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Polyols - What do we know about their impact on the gut microbiome?

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Summary:
Introduction and purpose:
Even though sweeteners' popularity is increasing as they are approved by the Food and Drug Administration (FDA) and generally considered to be safe, their whole impact on the human body is still confusing. Polyols are among one of the most used sweeteners, therefore in this review we will focus on their impact on the gut microbiome as this community of various bacteria influences many aspects of overall health.
Brief description of the state of knowledge:
The current conclusions mostly present prebiotic benefits of polyols and their ability to increase the number of Bifidobacteria, there is research supporting the evidence of it conducted on isomalt, maltitol, lactitol and xylitol. It is possible, as most of them are able to reach the colon. We also investigate other ways sweeteners are shaping the gut microbiome such as multiplication of short chain fatty acids (SCFAs) or decreasing the numbers of Clostridium difficile.
Conclusions:
The impact of polyols on the gut microbiome has many knowledge gaps. More long-term studies are needed in order to consider the individual diversity of the participants' gut microbiota. In order to conduct more valuable conclusions dietary and lifestyle habits should be taken into consideration. All things considered, there is not enough data to clearly determine polyols' role in modifying the gut microbiota.
Key words: sweeteners; polyols; microbiota

1.Introduction

The increased prevalence of obesity and its metabolic comorbidities have led to a growing consumption of sugar-free products, where sugars are replaced by low-calorie sweeteners [1]. Because they can affect body weight, glucose tolerance, appetite and taste sensitivity, they are consumed both by people with diabetes and the general population [2]. They are added to a wide variety of food, drinks, drugs and hygiene products, thus it can be assumed that each of us uses artificial sweeteners knowingly or not [3]. Although they are commonly accepted and considered safe and well tolerated, their impact on the composition of the gut microbiota is still unclear and controversial [4]. Sweeteners can be classified by their origin being either natural or synthetic. An important part of natural sweeteners are sugar alcohols, the so-called polyols [5]. Because of the poor absorption of the majority of polyols in a small intestinal, the main part of them reaches the colon and is fermented by the microbiome, which plays a significant role in human health and disease. It may affect metabolism, immunity, growth and fermentation of undigested carbohydrates. Diet can rapidly modulate and alter the composition and function of the microbiome [1]. This review critically discusses the evidence supporting the effects of polyols on the intestinal microbiome.

2.State of knowledge

Polyols are a specific group of sugar alcohols that are formed via the catalytic hydrogenation of carbohydrates. They are naturally present in certain fruits, vegetables and fungi and are also added to foods as sweeteners in products such as chewing gum, candies, and beverages [6]. Polyols can be considered a better alternative to other sweeteners, because they provide fewer calories per gram while also not increasing blood glucose response [5,7]. The interest in polyols arises also because of their low-insulinemic, low-digestible and osmotic qualities [8].They are also non cariogenic [9]. The Food and Drug Administration (FDA) has currently approved the use of eight different polyols, which include erythritol, hydrogenated starch hydrolysates, isomalt, lactitol, maltitol, mannitol, sorbitol and xylitol [6]. Despite many advantages, they have also been shown to spark gastrointestinal symptoms and exert an influence on laxative effects when consumed in excess [10].

2.1 Maltitol

Maltitol (E-965) is a sweetener reached by the hydrolysis, reduction and hydrogenation of starch. Its sweetness resembles the flavor of sugar in 90% and for this reason it is the sugar of choice for use in the production of no-sugar-added–labeled chocolate [11]. Maltitol is fermented in the colon and is characterized by the very slow digestion rate [12]. Therefore, it is expected that it could be fermented by the gut microbiota.

Studies on the impact of maltitol on the human microbiome are limited and further research is needed to determine its role [9]. However, current conclusions highlight prebiotic benefits of maltitol usage.

For example, in a human study 40 volunteers were divided into three groups and obtained to eat either a chocolate containing 22.8 g of maltitol or one with maltitol and polydextrose or chocolate enriched with maltitol and starch for 14 consecutive days. After that time the doses of the chocolate were increased twice every 2 weeks over a 6 weeks period. At the end of the study numbers of faecal Bifidobacteria significantly increased in all three groups. Chocolate with addition of polydextrose had a significant impact also on the level of faecal lactobacilli, faecal propionate and butyrate. Consumers tolerated all the chocolates with no significant change in bowel habit or intestinal symptoms even at a highest dose [13].

2.2 Lactitol

Lactitol (E-421) is a disaccharide analogue of lactose usually used in combination with other sweeteners because of its limited sweetness. Lactitol is fermented in the lower gut as it can not be absorbed in the small intestine, because of its lack of the appropriate β-galactosidase [14]. When consumed in higher dosage, for example 74 g a day, this sweetener can cause a laxative effect [15]. Impact of lactitol on the gut microbiota still has not been determined, however current studies mentioned its prebiotic properties.

For example in rats, lactitol caused the rise of the production of butyrate and IgA secretion with no signs of mucosal inflammation [16].

Li et al. studied the effect of lactitol on the gut microbiota in constipated patients. After two weeks protocol they noted a significant decrease in symptoms. Analysis of the faecal flora showed an increase of Actinobacteria, Actinobacteria, Bifidobacteriales, Bifidobacteriaceae and Bifidobacterium. These results showed that lactitol may be considered a good prebiotic option for patients with constipation [17].

Another study by Finney et al. aimed at a group of 75 non-adapted healthy adults showed that low doses, 10 g a day, of lactitol have beneficial effects on the gut microbiota and, as previously mentioned paper also noted an increase of Bifidobacteria [18].

In a study by Ouwehand et al. which was conducted on elderlies consuming a combination of lactitol and Lactobacillus acidophilus NCFM twice a day for fourteen days, showed a significant increase in faecal L. acidophilus NCFM levels. This study also highlighted improvement markers of the intestinal microbiota composition and mucosal function after the treatment [19].

Ballongue et al. examined the effects of lactitol on a group of healthy volunteers. After nine weeks of treatment numbers of bacterial populations of Bacteroides, Clostridium, coliforms, and Eubacterium were decreased. Lactitol also caused a decrease in fecal pH [20].

2.3 Sorbitol

Sorbitol (E-420) is also known as D-glucitol and is obtained by the hydrogenation of glucose with subsequent purification [9]. It may cause osmotic diarrhea if consumed in higher doses (20-50g) [21]. Many symptoms such as abdominal pain, bloating, and diarrhea have been observed in particular in children [22].

Badiga et al. also concluded that many diabetics are intolerant to sorbitol and regular sorbitol consumption may explain the diarrhea for no apparent reason in some diabetics [23]. Those negative effects of sorbitol usage are caused by an osmotic load sorbitol created in the gastrointestinal tract. The tract causes bigger concentration of the water in the colon and results in greater laxative effect when compared to other polyols [9]. However, it is yet to be known why some people react poorly to sorbitol.

Hattori et al. showed that sorbitol induced diarrhea may be contained by the gut microbiome. Escherichia coli made it possible to degrade sorbitol and consequently suppress sorbitol-induced diarrhea [24].

2.4 Xylitol

Xylitol (E-967) is produced by the hydrogenation of D-xylose and is the sweetest of all polyols with sweetness equivalent to sucrose [25]. It is mostly digested in the intestine by bacteria [8]. Only a small part is absorbed by the small intestine and metabolized by the liver [26]. This polyol tends to be well tolerated. Nevertheless, higher doses**,** 50 g a day, have been associated with digestive symptoms such as bloating and diarrhea [27]. Apart from microorganism production it can also be extracted from natural sources such as corn or the bark of birch trees [6].Effects of xylitol on human microbiota are currently not widely researched and lots of studies were conducted on mice.

Uebanso et al. studied the effects of consuming xylitol on gut microbiota in mice. Researchers concluded that moderate doses of xylitol consumption, when added to high-fat diets, caused a decrease in Bacteroidetes proportion and increase in Firmicutes proportion [28].

Moreover, there were studies on mice which showed that xylitol rebalance the gut microbiome in a negative way. Tamura et al. acknowledged that xylitol affects the gut microbiota of mice and a group with a diet not enriched with xylitol have had higher bacteroidetes levels in comparison to the xylitol group [29].

Additionally, Nabeer et al. showed on a hamster model that the combination of lactobacilli and xylitol had some protective effect against Clostridium difficile infection [30].

Studies conducted on mice, rats and men showed that xylitol caused a clear shift in the rodent faecal microbial population from Gram-negative to Gram-positive bacteria. In humans this change was observed after a single 30 g dose [31].

Studies on humans tend to show prebiotic properties of xylitol. For example, Xiang et al. revealed that xylitol consumption increased synthesis of propionate in the colon [32].Similar findings have been published by Sato et al. Researchers evaluated butyrate production in in vitro human faecal cultures. Xylitol turned out to increase butyrate production [33].

2.5 Erythritol

Erythritol (E-968) is a natural sweetener as a four-carbon alcohol with no optical activity [1]. Mass production of erythritol is demanding and differs from production of other polyols [34]. On the industrial scale it is obtained through fermentation of yeasts, where the main primary carbon source that is formed is glucose. The main disadvantage of such a process is the cost of production which makes the products relatively expensive compared to other products made of table sugar. Even though, consumption of erythritol is growing, especially because it has a positive effect on metabolism conditions [35,36]. Erythritol is absorbed in up to 90% in the gastrointestinal tract and excreted in the urine in the same metabolic form [37]. The impact of erythritol on the gut microbiome is ambiguous.

Study shows that erythritol significantly decreases the glucose levels of serum, liver, and kidney in streptozotocin-induced diabetic rats. In addition, erythritol decreases the indicator of oxidative stress as 5-hydroxymethylfurfural [38].

Another study that analyzed the impact of erythritol on mice with metabolic problems show that consumption of erythritol can increase short-chain fatty acids (SCFAs) including those of acetic acid, propanoic acid, and butanoic acid. It also indicates that mice which consumed erythritol had lower body weight, better glucose tolerance and lesser fat deposition in the liver compared to the control group [39]. This shows the potential of erythritol in preventing metabolic diseases.

The study conducted by Mahalak et al. with humans in vitro microbial community did not find any impact on the bacterial growth. Furthermore, none of the negative impact of steviol glycosides and erythritol on the gut microbial community was found. However, the same study shows that butyric and pentanoic acid production can be extended during the test on the human gut microbial community [40].

2.6 Isomalt

Isomalt (E-953) is a mixture of alpha-D-glucopyranosido-1,6-sorbitol (GPS) and alpha-D-glucopyranosido-1,6-mannitol (GPM) made from sucrose. Isomalt is 0.5 – 0.6 times as sweet as sucrose. It is obtained by enzymatic conversion and hydrogenation process. Isomalt, like other polyols, is commonly used in the food industry as a table sugar replacement. Due to the fact that isomalt is stable in high-temperature and does not have any aftertaste, it can be used in bakery products [41]. According to that, only a low level of isomalt is absorbed in a small intestinal and the main part reaches the colon where 90 % is fermented. Due to this fact isomalt might have an impact on the gut microbiota [8,11].

The double-blind, placebo-controlled, cross-over study conducted by Gostner et al. was focused on the effects of isomalt on the intestinal microflora. The nineteen healthy participants consumed 30 g isomalt or 30 g sucrose everyday for four weeks. After that the faecals samples were analyzed. The results showed that consumption of

isomalt causes an increase of Bifidobacteria and decrease of bacterial β-glucosidase in contrast to consumption of sucrose. In this study the author suggested that high butyrate synthesis was correlated with an increase of Bifidobacteria [42]. Therefore, using isomalt as a prebiotic deserves attention [43,44].

2.7 Mannitol

Mannitol (E-421) is one of the most abundant polyols in nature. It can be biosynthesized by diverse organisms like bacteria, yeasts, fungi, algae and lichens [45].This polyol can be used as a sweetener, in pharmaceutical and medicine industries. Its properties are really close to sucrose and it has a desirable cooling effect which is useful in masking bitter tastes [46]. Mannitol is expected to have some benefits as an antioxidant and non-metabolizable sweetener [47]. However, we have no data determining the effects of mannitol intake on the gut microbiota.

2.8 Hydrogenated starch isolates

Hydrogenated starch isolates are made from a connection of polyhydric alcohols such as sorbitol, maltitol and higher-order sugar alcohols [48]. Sometimes they are being listed as a maltitol syrup, hydrogenated glucose syrup, polyglycitol, polyglucitol, or simply HSH [9].They are mainly used as viscosity or bodying agents, humectants, crystallization modifiers and rehydration aids so their impact on the gut microbiome is not the subject of the studies [48].

Conclusions:

WHO in their latest nutrition recommendation advises limitation of monosaccharides to 10%, so the sweeteners can be helpful in order to make a target and therefore attract global attention. Besides low caloric of sweeteners, we can also expect other health benefits as the majority of polyols are absorbed partly in a small intestinal, so that most of them reach the colon and are fermented by microbiome. In this way, a certain amount of polyols stimulate the growth of bacteria. If a compound induces the growth of beneficial microorganisms as Bifidobacteria, it is called a prebiotic. Some studies show that polyols like isomalt, maltitol, xylitol and lactitol may cause such action, resulting in being considered as a prebiotic.Additionally, a diet with some polyols may increase the SCFAs. For example, erythritol has a positive impact on the production of acetic, propanoic and butanoic acids. Also, diet with maltitol and polydextrose has a significant impact not only on the level of faecal propionate and butyrate acids, but on faecal lactobacilli as well.

On the other hand, the effect of polyols is not limited to increasing the number of specific bacteria in the microbiota, but also reducing the amount of some pathogenic bacterias.The study on a group of healthy volunteers showed that the consumption of lactitol decreased the numbers of Clostridium. Similar effect as protective against Clostridium Difficile was observed using lactobacilli and xylitol in study on a hamster model. Some other authors also describe not only a lower number of Clostridium, but also Bacteroides, coliforms and Eubacterium after a lactitol treatment. Therefore, lactitol and xylitol may have a positive effect in chronic disease caused by Clostridium.

Based on the literature review, our knowledge about the impact of polyols on gut microbiome is still unclear. Thus, we have no data determining the effects of mannitol, sorbitol and hydrogenated starch isolates intake on the gut microbiota. Because of many variables that may change the composition of the gut microbiome, such as place to live, age, lifestyle or even different types of child delivery it is difficult to form or conduct studies with repeatable results. Moreover, there are not enough relevant studies available in the literature. Thus, further investigation and broader analysis is crucial in order to evaluate the impact of polyols on the intestinal flora.

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