Immunology and Infections

REVIEW ARTICLE

Role of Butyric Acid in Food and Intestinal Health

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Abstract

Butyric acid is a short chain fatty acid that contains 6 carbon atoms. It is found naturally in the digestive tract and its use in pathologies with intestinal involvement. It is the main energy substrate of the enterocyte and stimulates the absorption of sodium and water in the colon and presents trophic action in the intestinal cells. Its properties and the role it plays in the gastrointestinal tract have been known since ancient times; however, recent research shows that it remains a molecule with great potential.

Key words: Butyric Acid, Short Chain Fatty Acids, Intestinal Health

Introduction

Butyric acid is a short-chain fatty acid that contains six carbon atoms. It is found naturally in the digestive tract and highlights its use in pathologies with intestinal involvement. The butyric acid is the main energetic substrate of the colonocyte and stimulates the absorption of sodium and water in the colon and presents trophic action in the intestinal cells. In addition, they modulate the immune response in the intestine [1-10].

Figure 1 shows the chemical formula of butyric acid.

The properties of butyric acid, and the role it plays in the gastrointestinal tract, have been known for many years. However, recent research shows that it still presents a potential [11-29].

It is present in some fats in small amounts, such as butter, and is the final product of the fermentation of carbohydrates by the microorganisms of the intestine. The concentration in butter increases as it becomes rancid, and also gives it its characteristic odor when combined with other elements to form butyrine [1-3, 15, 25].

It is believed that butyric acid has a beneficial role in the gastrointestinal tract. Butyric anion is easily absorbed by enteric cells and is used as the main source of energy. It is also an important regulator of the proliferation and apoptosis of colonocytes, the motility of the gastrointestinal tract and the composition of the bacterial microflora, in addition to its involvement in many other processes, including immunoregulatory and anti-inflammatory activity [19-27].

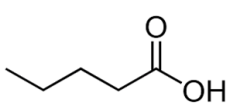

Figure 1: Chemical formula of butyric acid.

Crohn's Disease [CD] and Ulcerative Colitis [UC] appear to derive from a reaction to a luminal agent, driven by the intestinal microflora, which positively regulates the synthesis and release of different proinflammatory mediators, thus contributing to tissue damage characterizes these intestinal conditions [5-11].

Table 1 summarizes the main and different actions, in addition to the effects in which the butyric acid participates.

Role of Butyric Acid in Health

Butyrate is absorbed by the epithelial cells and by oxidation, facilitates the formation of ATP which is the main source

- Energy for the colonocytes
- Inflammation and oxidative status
- Synthesis of mucus
- Production of cytokines
- Control of pathogens
- Intestinal motility
- Absorption of nutrients
- Regulation of apoptosis
- Proliferation, differentiation and cell maturation
- Control of the intestinal barrier effect

Table 1: Different actions in which butyric acid is involved [1, 15, 23].

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Received: Sep 10, 2018; **Accepted:** Sep 27, 2018; **Published:** Oct 01, 2018

of energy for cellular functions. This energy is used by the sodium-potassium pump, responsible for maintaining the osmotic balance in the intestine allowing the absorption of water in the intestine [1, 15, and 27].

Butyrate also promotes intestinal health against different bacterial agents and restores the balance of the intestinal microbiota when it is altered by the use of antibiotics [30, 31].

The loss of oxygen causes the intestinal epithelium to become hypoxic, and the intestinal lumen becomes more anaerobic, which favors the establishment of anaerobic bacteria, Clostridium saprophytes, responsible for the production of endogenous butyrate. *S. typhimurium* infections produce a reduction in *Clostridium* saprophytes, and have an important role in controlling the proliferation of *E. coli* and maintaining the balance in the intestinal microbiota [2, 15].

While, on the contrary, an increase of oxygen in the intestinal light, favors the growth of aerobic bacteria, such as Salmonella and other intestinal pathogens that when proliferating increase the risk of disease, excretion to the environment and transmission to other animals.

The possibility of supplementing the endogenous levels of butyrate may be a way to limit the effects of an enteric infection by Salmonella, since it favors the bacteria, through the use of probiotics and prebiotics or the direct supply of SCFA through the use of protected or esterified acids [3, 26, 27, 29, and 32].

The forms of butyric acid supplementation in animal nutrition are based: In the form of sodium and calcium salts. In the form of protected salts, involving the active principle, salts of butyric acid in fats. And as esters of butyric acid, up to 3 molecules of butyric acid can be bound in each glycerol, forming the tributaries [15, 33, and 31].

In order for the supplemented butyric to reach the intestine, it must be protected against different manufacturing processes and also in the first part of the digestive tract, to prevent it from being released before reaching the intestine, since its availability would be reduced [15, 19]. Protected butyric acid salts are used as protection to overcome the gastric acidity of the stomach, but 70% of the weight of the product is compromised, limiting the amount of butyrate provided. While esterified forms, tributyrin supplies butyric acid in a concentrated, efficient and direct form [26, 34, and 31].

Therefore, tributyrins, are formed by butyric acid esterified with glycerol and the covalent bonds that bind them resist the processes of manufacture of feed and gastric digestion, which ultimately break by the action of pancreatic lipase, releasing the acid butyric in the intestine [15, 31].

Butyrate exerts potent effects on a variety of functions of the colonic mucosa, such as the inhibition of inflammation and carcinogenesis, reinforcing several components of the colon defense barrier and decreasing oxidative stress. In addition, butyrate can promote satiety [1, 21, 26, and 35-33].

Two important mechanisms have also been found, including the inhibition of nuclear factor kappa B activation and histone deacetylation. However, the observed effects of butyrate depend to a large extent on the concentrations and models used, since human studies are still limited [12, 27, 29, and 35].

Several studies have reported that Inflammatory Bowel Disease [IBD] is associated with the deterioration in the production of short chain fatty acids [SCFA], mainly acetate, propionate and butyrate. These are produced in the large intestine by the anaerobic bacterial fermentation of undigested carbohydrates and fiber polysaccharides, considering butyrate as the main fuel source for the colonocytes. It has been proposed that these SCFAs play a key role in the maintenance of colonic homeostasis. [30, 31].

The production and absorption of SCFA is closely related to the nutrition of the colonic mucosa, its production from dietary carbohydrates is a mechanism by which considerable amounts of calories can be produced in patients with short bowel with remaining colonic function and are maintained in an appropriate dietary regime. SCFA enemas or oral probiotics are novel and promising treatments for ulcerative colitis [3, 15, 21, 27, and 32].

Dietary fibers are nondigestible food ingredients that reach the colon and are then fermented by colonic bacteria, leading to the formation of SCFA such as acetate, propionate and butyrate. These SCFAs, especially butyrate, are recognized for their potential to act on secondary chemoprevention by slowing growth and activating apoptosis in colon cancer cells. In addition, SCFA can also act in primary prevention by activating different drug metabolizing enzymes. This can reduce the burden of carcinogens and, therefore, decrease the number of mutations, reducing the risk of cancer [17-19, 23].

It has been observed that butyrate has had differential effects on colon cells at different stages of cancer development. The functional consequences of this activation include a reduction in DNA damage caused by carcinogens such as hydrogen peroxide or 4-hydroxynonenal [HNE], in colon cells treated with butyrate [2, 20, 32, and 34].

In addition, more studies in animals and humans are also needed to define the exact role of dietary fiber and butyrate in the induction of Glutathione S Transferase [GST] activity and the reduction of the risk of colon cancer [1, 15, 2, and 3]. The effects have been attributed to the oxidation of SCFA in the colonocytes and to the ability of the butyrate to induce enzymes, such as transglutaminase, that promote the restitution of the mucosa. This evidence is increasing with respect to the effects of butyrate on several cellular functions whose importance requires further investigation [1, 27, and 29].

In recent years, the interest in short-chain fatty acids [SCFA] has been revived with the appearance of prebiotics and probiotics aimed at improving gastrointestinal health [3, 27, and 32]. Dietary carbohydrates, specifically resistant starches and dietary fiber, are substrates for fermentation that produce SCFA, mainly acetate, propionate and butyrate, as end products. The speed and amount of production of SCFA depend on the species, the amounts of micro flora present

in the colon, the source of the substrate and the intestinal transit time. SCFA is easily absorbed and butyrate is the main source of energy for the colonocyte. The liver also absorbs a large amount of propionate. The acetate enters the peripheral circulation to be metabolized by the peripheral tissues. Specific SCFA can reduce the risk of developing gastrointestinal disorders, cancer and cardiovascular diseases. Acetate is the main SCFA in the colon, and after absorption it has been shown to increase cholesterol synthesis. However, it has been shown that propionate is a gluconeogenerator, since it inhibits the synthesis of cholesterol. Therefore, substrates that can decrease the acetate/propionate ratio can reduce serum lipids and possibly the risk of cardiovascular disease [1-3, 15].

Butyrate has also been studied for the role it plays in the nutrition of the colonic mucosa and in the prevention of colon cancer, promoting cell differentiation, the arrest of the cell cycle and the apoptosis of transformed colonocyte; inhibit the enzyme histone deacetylase and decrease the transformation of primary bile acids to secondary as a result of colonic acidification. Therefore, a greater increase in the production of SCFA and potentially a greater administration of SCFA, specifically from the butyrate to the distal colon, may result in a protective effect. Irrigation with butyrate, in the form of an enema, has also been suggested in the treatment of colitis. Although more studies are needed, especially given the diverse nature of the carbohydrate substrates and the SCFA patterns resulting from their fermentation. In particular, more short-term and long-term human studies on SCFA are required in relation to cancer risk markers. These will be key to the success of dietary recommendations and to maximizing the prevention of colonic disease [35, 33].

There is different information on the effectiveness of dietary fiber in the different tests carried out and designed. In the different studies, we are trying to clarify and justify the available evidence for the use of dietary fiber and its mechanisms of action in the treatment and prevention of IID [12, 13, 15, and 17].

Table 2 shows and summarizes the different intestinal pathologies in which SCFAs have been studied, especially butyric acid.

The direct quantitative determination of SCFA in the laboratory, including butyric acid, is done by gas chromatography with flame ionization detector, although there are different methodological modifications of these applications [36-38].

- Constipation
- Diarrhea
- Traveler's diarrhea
- Diarrhea associated with antibiotics
- Irritable bowel syndrome (IBS)
- Intestinal bowel disease
- Ulcerative colitis (UC)
- Crohn's disease (CD)
- Colon cancer

Table 2: Different pathologies in which butyric acid and SCFA have been studied [5-12].

Conclusions

Short chain fatty acids [SCFA], especially butyrate, play a central metabolic role in maintaining the mucosal barrier in the intestine. The lack of SCFA leads to endogenous deprivation of enterocytes and may be the cause of ulcerative colitis [UC] and other inflammatory conditions [5-11].

The main source of SCFA is dietary fiber, but it can also be derived from structured lipids such as tributyrin. Once absorbed by the non-ionic diffusion or exchanges of anions mediated by the carrier, the SCFAs are used locally as fuel for the enterocytes or enter the portal bloodstream. It has also been shown that butyrate also promotes wound healing and reduces inflammation in the small intestine [15, 22, 27, 28].

In the colon, butyrate is the dominant energy source for epithelial cells and affects cell proliferation and differentiation by mechanisms that have not yet been well elucidated. Recent studies suggest that luminal provision of butyrate may be an appropriate means to improve wound healing in intestinal surgery and to improve the symptoms of inflammatory bowel diseases [28, 33].

The use of oral supplements with butyric acid is a novel and promising strategy in diseases such as inflammatory bowel diseases and IBS. Numerous advances have been made in the different bioactive formulations of butyric acid that have acceptable organoleptic characteristics, such as tributyrins [2, 5, 8, 11, and 35].

Therefore, it is reasonable to consider new therapeutic approaches that increase the production of colonic SCFA, since this can be achieved by administering dietary fiber to patients with intestinal bowel disease [9, 30-34].

Conflict of Interests

The authors declare no conflict of interest.

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Citation: Miguela AS, Salgado MT, Rodrígueza MSM, Pachónb J, Martín MAS, et al. (2018) Role of Butyric Acid in Food and Intestinal Health. Immunol Infect 1: 001-005.