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Is xylitol a sweet revolution? - A literature review of its metabolic effects and innovative applications

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ABSTRACT

Introduction: Xylitol is a natural sweetener clasified as a sugar alcohol. It tastes and looks like sugar, but has a 40% lower caloric value. Sugar alcohols are becoming more popular not only in overweight or diabetic patients, but also in everyday life of young, athletic people. Xylitol has been studied since the 1960s for its antihyperglycemic, antiobesogenic and antidiabetic potential [1], and its health effects have been confirmed in many studies over the years, which is why they are often used in dental care products and chewing gums [2]. This polyol seems to be very promising in supporting treatment of various diseases. It is known

that its metabolic effect is different from glucose metabolism, but the effects of xylitol on the body are still not fully understood, which creates a wide range of potential applications for xylitol.

Aim of the study: The purpose of this study is to evaluate the influence of xylitol on human metabolism and to review innovative ideas of its use based on randomized clinical trials and clinical trails published in the last five years.

Material and Methods: Review and analysis of randomised clinical trials and clinical trials from 2020-2025 available on PubMed and Google Scholar.

Conclusions: Xylitol is definitely promising as an alternative sweetener. With its sweetness and slightly impact on postprandial glycemia it can be consumed as a sugar substitute, also in combination with a high protein meal. However, xylitol may gain much wider application than just a sweetener - by supporting the symptomatic treatment of gastroesophageal reflux disease (GERD) and good osmometabolic properties during peritoneal dialysis (PD), it seems to maintain the benefits of traditional therapies while avoiding side effects. Most of the studies published so far on innovative use of xylitol were pilot studies, therefore metabolic regulation, brain network modulation and general long-term impact of xylitol on health needs extensive studies.

Keywords: *xylitol, sugar alcohol,alternative sweetener, xylitol metabolism, metabolic effect, innovative application*

INTRODUCTION

Xylitol is a five-carbon polyol widely used as a sugar substitute in food and pharmaceutical industries. Due to its sweet taste and significantly lower caloric content than white sugar (sucrose), amounting to 2.4 kcal/g [3], xylitol has become the focus of interest for individuals following weight-loss diets, athlets and patients with obesity. Xylitol is characterized by a low

glycemic index (GI) of 7 [4], which means that it has a minimal effect on postprandial glycemia and, therefore, can be consumed by patients with diabetes.

One of the reasons why xylitol is among the most frequently used sucrose substitutes is also its physical properties: it is easily soluble in water, colorless, and stable at high temperatures, which facilitates food processing. Initially, birch wood was used to obtain xylitol, hence it was originally called "birch sugar." Naturally, xylitol is also found in certain vegetables and fruits, such as strawberries, plums [5], pumpkins and cauliflower. Currently, due to high consumer demand, xylitol is produced through the catalytic reduction of D-xylulose or microbial fermentation and enzymatic biotransformation.

The metabolism of xylitol differs from the pathways that glucose undergoes. Xylitol is absorbed in the small intestine by simple diffusion at a rate of 49-95% [6] and transported to the liver. There, it is metabolized to glucose-6-phosphate (via the pentose phosphate pathway) and subsequently to pyruvate and acetyl-CoA. This mechanism is considered one of the reasons for the lower postprandial glycemia and reduced insulin levels compared to glucose. The unabsorbed portion of xylitol is fermented by bacteria in the large intestine into short-chain fatty acids and gases [7], which may contribute to side effects of xylitol, such as bloating, increased bowel sounds**,** or diarrhea.

Effects on dental and oral cavity health

The beneficial effect of xylitol on oral health is one of the best documented effects of its consumption. It has been studied that xylitol not only inhibits the growth of bacteria responsible for the development of caries (mainly *Streptococcus Mutans*), but also effectively reduces their number in dental plaque. Moreover, unlike mono- and disaccharides, it is not fermented by oral bacteria, and thus does not lower the pH in the oral environment. In the bacterial cell, xylitol is first phosphorylated to xylitol-5-phosphate, which induces degradation of the cell membrane and, consequently, death of bacteria. These changes are responsible for lower production of acid plaque, so regular use of xylitol plays a role in reducing caries and increased mineralization of the enamel [8]. Additionally, xylitol increases salivary secretion [9], which has antibacterial effects and neutralizes dietary acids [10]. Due to numerous research results clearly indicating the benefits of xylitol for dental health, it is commonly used in chewing gums, toothpastes and mouthwashes. Using fluoride toothpaste containing 10% xylitot can reduce the risk of caries by up to 13% compared to fluoride-only toothpaste [11] [12]. Another common oral disease linked to the sugar intake is candidosis. It is a fungal

infection of the oral cavity is usually caused by *Candida Albicans*. This yeast is a part of the normal human microflora, but can also be infectious, especially in patients with immunosupression. Sugar consumption contributes to the growth of *Candida Albicans*, where xylitol has an inhibitory effect on this fungus with MIC=20×10^4 μg/mL [13].

Effects on gastric emptying

Ingestion of xylitol affects gastric emptying – it has been studied that in healthy volounteers intake of 25 g of xylitol before the solid meal could prolong gastric emptying for 56,9% [14]. Intragastric administration of 50 g xylitol dissolved in 300 ml water was also associated with delayed gastric emptying, which has been observed in obese patients with impaired glucose control as well as in healthy standard-weight participants [15]. Gastric motility is regulated by, among others, cholecystokinin (CCK) and glucagon-like peptide (GLP-1). Xylitol, both orally and intragastrically administered, stimulates increased secretion of CCK and GLP-1, which seems to be the cause of prolonged gastric emptying time and consequently may cause a feeling of satiety and prevent food intake.

Effects on glycemic control

Xylitol causes a small increase in postprandial glycemia and has minimal effect on insulin secretion. As a result, it may reduce the risk of insulin resistance and be a safer alternative to sugar, especially in patients with type 2 diabetes mellitus (DM2). Compared to glucose, the increase in glycemia in healthy, non-obese subjects after oral administration of xylitol is significantly lower at 30 and 60 minutes after administration, although lower glycemia has been documented after glucose ingestion at 150 and 180 minutes [16]. The AUC after xylitol ingestion is significantly lower than after glucose ingestion, therefore the GI for xylitol is 7 (GI for glucose = 100). Reactive hypoglycemia was not observed after xylitol administration [16]. All these observations lead to the conclusion that xylitol is much more beneficial than glucose due to its lower impact on glucose level and insulin response. It contributes to better glycemic control and reduce the risk of metabolic disorders [15].

Effects on lipid metabolism

After animal studies, xylitol was very promising as a substance that reduces the accumulation of visceral fat, lowers total cholesterol, and also causes significant up-regulation of PPAR-γ receptors in mesenteric adipose tissue [17]. PPAR-γ receptors are responsible for adipocyte

differentiation and control of insulin sensitivity. Their activation increases insulin sensitivity, and this effect has been used for years by using glitazones in the treatment of DM 2 [18]. Unfortunately, during pilot studies conducted on humans, no statistically significant effect of xylitol on the concentration of triglycerides, total cholesterol, free glycerol, nonesterified fatty acids, alpha-lipoproteins, beta-lipoproteins was observed [19], however, the topic has not yet been fully explored and requires further research.

REVIEW OF LITERATURE

Over the past five years, xylitol has been studied in various fields of medicine. In 2021, Sridonpai et al. documented that consumption of a meal containing xylitol by patients with DM2 had a beneficial effect on postprandial glycemia, insulin levels, and GLP-1 concentration [20].

Two isocaloric meals with very similar nutritional values were compared: a whey protein-based multi-ingredient nutritional drink containing 23.89% xylitol and a typical Thai breakfast consisting of white rice and chicken. A higher AUC for active GLP-1 was documented for the meal containing the nutritional drink, as well as a significantly lower AUC for blood glucose levels after consuming this drink. These observations suggest a significantly higher metabolic benefit of the drink containing xylitol. Furthermore, no statistically significant difference in postprandial insulin levels was observed between the two meals. For patients with DM2, a meal combining protein and xylitol may provide substantial benefits for glycemic control and should be considered as a substitute for a typical breakfast.

Perspectives for xylitol in peritoneal dialysis therapy

Nowadays approximately 850 million people worldwide suffer from kidney disease [21], which, if left untreated, can lead to end stage renal disease and the need for dialysis. Peritoneal dialysis is a more economical yet less frequently used form of therapy compared to hemodialysis [22], however it has a serious drawback – glucose-associated toxicity. In adult patients with end stage renal disease using continuous intraperitoneal dialysis therapy, the use of xylitol with L-carnitine and a small amount of glucose in the dialysis fluid instead of the standard glucose allows for the suppression of negative metabolic effects associated with glucose overload [23]. Standard dialysate containing glucose has a concentration about 10-50 times higher than blood glucose level, which is necessary for the migration of water,

electrolytes and toxins, but it also promotes the development of DM2, insulin resistance and cardiovascular disease (CVD).

Dialysate containing xylitol and L-carnitine demonstrates favorable osmometabolic properties and was well tolerated by patients, with no side effects reported during a 28-day preliminary randomized study. Moreover, it does not cause toxicity related to peritoneal glucose overload, does not impair the peritoneal ultrafiltration mechanism, and does not induce the systemic negative effects of hyperglycemia. The parameters of dialysis efficiency remained stable throughout therapy with xylitol- and L-carnitine-containing dialysate. The results of this study suggest that using these osmolytes in peritoneal dialysis therapy reduces glucose overload and glucose-induced toxicity without compromising efficacy [23].

Xylitol-malic acid tablets in managing GERD symptoms

In 2020 Sánchez-Blanco et al. examined impact of xylitol-malic acid lozenges (3 times per day) on salivary secretion in adult patients with GERD diagnosis. It has been demonstrated that after six months of taking xylitol-malic acid tablets, salivary secretion significantly increased and xerostomia was present in only 14.3% of patients compared to 100% of participants experiencing it without the tablets [24]. Additionaly, an increase in salivary buffering capacity and a significant reduction in esophageal reflux symptoms, such as regurgitation, retrosternal burning, and heartburn, were also documented. The use of xylitol-malic acid tablets was well tolerated by participants and appears to significantly improve the quality of life in adult patients with GERD.

Impact of xylitol on brain activity

In 2022 Meyer-Gerspach et al. conducted the first study focusing on the acute effects of xylitol ingestion on brain activity. After intragastric administration of 50g of xylitol (dissolved in 300 ml) in healthy subjects, increased resting cerebral blood flow (rCBF) in the hypothalamus was observed, while equisweet load of glucose was associated with a decrease in rCBF [25]. At 6 and 21 min after intragastric administration, blood-oxygen-level–dependent (BOLD) functional magnetic resonance was performed and showed similarities in the effects of glucose and xylitol on brain network properties - both sweeteners increased betweenness centrality in the hypothalamus, which implies that this is an important brain region in the integration of signals after glucose and xylitol administration. However, some differences were noted: xylitol caused increased activity in the nucleus accumbens but

decreased activity in the left orbitofrontal cortex, while glucose had the opposite impact. Both substances caused changes in the activity of the basal ganglia, but with different effects, suggesting different influence on the reward system and appetite control.

Gastrointestinal study on xylitol

In a study conducted in 2020, Meyer-Gerspach et al. demonstrated a dose-dependent increase in the concentration of gut hormones—cholecystokinin, GLP-1 analog, and PYY—after xylitol administration in healthy adult participants [26]. None of the tested doses of xylitol (7 g, 17 g, and 35 g) had an effect on motilin or GIP-1 levels. The concentration of blood lipids also remained unchanged. Glucagon levels were not significantly changed after xylitol administration, although the intake of 35 g of the sweetener led to a higher glucagon concentration at 120 minutes compared to the 17 g dose. At the same time, plasma glucose levels did not increase. This observation does not allow for a definitive conclusion regarding xylitol's effect on glucagon, therefore, further studies with longer observation periods and chronic xylitol use are needed.

In healthy adults, single doses of up to 35 g of xylitol were well tolerated—it did not cause abdominal pain, nausea, or vomiting, with the only reported side effect being a subjective sensation of increased bowel sounds. However, it should be noted that in studies involving repeated xylitol intake (30–90 g per day), the vast majority of participants reported diarrhea and flatulence [27] [28].

The only study conducted so far on chronic xylitol intake was conducted in obese participants, assessing glucose absorption after 5–7 weeks of xylitol consumption (3 × 8 g per day). In the oral glucose tolerance tests (OGTT) performed after this period, no statistically significant alteration in intestinal glucose absorption were observed [29]. This suggests that despite a slight increase in glycemia after acute xylitol ingestion [15] [30], chronic intake does not lead to reduced glucose absorption by decreasing the number of glucose transporters in the intestine. However, to draw definitive conclusions, a simultaneous analysis of both the effects of chronic xylitol intake and the acute response to a single dose of this sweetener is necessary.

CONCLUSIONS

Xylitol appears to be a promising adjunct in the management of various common diseases. It should be considered as an alternative to sugar, especially in prediabetic and diabetic patients. Based on this review we noted several important observations:

- The reduction of persistent esophageal symptoms in patients with GERD in the pilot study was achieved, which seems very promising for patients with this condition.
- The use of xylitol in dialysate for patients undergoing peritoneal dialysis appears to offer only benefits related to a lower glucose load while not affecting its efficiency.
- Due to its minimal impact on glycemia and insulin secretion in healthy individuals and patients with DM2, xylitol may provide significant benefits for prediabetic and diabetic patients. Recent studies have confirmed xylitol's effect on increasing the levels of anorexigenic gut hormones. This effect is observed both when xylitol is consumed with a high-protein meal and when taken alone. However, prolonged xylitol consumption seems to be associated with intestinal disturbances, while intestinal glucose absorption remains unchanged.
- Xylitol affects basal ganglia activity differently than glucose; however, the consumption of both substances increases neuronal communication between the hypothalamus and other brain regions. Nevertheless, this topic definitely requires further studies.
- No effect of low doses of xylitol on prokinetic motilin and GIP-1 has been demonstrated.

The impact of xylitol on human metabolism has not yet been fully explored. Most studies focus only on the acute effects of xylitol intake. Longer observation and chronic exposure require further investigation, as does the effect of xylitol when consumed with other meals differing in processing level or temperature.

Disclosure

Author's contribution

Conceptualization, M. Blecharczyk; methodology, I. Zydlewski and M. Pacanowska; software, M. Kosiński; check, M. Sękulski, and P. Jakubiec; formal analysis, A. Nowik and M. Mrozek; investigation, M. Pacanowska; resources, I. Zydlewski; data curation, M. Sękulski and M. Kosiński; writing - rough preparation, P. Jakubiec; writing - review and editing, M. Mrozek; visualization, A. Nowik; supervision, M.Blecharczyk; project administration, M. Blecharczyk; All authors have read and agreed with the published version of the manuscript.

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