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Erythritol as a Next-Generation Sweetener: properties, metabolism, cardiovascular risk and gut health implications – A literature review

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ABSTRACT

Introduction and Purpose:

The global epidemic of metabolic diseases has prompted a growing interest in modifying dietary habits. Sucrose, a commonly used sweetener, is ubiquitous in food products, contributing to its excessive global consumption. Due to its numerous drawbacks there is increasing demand for low-calorie sugar substitutes in human nutrition. Among the most frequently selected sugar substitutes is erythritol, a four-carbon polyol that is industrially produced through the fermentation of glucose by yeast. The aim of this study is to highlight the key characteristics of erythritol, examine its potential adverse effects, evaluate its advantages among other polyols, discuss its possible health-promoting properties, impact on the gut microbiota, and identify directions for future research.

Material and methods:

The review was is based on the thorough analysis of the materials selected from PubMed, Scopus, Google Scholar and Science Direct using the following key words: erythritol, erythritol metabolism, gut microbiota, polyols, non-nutritive sweeteners, butyric acid.

Conclusions:

Erythritol is a well-tolerated, low-calorie sugar alcohol with minimal systemic metabolism and negligible impact on blood glucose levels. It is largely absorbed in the small intestine and excreted unchanged, with limited fermentation in the colon. While human studies show no significant impact on gut microbiota, ex vivo findings suggest a potential for increased production of beneficial short-chain fatty acids. Recent observational studies have raised concerns about potential associations with cardiovascular risk. However, these findings are inconclusive and require further investigation. Emerging animal data indicate erythritol may modulate gut epithelial structure via microbiota-derived metabolites. Overall, erythritol remains a promising sugar substitute, but its long-term health effects warrant additional high-quality clinical research.

Key words: erythritol, sweetener, gut microbiota, gastroenterology, butyric acid

INTRODUCTION:

The global shift toward healthier lifestyles has significantly increased interest in sugar alternatives, particularly those that offer sweetness without the metabolic drawbacks of sucrose. Among these, erythritol - a naturally occurring polyol - has gained popularity not only for its organoleptic properties but also for its favorable safety and metabolic profile. Originally isolated in the mid-19th century, erythritol did not reach the consumer market until the 1990s, when technological advances enabled its production via microbial fermentation. [1,2] While its role as a non-caloric sweetener is well established, erythritol's potential impact on

human health extends beyond simple energy substitution. Unlike high-intensity sweeteners, erythritol does not exhibit a synergistic sweetness effect but instead mimics the bulk and mouthfeel of sugar, making it a preferred ingredient in low-calorie food formulations. Its stability under heat and across a broad pH range has expanded its utility in processed foods, pharmaceuticals, and oral health products. [3] Erythritol has also emerged in recent scientific discourse surrounding cardiometabolic risk. A 2023 study sparked debate by reporting associations between elevated circulating erythritol and increased platelet reactivity, raising questions about its long-term safety in vulnerable populations. [4-6] However, causality remains unconfirmed, and these findings highlight the need for nuanced interpretation and further investigation in clinical contexts. In the realm of gastrointestinal physiology and gut microbiota, erythritol occupies a unique niche. Unlike many polyols that are extensively fermented in the colon, erythritol is largely absorbed in the small intestine and excreted unchanged, thereby minimizing common adverse effects such as gas production and osmotic diarrhea. [7-9] Nonetheless, new experimental models suggest that erythritol may influence intestinal remodeling and microbiota-host interactions through indirect mechanisms—an area of growing interest in sports science, metabolic health, and immunonutrition. [10-12]

Erythritol: Properties and Applications

Erythritol is a four-carbon organic compound classified as a polyol. It is used as a food additive with sweetening properties and is also an ingredient in cosmetics and pharmaceuticals. Although it was first isolated in 1852, erythritol only entered the market in 1990 as a new natural sweetener in Japan. [13] Its sweetness is approximately 70% that of sucrose, and it produces a mild cooling sensation in the mouth upon consumption. [14] Consequently, a larger quantity is needed to achieve a comparable level of sweetness. The caloric value of erythritol has been estimated at less than 0.4 kcal/g. [15] However, for the purposes of nutritional labeling, erythritol is considered to provide 0 kcal/g, compared to 2.4 kcal/g for other sugar alcohols [16] Erythritol occurs naturally in a variety of fruits such as watermelon, melon, pears, and grapes, as well as in vegetables and fermented food products. [8,17,18] It is also present in human and animal tissues. [19-21] Industrial production via chemical synthesis is not economically viable; therefore, erythritol is currently produced on an industrial scale by fermenting glucose with yeast. [22] Its properties are utilized in the manufacture of pharmaceuticals, toothpaste, and mouthwashes. An important advantage of erythritol is its high stability: it does not react with most active ingredients, remains stable

during storage, withstands temperatures up to 160°C, and is stable within a pH range of 2–10.2. [23] Furthermore, in oral hygiene products, in addition to providing a sweet and pleasant taste, erythritol inhibits the growth of *Streptococcus mutans* in the oral cavity, thereby reducing the risk of dental caries. [14,17,24]

Adverse Effects of Erythritol Consumption

Compared to other sweeteners in the polyol group, erythritol is the most well tolerated and can be consumed in relatively high doses without causing adverse effects. [17] In a study comparing the effects of sucrose, xylitol, and erythritol consumption, a statistically significant difference was observed following ingestion of 20, 35, and 50 g of xylitol compared to equivalent doses of erythritol. A 50 g dose of erythritol caused only statistically significant nausea. In contrast, a 50 g dose of xylitol caused statistically significant nausea, bloating, borborygmi, colic, and watery stools. Consumption of 50 g of either erythritol or xylitol was associated with a significant increase in the mean number of symptoms compared to 45 g of sucrose. However, 20 and 35 g of erythritol, as well as 20 g of xylitol, did not significantly increase symptom presence. [7]

According to the European Food Safety Authority (EFSA)'s re-evaluation of erythritol as a food additive, erythritol may cause diarrhoea when consumed at doses above 0.5 g/kg body weight per day. EFSA has adopted this value as the acceptable daily intake (ADI). Although some observational studies suggest a correlation between elevated erythritol plasma concentrations and cardiovascular risk, current evidence is insufficient to establish a causal link between erythritol consumption as a food additive and increased cardiovascular disease risk. Based on available human studies, EFSA identified diarrhoea as the most sensitive adverse effect endpoint. [25]

In recent years, publications have reported a possible correlation between higher erythritol plasma levels and cardiovascular disease or associated risk factors. [4-6] A 2023 study published in the journal *Nature Medicine* investigated the potential link between erythritol intake and the risk of major adverse cardiovascular events (MACE), such as myocardial infarction, stroke, and death. Untargeted metabolomic analyses in patients undergoing cardiovascular risk assessment showed that elevated plasma levels of polyols, including erythritol, correlated with an increased risk of MACE over three years. This correlation was later confirmed by targeted analyses in independent validation cohorts comprising patients undergoing elective

cardiovascular evaluation. In vitro experiments showed enhanced platelet reactivity in response to erythritol, suggesting a prothrombotic effect. In vivo studies in mouse models demonstrated increased thrombogenesis following erythritol administration. Furthermore, a prospective pilot intervention study found that healthy volunteers who consumed an erythritol-sweetened beverage exhibited a greater than 1,000-fold increase in blood erythritol levels, persisting for more than two days. These concentrations significantly exceeded thresholds associated with increased thrombotic potential in prior in vitro and in vivo studies. [4] Nevertheless, caution is warranted in interpreting these observational data. There is currently insufficient evidence to confirm that dietary erythritol directly increases cardiovascular disease risk. Elevated erythritol levels in plasma may instead be markers of pre-existing metabolic disturbances rather than their cause. [25,26]

Erythritol Metabolism and Its Effect on Human Gut Microbiota

Erythritol is rapidly absorbed in the small intestine by passive diffusion and is primarily excreted in the urine. Therefore, erythritol does not affect blood glucose or insulin levels. [27,28] Only a small fraction (approximately 10%) reaches the colon [8] There is some evidence that a minimal amount may be oxidized in the bloodstream to erythronate [29,30] The limited amount of erythritol reaching the colon may explain the lack of clinical evidence for its impact on the human gut microbiota. [31] A 2005 study using a 24-hour in vitro fermentation model with fresh human feces demonstrated that erythritol was not fermented by the human microbiota. In contrast, maltitol and lactulose underwent fermentation, as evidenced by increased gas production and decreased pH. [32] Low concentrations of erythritol (25, 50, and 100 μg/mL) had no effect on the growth of *Escherichia*, *Enterococcus*, *Lactobacillus*, *Ruminococcus*, or *Bacteroides* species in the human gut microbiota. However, a significant increase in butyric and pentanoic acid concentrations was observed following erythritol consumption, which is attributable to the 10% of erythritol reaching the colon [10] Notably, butyric acid has been shown to alleviate symptoms of irritable bowel syndrome (IBS) and prevent obesity. [33,34] Butyric acid and valeric acid (pentanoic acid) have recently been identified as histone deacetylase (HDAC) inhibitors. Since HDAC overexpression is associated with various diseases, including cancer, these acids may represent promising therapeutic targets. [35]

These findings are supported by promising ex vivo studies suggesting potential prebiotic benefits of erythritol, including increased butyrate production. Moreover, an increase in the abundance of bacterial families *Eubacteriaceae* and *Barnesiellaceae* was observed. This study employed human stool samples and the SIFR® (Standardized In Vitro Fermentation)

technology, which enables the simulation of colonic conditions in a controlled laboratory environment. However, there is still a lack of in vivo evidence, and further clinical studies are necessary. [11]

Impact of Erythritol on Intestinal Epithelial Remodeling

A published mouse model study indicated that erythritol modulates intestinal epithelial structure and function via two distinct mechanisms. The first involves hyperplasia of tuft cells (TCs) and goblet cells (GCs). Short-term erythritol consumption in mice led to an increase in these cell populations. TCs serve as chemosensory cells detecting luminal signals, while GCs are responsible for mucus secretion, which protects the mucosal lining. Their proliferation may indicate an adaptive epithelial response to erythritol. The second mechanism involves increased intestinal stem cell activity in response to erythritol. This activation was dependent on the gut microbiota, as antibiotic administration abolished the effect, while fecal transplantation from erythritol-fed mice restored it in recipient mice. Acetate was identified as the key metabolite mediating this effect, highlighting the importance of microbial fermentation products in modulating epithelial function. [12]

CONCLUSION

Erythritol is a four-carbon sugar alcohol characterized by favorable physicochemical and metabolic properties, including high digestive tolerance, negligible caloric contribution, and chemical stability across a broad range of environmental conditions. Its widespread application in the food, pharmaceutical, and oral care industries is supported by its organoleptic qualities and safety profile. Current evidence indicates that erythritol is rapidly absorbed in the small intestine and largely excreted unchanged in the urine, with minimal effects on glycemic response and insulin secretion. Its limited fermentation in the colon further supports its gastrointestinal tolerability and lack of adverse impact on the gut microbiota in humans.

Emerging studies have proposed a potential association between elevated plasma erythritol levels and increased cardiovascular risk. However, these findings are observational in nature and do not establish causality. Elevated erythritol concentrations may instead serve as

biomarkers of pre-existing metabolic dysfunctions, rather than being a direct consequence of dietary intake. Experimental data suggesting prothrombotic effects at supraphysiological concentrations warrant further investigation through longitudinal and mechanistic clinical studies.

Preliminary in vitro and ex vivo studies have indicated a possible prebiotic potential of erythritol and its modulatory influence on intestinal epithelial cell dynamics via microbiota-mediated pathways. Nevertheless, the translational significance of these findings remains uncertain and necessitates validation in controlled human studies.

In conclusion, erythritol appears to be a well-tolerated and functionally versatile sugar substitute. While current evidence supports its safety at levels commonly used in food products, further high-quality research is required to clarify its long-term health effects, particularly with respect to cardiometabolic outcomes.

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Author's Contribution:

Conceptualization: Julia Skowrońska-Borsuk, Bartłomiej Czerwiec, Adam Borsuk; methodology: Julia Borkowska, Julia Sposób ; check: Bartłomiej Czerwiec, Adrianna Pękacka, Martyna Narożniak; data curation: Malwina Wojtas, Joanna Pergoł; investigation: Julia Skowrońska Borsuk, Joanna Pergoł, Julia Sposób, Zuzanna Krupa; resources: Julia Sposób, Malwina Wojtas; writing-rough preparation: Julia Skowrońska-Borsuk, Adam Borsuk, Martyna Narożniak, Adrianna Pękacka; writing-review and editing: Julia Skowrońska-Borsuk, Zuzanna Krupa, Julia Borkowska; visualization: Julia Skowrońska-Borsuk; supervision: Julia Skowrońska-Borsuk, Adam Borsuk; project administrator: Julia Skowrońska-Borsuk

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