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Sodium Butyrate in The Treatment of Irritable Bowel Syndrome - Literature Review

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Abstract

Purpose of the research:

The purpose of this study is to present current knowledge on the use of sodium butyrate in the treatment of irritable bowel syndrome (IBS), with a particular focus on its effects on the microbiota and intestinal barrier.

Material and Methods:
The study is based on a review of the scientific literature, including clinical and experimental studies on the effects of sodium butyrate on the gastrointestinal tract.
Results:
Sodium butyrate strengthens the intestinal barrier, exhibits anti-inflammatory effects and influences the microbiota. Clinical studies confirm that its supplementation reduces abdominal pain, improves bowel rhythm and reduces bloating in IBS patients, resulting in a better quality of life.
Conclusions:
Sodium butyrate has the potential to be an effective support for IBS therapy, but further research is needed to determine its long-term safety and optimal dosage. In addition, changes in faecal levels of short-chain fatty acids (SCFAs) may act as a potential biomarker for IBS, but extra studies are needed to confirm their diagnostic value and define accurate reference levels.

Keywords: sodium butyrate; irritable bowel syndrome; butyric acid; SCFAs

Introduction

In the past few years, sodium butyrate has gained popularity as a supplement to help treat various gastrointestinal disorders. A growing number of studies indicate its potential benefits in alleviating symptoms of irritable bowel syndrome (IBS), inflammatory bowel disease (IBD) as well as many other health conditions. As a result, more and more studies are emerging on the effectiveness of butyrate supplementation in specific groups of patients. On the internet, there are guides comparing various supplements containing this chemical compound, as well as articles regarding the correct use of butyrate.

Butyric acid is one of the three short-chain fatty acids (SCFAs) which are physiologically produced in the intestines. Despite the fact that butyric acid content is the lowest among SCFAs - 15%, it has a number of functions in the human body [1].

Among the roles that butyric acid plays include modulation of visceral sensation, anti-inflammatory effects, strengthening of the intestinal barrier and effects on colonocyte proliferation [2]. Decreased levels of sodium butyrate are not a direct cause of IBS, but may play a role in its pathogenesis, affecting the weakening of the intestinal barrier and the occurrence of inflammation. The disease itself, meanwhile, leads to a disturbed microbiota and reduced SCFA production, which can exacerbate symptoms.

This study explores the mechanisms of action of butyric acid, its impact on the intestinal microbiota, and the potential therapeutic benefits observed in clinical and experimental research. The aim of this study is to analyze the role of butyric acid in IBS treatment based on existing scientific literature.

Material and Methods

An extensive literature review was conducted using Google Scholar, PubMed and Scopus to assess the potential benefits of sodium butyrate in the treatment of irritable bowel syndrome. The research focused on human studies and included a range of sources, including meta-analyses observational studies and randomised controlled trials.

Keywords such as ‘sodium butyrate’, ‘irritable bowel syndrome’, ‘IBS’, ‘butyric acid’ and ‘SCFA’ targeted the search process. The collected studies were analysed on the basis of their results related to efficacy, safety, impact on symptoms and improvement in patients' quality of life.

Sodium butyrate - basic information

Sodium butyrate is the salt of butyric acid, a member of the short-chain fatty acid (SCFA) group. Butyric acid plays a crucial role in maintaining intestinal health, being the main source of energy for intestinal epithelial cells. Due to its low stability and unpleasant smell, the supplement has been replaced by a sodium salt formula [3, 4].

In the large intestine, butyric acid is produced by the gut microbiota through the fermentation of nutrients that have not been digested in the small intestine [5]. These include compounds such as resistant starch, lactose, oligofructose, inulin, insoluble dietary fibre fractions and sugar alcohols such as mannitol and sorbitol. The total concentration of SCFAs in the intestines ranges from 60 to 150 mmol/kg [1]. There are many strains of bacteria that naturally colonize the intestines and ferment sugars, including Eubacterium spp., Fusobacterium spp., Clostridium spp., Butyrivibrio spp., Megasphaera elsdenii, Mitsuokella multiacida and Faecalibacterium prausnitzii [6, 7]. The main SCFAs are acetate, propionate and butyrate; their production depends on the diet, the site of fermentation and the composition of the intestinal microbiota [8]. Another way SCFAs are formed is through a mechanism called 'cross-feeding,' which is a process in the gut microbiome in which bacteria use each other's metabolites to produce short-chain fatty acids [7].

Butyric acid has a number of functions in the human body. This compound is the primary source of energy for colon epithelial cells and stimulates their growth and differentiation [9]. Butyrate strengthens the integrity of the intestinal barrier by maintaining proper tight junctions, expressing mucin-2 and influencing the reduction of intestinal leakage
[10]. As a result, it effectively protects the body against the infiltration of pathogens and reduces the risk of inflammatory reactions. Butyrate also exhibits anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines (TNF-α, IL-1b, IL-6, IL-8) and stimulating the expression of anti-inflammatory cytokines such as IL-10 [10, 11, 12]. Receptors for the SCFA in question are found in almost all GALT (gut-associated lymphoid tissue) immune cells, indicating that this substance has immunoregulatory functions. An example of such a function is, for example, promoting the differentiation of regulatory T cells. Butyric acid also plays an important role in preventing carcinogenesis by inhibiting histone deacetylase (HDAC) activity. This promotes chromatin loosening and thus allows activation of genes that regulate proliferation and apoptosis [13]. This is particularly important in the context of colorectal cancer, since butyric acid can affect the proliferation of normal colonocytes and inhibit the division or induce apoptosis of abnormal colon cells with malignant potential [9]. In addition, SCFAs affect the regulation of gastrointestinal motility, the gut-brain axis and intestinal pH, which promotes the development of beneficial microflora [13].

Consumption of foods rich in dietary fiber and resistant starch promotes the natural production of butyric acid. These products include cow's milk and its products (especially hard cheeses, such as Parmesan), goat's and sheep's milk, pickled vegetables (cabbage, cucumbers) and fermented soy products. However, butyrate supplied from the diet is broken down before reaching the large intestine, which limits its effectiveness [14]. The sodium butyrate molecule is prone to rapid degradation, and the residue is immediately consumed upon release.
In order to increase the bioavailability of butyrate, microencapsulation technology was developed to lock the active ingredient into lipid microgranules. This makes it possible to delivery of butyrate to the large intestine - the site of its intended action. The encapsulation of the microgranules in a gel capsule further protects them from digestion in the stomach and eliminates the unpleasant odor of butyric acid [4].

Irritable bowel syndrome - characteristics and role of sodium butyrate in therapy

Irritable bowel syndrome (IBS) is a chronic disorder of gut-brain interaction, characterized by recurrent abdominal pain, changes in bowel movements (diarrhea, constipation or their alternation) and abdominal discomfort, in the absence of obvious structural changes detected by diagnostic tests [15]. The condition affects people worldwide, regardless of gender and age, although women and younger people are more often affected [16, 17, 18]. Educated, wealthy people and students are a particularly vulnerable group [19]. The prevalence of IBS is put at 4.1-15% of the global population [15, 16, 20, 21]. As can be seen, it is difficult to determine the exact prevalence of this syndrome due to the lack of a universally accepted accepted biomarker specific for IBS. Irritable bowel syndrome is a disorder that significantly worsens patients' quality of life and makes daily functioning difficult. Persistent symptoms can cause reduced productivity at work, frequent absences from work/school/social gatherings.
To diagnose IBS, the Rome IV Criteria are used, according to which the following are necessary to diagnose the disease: the presence of recurrent abdominal pain, which occurs on average min. 1 day per week (in the last 3 months) and is associated with at least two of the following: 1) defecation 2) change in frequency of bowel movements or 3) change in appearance of stools [11]. Symptoms should first occur at least 6 months before diagnosis [15]. There are 4 subtypes (Table 1) of irritable bowel syndrome which include: diarrheal form (IBS-D), constipation form (IBS-C), mixed form (IBS-M) and unclassified form (IBS-U) [22]. The Bristol Stool Form Scale (BSFS) is recommended to assess a patient's bowel movements. Importantly, the disease subtype should be checked routinely, as more than half of IBS patients develop a change in disease subtype within a year [15].

Table 1 Definitions of IBS subtypes according to Rome IV criteria

IBS subtype	Definition regarding bowel movements
IBS-C	≥25% of bowel movements associated with BSFS 1 or 2 with BSFS 6 or 7 occurring in less than 25%
IBS-D	≥25% of bowel movements associated with BSFS 6 or 7 with less than 25% of bowel movements with BSFS 1 or 2
IBS-M	≥25% of bowel movements associated with BSFS 1 or 2 and ≥25% of bowel movements associated with BSFS 6 or 7
IBS-U	can't be determined

The pathogenesis of IBS is multifactorial and results from the interaction of multiple abnormalities, including abnormal intestinal motility, visceral hypersensitivity, disregulation of the gut-brain axis, increased permeability of the intestinal barrier and altered mucosal immune function. These disorders are associated with intestinal dysbiosis, that is, qualitative and quantitative changes in the microflora (including a reduction in beneficial bacteria, such as Lactobacillus and Bifidobacterium, and an increase in potentially pathogenic microorganisms) [16, 23, 12]. In addition, dysregulation of the hypothalamic-pituitary-adrenal axis and neuroendocrine changes, often induced by stress, contribute to increased visceral sensitivity, resulting in abdominal pain and gastrointestinal motility disorders [11]. As a result, the interplay of these mechanisms leads to the appearance of the characteristic symptoms of IBS. It is also worth mentioning that psychiatric disorders and psychosocial factors influence the course of the disease and treatment psychosocial factors [11].

Studies show that patients with IBS experience significant changes in the composition of the intestinal microbiota. Analyses of fecal samples reveal a decrease in the number of bacteria from the genera of Bifidobacterium, Lactobacillus and Faecalibacterium prausnitzi - a key producer of butyric acid - while the proportion of bacteria belonging to the Firmicutes group increases [23]. In particular IBS-D and IBS-M patients showed a significant reduction in the number of butyrate-producing bacteria, which may affect intestinal function. In addition, a reduced abundance of methane-producing bacteria has been observed, which may contribute to increased local oxygen reserves and increased bloating [24, 25]. Modern sequencing techniques have also revealed subtle microscopic and molecular changes in the intestinal mucosa that were previously undetectable by standard histology [11].

Given the deficiency of butyrate found in IBS patients, the use of a microencapsulated preparation that allows precise delivery of this substance to the distal portions of the intestine was considered a promising therapeutic strategy [26].

A study by Lewandowski et al. evaluated the efficacy of microencapsulated sodium butyrate in the treatment of IBS. In 2990 patients, significant relief of abdominal pain, bloating, diarrhea and constipation, as well as improvement in quality of life ($p < 0.001$), as assessed by a 0-10 scale in terms of occupational, social and daily functioning, were found after 12 weeks of 300mg/d therapy. 93.9% of participants said they wanted to continue treatment [3].
A randomized, double-blind, placebo-controlled study described by Banasiewicz et al. showed that supplementation with microencapsulated sodium butyrate significantly reduced the frequency of pain during bowel movements and improved defecation rhythm after 12 weeks of therapy [26]. However, there was no significant effect on the overall severity of abdominal pain and bloating. The results suggest that sodium butyrate may be an effective adjunct to standard IBS treatment.
Tarnowski et al. conducted a study evaluating the effect of sodium butyrate supplementation on irritable bowel syndrome symptoms [27]. In the randomized trial, patients received 300 mg of sodium butyrate daily for 6 weeks in addition to standard therapy (trimebutynin or mebverine). At the end of the study, the group receiving sodium butyrate had a significant reduction in the severity of abdominal pain, an improvement in bowel movements and a reduction in bloating compared to the control group. In addition, patients supplementing with sodium butyrate showed a significant improvement in quality of life, as assessed by the IBS-QoL scale, suggesting a beneficial effect of this therapy on daily functioning.

Conclusions

Sodium butyrate plays a key role in maintaining intestinal homeostasis by supporting the intestinal barrier, exhibiting anti-inflammatory effects and modulating the microbiota. Its deficiency may contribute to gastrointestinal disorders, including irritable bowel syndrome, which justifies the growing interest in its supplementation as a potential therapeutic support. A review of clinical studies indicates that supplementation with microencapsulated sodium butyrate may benefit IBS patients by reducing the frequency of pain with bowel movements, improving defecation rhythm and reducing bloating. These benefits were observed after both short-term (6 weeks) and long-term (12 weeks) therapy, resulting in improved quality of life for patients [3, 28, 27].
Although the results of the study are optimistic, further studies are needed to precisely determine the mechanisms of action of sodium butyrate in different subtypes of IBS. Butyric acid in high concentrations, like other SCFAs, may increase visceral sensitivity and affect intestinal motility [28]. Therefore, further research is also needed on the optimal dosage and long-term safety of its use in different patient groups.
A study described in 2019 by Sun Q et al. indicates that changes in fecal short-chain fatty acid (SCFA) levels may be a potential biomarker of IBS [29, 30, 31]. They found lower levels of propionate and butyrate in IBS-C patients and elevated levels of butyrate in IBS-D, which may reflect a disruption of the gut microbiota [29]. Although these results suggest potential diagnostic value, further studies are needed to confirm them and establish a precise reference thresholds.

Disclosure
Author's contribution:
Conceptualization, Joanna Lara, and Martyna Grabowska;
Methodology, Wiktoria Kosucka;
Software, Dominik Balik;
Check, Jakub Dąbek, Aleksandra Wiśniewska and Joanna Lara;
Formal analysis, Jagoda Kubicka;
Investigation, Dominik Balik;
Resources, Anna Kwaśniewska;
Data curation, Wiktoria Kosucka;
Writing - rough preparation, Martyna Grabowska;
Writing - review and editing, Karolina Grabowska;
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