria that, when ingested in proper amounts, they change the microflora and lead to a health benefit for the host. IBD patients suffer from a loss of intestinal flora which may affect the course of the disease.[11]

Polyphenols are natural occurring nutrients found in plant-based substances. They are largely found in fruit, vegetables, cereal, coffee and red wine. They act as antioxidants, preserving cells and body chemicals against any damage that may be caused by free radicals, reactive atoms that may cause harm to the tissues in the body. They are considered a protective method for the body. Polyphenols are known to be the most abundant antioxidant in the human diet, they are consumed, "10 times more than vitamin C and 100 times more than vitamin E and carotenoids". Polyphenols are ingested by an average of 900 mg/day.[12]

The Codex Alimentarius Commission has defined fibers as "carbohydrate polymers with ten or more monomeric units, which are not hydrolyzed by the endogenous enzymes in the small intestines of humans and belong to subsequent categories". The influence of fibers in the etiology of CD and UC are poorly understood. Low residue diets may be recommended in those patients with active forms of disease, but in inactive patients, dietary fiber is seldom considered due to individual differences in dietary tolerances. Health effects vary among the various types of fibers, but may include reducing diarrhea/constipation, producing short-chain fatty acids, down-regulating inflammation, and promoting tissue healing. These effects all play a role in the prevention of colorectal cancer onset in susceptible IBD patients.[13]

Omega 3 and Omega 6 fatty acids are very important substances in human diet; however, there seems to be some discrepancy between their consumption. Linoleic acid has been consumed in higher amounts since the last century, which has been tied to some increase in the prevalence of CD and UC. On the other hand, higher amounts of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) is considered helpful. They have shown to replace arachidonic acid and inhibit pro-inflammatory mediator production, being indispensable to resolving inflammation processes. These acids are directly related to improved blood lipid levels and attenuation of inflammation processes seen in inflammatory diseases. The anti-inflammatory actions may be associates with their ability or change cell composition of the cell membrane, which in turn, alleviates symptoms and discomfort related to IBD.[14]

As IBD has become a more prevalent problem in the Western world, many scientists have been studying various diets to potentially find a way to ease patient's lifestyle and progression of disease. Many substances have been advised against by physicians worldwide, such as coffee, spicy foods, alcohols as they have been noted to worsen patient's condition and decrease comfort. With this being said, there are some substances that have been noted to ameliorate the quality of life in IBD patients by reducing their IBS-like symptoms. It is estimated that more than 30% of patients with IBD have concomitant IBS and that functional gastrointestinal symptoms are observed approximately 3 times more frequently in patients with IBD compared to the general population.[15]

CONCLUSION

Many patients reached some remission, and those that did not, did not have any worsening progression of disease. This suggests that in the worst-case scenario, there is no negative effect after implementing these substances into the diet. However, that being said, there is a need for further studies to gauge the right amount of each substance to generate the highest yielding results. Implementing fibers, polyphenols, and fatty acids, as well as keeping a low-saccharide diet for those patients with CD and UC can improve quality of life and invoke clinical remission. Some polyphenols, specifically curcumin and resveratrol, have proved to decrease disease activity in studies reviewed. This may also be a cheaper option to some of the current therapies on the market, or may also be used in conjunction with therapies to help with symptoms and clinical remission. Regardless of the substance, diets and implementation of these substances should be done with the guidance of a dietician or doctor familiar with the effects. This will also allow for the proper dosage to achieve optimal treatment results.

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