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Erythritol: Evaluation of its Potential Therapeutic Applications and Discussion on Safety Issues - A Review

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Summary:

Introduction: Erythritol is a sugar alcohol that has become increasingly popular as a low-calorie sweetener due to its unique characteristics. It is a naturally occurring substance that is found in various foods such as fruits and vegetables. In recent years, erythritol has gained attention as a potential alternative to traditional sugars due to its minimal impact on blood glucose level.

The aim of the study: This review aims to provide an overview of the characteristics of erythritol and its potential therapeutic applications. Specifically, the review focuses on the role of erythritol in managing diabetes type 2 patients and obesity.

Material and Methods: A systematic search was conducted on various academic databases, including PubMed and Google Scholar. Articles published mainly between 2013 and 2022 were included in the study. In addition, some older articles were included in the analysis if they provided essential information for a comprehensive understanding of erythritol. The articles were analysed, and relevant information was extracted.

Description of the state of knowledge: The study is based on an analysis of various scientific publications, including original articles and reviews, that provide insights into the features of erythritol and its potential therapeutic applications. The review provides a comprehensive understanding of erythritol, highlighting its properties and the potential applications that could be explored in the future.

Conclusions: Overall, erythritol appears to be a promising low-calorie sweetener that may have various potential therapeutic applications, particularly in managing diabetes type 2 patients and obesity. While further research is needed to fully understand its potential benefits, the current evidence suggests that erythritol could be a valuable tool in promoting better health outcomes.

Keywords: "erythritol", "sugar substitute", “polyol”, "glycemic control", "diabetes", "weight loss"

Introduction:

Erythritol, an organic chemical compound belonging to the group of sugar alcohols, is gaining recognition in the world of science and the food industry as an effective and safe sugar substitute [1,2]. Due to its low-calorie nature and antidiabetic and anti-obesity properties, erythritol is becoming increasingly popular as an ingredient in food products [3,4].

Erythritol occurs naturally in small amounts in fruits, vegetables, and fermentation products such as wine, soy sauce, and cheese [5,6]. Due to its low caloric values (0.2 kcal/g) and a sweetness equal to about 60-80% of the sweetness of sucrose, erythritol is an attractive alternative for people concerned about their health and weight control [1,4].

Scientific research has shown that erythritol does not affect blood glucose levels or insulin secretion, which is significant for people with diabetes and insulin resistance [2]. Moreover, due to its low fermentation by gut bacteria, erythritol does not cause bloating or other food intolerance symptoms [1]. Erythritol also exhibits antibacterial activity against bacteria responsible for tooth decay, making it friendly to oral health [7].

The aim of this scientific paper is to present the characteristics of erythritol and discuss its potential uses in supporting the treatment of various diseases. The review of scientific literature includes the analysis of the chemical, physical, and biological properties of erythritol, its impact on human health, and the possibilities of using it in adjunct therapy for diseases related to diabetes, obesity, and dental caries.

Materials and Methods:

Materials and methods: A systematic search was conducted on various academic databases, including PubMed and Google Scholar. Articles published mainly between 2013 and 2023 were included in the study. Furthermore, to provide a comprehensive overview of erythritol and its potential therapeutic applications, some older articles were also included in the analysis if they were deemed essential. The articles were analysed, and relevant information was extracted. The materials and methods were based on a thorough research process. In the first step, keywords and phrases related to the topic of erythritol were defined, such as "erythritol", "sugar substitute", “polyol", “glycemic control", "diabetes", "weight loss", and others. Then, using these keywords, a search was conducted in the aforementioned academic databases.

To ensure the quality of the review, only articles published in peer-reviewed scientific journals were included. After collecting an appropriate number of articles, a critical appraisal was conducted to evaluate the value and credibility of the presented data. This involved assessing research samples, methodology, statistical analysis, and conclusions.

After completing the critical appraisal process, relevant information was extracted from each article, such as the number of participants, research methods, results, and conclusions. This information was then compiled for comparison and analysis of the results from different studies.

Erythritol: General characteristics

Erythritol is one of the sugar alcohols, also known as polyols, which are widely used as low-calorie sweeteners [1]. Polyols are carbohydrates that have a hydroxyl group attached to each carbon atom, giving them properties similar to sugars and alcohols [1]. Erythritol synthesis mainly occurs through the fermentation of glucose using yeast and bacterial strains [2]. Erythritol is naturally present in fruits, vegetables, and fermentation products, such as wine, soy sauce, and cheese, albeit in small amounts [3,4]. Erythritol exhibits numerous beneficial properties that make it an attractive sweetener for consumers and the food industry. It has a very low energy value, approximately 0.2 kcal/g, making it appealing to health-conscious individuals and those managing their weight [5]. Erythritol is sweeter than some other polyols, with a sweetness intensity of about 60-80% of sucrose, which makes it a practical sugar substitute in many food products [5]. Erythritol appears as a white, crystalline, odorless powder [1]. It is soluble in water, with a solubility of approximately 37 g/100 mL at 20°C. It is stable across a wide range of temperatures, allowing for its use in various food manufacturing processes, such as cooking, baking, or freezing [6].

Erythritol: Absorption, Metabolism, and Excretion

Erythritol demonstrates distinct absorption kinetics in comparison to other polyols. Owing to its small molecular size, erythritol is quickly absorbed in the small intestine [1][8]. Unlike other sugar alcohols such as xylitol and sorbitol, erythritol is absorbed in 80-90% [1][8][9].

Metabolism of erythritol in the human body is limited. Studies involving humans have found that about 90% of ingested erythritol is excreted unchanged in urine [1][8][9]. Research indicates that a portion of ingested erythritol can be oxidized to erythrose or converted to erythronate, both of which are also excreted in urine [8]. A small portion of erythritol is converted to glycerol, but this process has marginal significance in energy balance [10]. Erythritol is not fermented by gut bacteria, meaning it does not cause bloating or diarrhea as occurs with the consumption of other sugar alcohols [11].

The excretion of erythritol by the kidneys is rapid and efficient [2]. Most ingested erythritol is excreted by the kidneys within 24 hours of consumption, as confirmed in human studies [6]. Erythritol excretion does not burden the kidneys, as erythritol concentration in urine does not affect urine osmolality or pH [11].

In summary, erythritol is quickly absorbed in the small intestine and its metabolism in the human body is minimal. Most ingested erythritol is excreted unchanged in urine within 24 hours. Rapid and efficient excretion of erythritol and the lack of fermentation by gut bacteria make erythritol well-tolerated by humans, even at higher doses.

Safety of Erythritol:

The safety of erythritol as a low-calorie sweetener has been extensively evaluated in numerous studies, with a wealth of research findings supporting its safe use in food and beverages. A detailed evaluation conducted by the European Food Safety Authority (EFSA) Panel on Food Additives and Nutrient Sources offers robust evidence for the safety of erythritol [10]. Within this evaluation, the panel examined the potential risks associated with the proposed expansion of erythritol's use (E 968) as a food additive, considering the available toxicological and clinical data.

Upon evaluating the evidence, the EFSA panel determined that erythritol is safe for consumption at the proposed usage levels, encompassing a wide variety of food products, such as soft drinks, confectionery, and bakery items [10]. This conclusion aligns with previous research that has similarly demonstrated the safety and effectiveness of erythritol as a food additive [1][2].

Notably, the EFSA panel established an acceptable daily intake (ADI) for erythritol as "not specified" [10]. This classification suggests that no adverse effects are anticipated when erythritol is consumed within the scope of typical dietary exposure. The decision to assign an ADI of "not specified" reflects the panel's confidence in erythritol's safety, based on a thorough evaluation of the available data.

Erythritol: Tolerance and Possible Side Effects

While erythritol is generally considered safe and well-tolerated as a low-calorie sweetener, it is important to discuss its potential side effects and tolerance levels. Some individuals may experience gastrointestinal discomfort when consuming erythritol in excessive amounts.

One of the common side effects associated with erythritol consumption is its laxative effect [7]. De Cock and Bechert highlighted that erythritol can cause digestive issues such as bloating, gas, and diarrhea when consumed in high quantities [7]. This laxative effect is primarily due to the fact that erythritol is not completely absorbed by the body and passes through the digestive system, which can lead to an osmotic effect in the intestines [1].

However, it should be noted that the gastrointestinal side effects of erythritol are generally mild and tend to occur only when consumed in excessive amounts [1][7][10]. Grembecka reported that erythritol is well-tolerated and has no significant side effects when consumed in moderate amounts. Furthermore, erythritol's tolerance level appears to be higher compared to other sugar alcohols, such as xylitol and sorbitol, which are known to cause gastrointestinal issues at lower doses [1].

In conclusion, erythritol is generally well-tolerated with minimal side effects, particularly when consumed in moderate amounts. However, excessive consumption of erythritol may lead to gastrointestinal discomfort. It is important to monitor individual tolerance levels and consume erythritol in moderation to minimize potential side effects.

The Use of Erythritol in Type 2 Diabetes

Erythritol, a natural sweetener, has demonstrated potential benefits for individuals with Type 2 diabetes. Studies have shown that erythritol can have a positive impact on endothelial function in patients with Type 2 diabetes [11][12][13][14]. Boesten and colleagues investigated the multi-targeted mechanisms underlying the endothelial protective effects of erythritol, a natural sweetener that is considered safe for diabetics [11]. The researchers found that erythritol demonstrated multiple protective mechanisms on endothelial cells, which play a crucial role in vascular health and are often impaired in individuals with type 2 diabetes [14]. They discovered that erythritol could protect endothelial cells from hyperglycemia-induced oxidative stress, reduce inflammation, and improve nitric oxide (NO) bioavailability, a vital molecule in the regulation of blood flow and vascular tone [11]. In Flint et al.'s (2014) pilot study, researchers investigated the effects of erythritol on endothelial function in patients with type 2 diabetes. Preliminary evidence suggested that erythritol consumption led to a significant improvement in flow-mediated dilation (FMD) of the brachial artery, which is a widely used non-invasive method for assessing endothelial function, indicating enhanced endothelial function [12]. These findings suggest that erythritol may not only serve as a safe alternative sweetener for people with type 2 diabetes but also provide additional benefits in maintaining vascular health.

Furthermore, erythritol has low glycemic properties, which may contribute to its potential health benefits as a sugar replacer [5][13]. Research on erythritol's potential as a biomarker for Type 2 diabetes and impaired fasting glucose has also been conducted. Menni et al. (2013) employed a nontargeted metabolomics approach to explore novel biomarkers for type 2 diabetes and impaired fasting glucose. In their study, they discovered erythritol as a potential

biomarker that could be used to identify individuals at risk for these metabolic conditions. This finding may contribute to better diagnostic tools and improved management of patients with type 2 diabetes and impaired fasting glucose [14].

Furthermore, erythritol's impact on satiety has been investigated in relation to its potential as a sugar substitute for individuals with Type 2 diabetes. Overduin et al. (2015) conducted a study examining the effects of erythritol on the release of gut hormones GLP-1 and PYY, which are associated with appetite regulation and satiety [15]. The study involved both lean and obese participants and compared the effects of sucrose replacement with erythritol on the release of these hormones and the size of a test meal. The results indicated that erythritol did not significantly alter the release of GLP-1 or PYY, nor did it affect the test meal size in either lean or obese participants [15]. This suggests that erythritol may not have a direct impact on satiety; however, its low-calorie nature and minimal impact on blood glucose and insulin levels still make it a viable sugar alternative for individuals with Type 2 diabetes.

In conclusion, erythritol has shown promise as a beneficial and safe sugar substitute for individuals with Type 2 diabetes due to its effects on endothelial function, glycemic control, and low glycemic properties [15][16]. Further research is needed to fully understand its potential role in the management and prevention of diabetic complications.

The Use of Erythritol in Obesity

Erythritol, a non-nutritive sweetener, has garnered increasing interest in the context of obesity management due to its potential role in promoting satiety and aiding weight control [16]. While some studies have not observed significant effects of erythritol on gut hormone release or meal size in lean or obese individuals [15]. Moreover, chronic consumption of erythritol has been linked to improved glucose absorption in individuals with obesity [16], and erythritol has been reported to ameliorate small intestinal inflammation induced by high-fat diets, leading to improved glucose tolerance [17]. These findings are complemented by evidence that erythritol influences gut sweet taste receptors and gastrointestinal satiation hormone release in humans, underlining its potential role in promoting satiety [18]. Although the effects of erythritol on gut hormone secretion and gastric emptying remain inconclusive [19], certain studies have indicated that erythritol may elicit different responses compared to other sweeteners such as xylitol [20]. In a randomized, controlled crossover trial, erythritol was found to reduce energy intake during a subsequent ad libitum test meal in healthy participants [21]. Furthermore, erythritol and xylitol have been reported to differentially impact brain networks involved in appetite regulation, potentially suggesting distinct

mechanisms underlying their effects on satiety [22]. In a pilot study, erythritol-sweetened beverages were found to induce satiety and suppress ghrelin to a greater extent than aspartame, supporting erythritol's potential role in promoting satiety and assisting in weight management [23]. However, caution is necessary when considering the use of erythritol and other artificial sweeteners for weight management, as their long-term effects on obesity and overall health are not yet fully understood [24].

Erythritol: Oral health and hygiene

Erythritol also has benefits for oral health. Unlike sucrose, erythritol is not metabolized by oral bacteria such as Streptococcus mutans, leading to lower acid production and reduced risk of tooth decay [7]. Additionally, erythritol can inhibit bacterial adhesion to tooth surfaces and decrease the formation of dental plaque [7]. Based on the research findings, erythritol affects the microstructure and metabolic profiles of the biofilm composed of Streptococcus gordonii and Porphyromonas gingivalis, which may lead also to a decreased risk of gum disease and tooth decay [25].

Erythritol: Potential long-term risks

A research study investigating the long-term effects of erythritol, an artificial sweetener, found that it was associated with an increased risk of major adverse cardiovascular events (MACE). This association was confirmed in independent US and European validation cohorts. At physiological levels, erythritol was shown to enhance platelet reactivity in vitro and increase thrombosis formation in vivo. In a pilot intervention study, erythritol ingestion in healthy volunteers led to significant and sustained increases in plasma erythritol levels, surpassing thresholds associated with heightened platelet reactivity and thrombosis potential [26]. The study examines the possible connections between the artificial sweetener erythritol and the risk of cardiovascular disease. While the research offers intriguing insights, it's crucial to emphasize that it does not conclusively prove that erythritol is harmful. The study primarily investigates plasma erythritol levels, which might not be directly linked to dietary consumption, as erythritol can be synthesized within the human body endogenously from glucose via the pentose-phosphate pathway (PPP) [27]. Moreover, the erythritol quantities used in the research may not accurately reflect common dietary intake in the UK and Europe. To gain a better understanding of the potential health effects of erythritol and determine safe usage levels, more research is needed, including long-term observational studies and well-designed clinical trials.

Conclusions:

Erythritol has emerged as a promising low-calorie sweetener due to its unique characteristics and potential therapeutic applications, particularly in the management of type 2 diabetes and obesity [1][2]. Research has shown that erythritol has minimal impact on blood glucose levels and insulin secretion [13], making it an attractive alternative to traditional sugars for people with diabetes type 2. Studies also indicate that erythritol may reduce calorie intake and aid in weight loss [15][16]. Moreover, erythritol has demonstrated potential anti-inflammatory effects in high-fat diet-induced small intestinal inflammation [17] and the capacity to modulate gastrointestinal satiation hormone release [18]. In the case of dental health, studies have shown that erythritol can be beneficial, particularly in preventing tooth decay and gum diseases [7][25]. While there is some evidence to suggest a possible link between the use of erythritol as an artificial sweetener and an increased risk of major adverse cardiovascular events, the underlying mechanisms remain unclear and further research is needed to confirm this association [26]. Although the current evidence suggests that erythritol may have some potential benefits, especially in the case of type 2 diabetes, obesity, and dental health, it is important to note that its risks and limitations have not been fully established. Therefore, further research is needed to better understand the potential drawbacks and determine if erythritol can be a safe and effective tool for improving health [5][7][11][12][14][19][20][26].

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