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Positioning on the Use of Polyols as Table Sweeteners

Posicionamento sobre o uso de polióis como adoçantes de mesa

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Abstract

Polyols are poorly digestible carbohydrates present in small amounts in some fruits and vegetables. Xylitol and erythritol are used as table sweeteners. These compounds are widely used in the food industry due to their low-calorie content. Erythritol is the only noncaloric polyol. Xylitol is the sweetest of the polyols, being the only one with sweetness equivalent to sucrose, but with one third of its calories. Clinical studies have shown reductions in the number of plaques, in counts of *Streptococcus mutans*, and in the number of dental cavities in individuals receiving erythritol and xylitol. Xylitol is also capable of reducing the growth and adherence to the oropharynx of bacteria that cause acute otitis media, such as *Streptococcus pneumoniae,* and several studies have shown that it reduces the risk of this bacterial infection in children. In addition to these effects, polyols can also have beneficial effects on metabolism. Both erythritol and xylitol have been approved by the European Union for use as sweeteners for several years, and replacing sugar with polyols decreases caloric intake, which can reduce body weight and blood glucose in individuals with obesity and type 2 diabetes mellitus. The safety of polyols is recognized by the Food and Drug Administration (FDA), who classifies them as compounds generally recognized as safe (GRAS). Thus, based on available scientific data, the daily consumption of both substances is associated with several benefits and does not represent any risk to human health.

Keywords
- polyols
- xylitol
- erythritol
- sweeteners
- benefits

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Resumo

Os polióis são carboidratos pouco digeríveis presentes em pequenas quantidades em algumas frutas e vegetais. Xilitol e eritritol são utilizados como adoçantes de mesa. Estes compostos são amplamente utilizados na indústria alimentícia devido ao seu baixo teor calórico. O eritritol é o único poliol não calórico. O xilitol é o mais doce dos polióis, sendo o único com doçura equivalente à sacarose, mas com um terço das calorias da mesma. Estudos clínicos mostraram reduções no número de placas bacterianas, nas contagens de *Streptococcus mutans* e no número de cáries em indivíduos recebendo eritritol e xilitol. O xilitol também é capaz de reduzir o crescimento e a adesão à orofaringe de bactérias causadoras de otite média aguda, como o *Streptococcus pneumoniae,* e vários estudos mostraram que ele reduz o risco desta infecção bacteriana em crianças. Além destes efeitos, os polióis também podem exercer efeitos benéficos sobre o metabolismo. Tanto o eritritol quanto o xilitol são aprovados pela União Europeia para uso como adoçante há vários anos, e a substituição do açúcar por polióis diminui a ingestão calórica, o que pode reduzir o peso corpóreo e a glicemia de indivíduos com obesidade e diabetes mellitus tipo 2. A segurança dos polióis é reconhecida pela Food and Drug Administration (FDA, na sigla em inglês), que os classifica como compostos geralmente reconhecidos como seguros (GRAS, na sigla em inglês). Assim, com base nos dados científicos disponíveis, o consumo diário de ambas as substâncias está associado a vários benefícios e não representa qualquer risco para a saúde humana.

Palavras-chave
- polióis
- xilitol
- eritritol
- adoçantes
- benefícios

Introduction

The palate represents a property of chemoperception located in the tongue, triggered by chemical compounds present in food and beverages. A wide variety of these compounds can be grouped into one of five taste categories, depending on the quality of the gustatory sensation evoked: sweet, umami, bitter, sour, and salty. Sweet and umami indicate the presence of sugars and amino acids, respectively, and are attractive to animals; on the other hand, bitter and sour represent potential toxins and spoiled ingredients, and are aversive. Finally, the salty taste is present in sodium chloride, and can be attractive or aversive, depending on the status of the hydroelectrolytic balance found in the organism.[1]

Until the 18th century, when sucrose was first taken, honey represented the main source of sweetness used by humans. After that, cane and beet sugar took a leading position. Nowadays, excessive sugar consumption is considered a public health problem in industrialized nations, which has fostered the acceleration of the search for alternatives.[2] Many synthetic sweeteners are available for industrial use, but the public interest in natural sweeteners has grown in recent years due to the increased concern of the population about their health and the content of artificial additives added to food.[2,3]

All sweet-flavored compounds are detected by a single type of receptor, the heterodum TAS1R2-TAS1R3, expressed on the surface of the taste buds. This receptor belongs to the superfamily of extracellular receptors coupled to g protein, with a cysteine-rich section and seven trans-mukic domains. It is known that different compounds can activate the receptor both in the extracellular part and in the cysteine-rich portion or in the transmid-brach loops, which explains the amplitude of the chemical space of sweeteners, including natural sugars, saccharic alcohols, terpenoid glycosides, some amino acids, polyphenols, and sweet-flavored vegetable proteins.[2]

►**Fig. 1** illustrates how the various types of sweeteners can be classified. In this classification, there are two large groups: intense sweeteners, that is, high sweetening potency and bulk sweeteners, which require a greater amount for sweetening similar to the sucrose molecule (international sweetness standard).[5] In the case of intense sweeteners, they are divided according to the origin of their molecules: synthetic and occurring in nature. Bulk sweeteners are divided between carbohydrate sweeteners and sugar alcohols or polyols, which can be found in nature. The polyols, which are the focus of the present review, are inserted in the context of bulk sweeteners being generally nutritious, except for erythritol, which does not alter glycemic levels.

Polyols

Saccharic alcohols, also known as polyhydric alcohols or polyols, are poorly digestible carbohydrates obtained by replacing an aldehyde group with a hydroxyl. Polyols are naturally present in small amounts in fruits and in certain types of vegetables or mushrooms and are recognized under regulatory aspect as generally recognized as safe (GRAS). Seven polyols are recognized by the European Union as sweeteners: sorbitol, mannitol, isomalt, maltitol, lactitol, xylitol, and erythritol (►**Table 1**); however, only the last two are used as table sweeteners. Polyols, if consumed in excess, can have laxative effect or cause gastrointestinal symptoms such as flatulence, distension, and abdominal pain.[6]

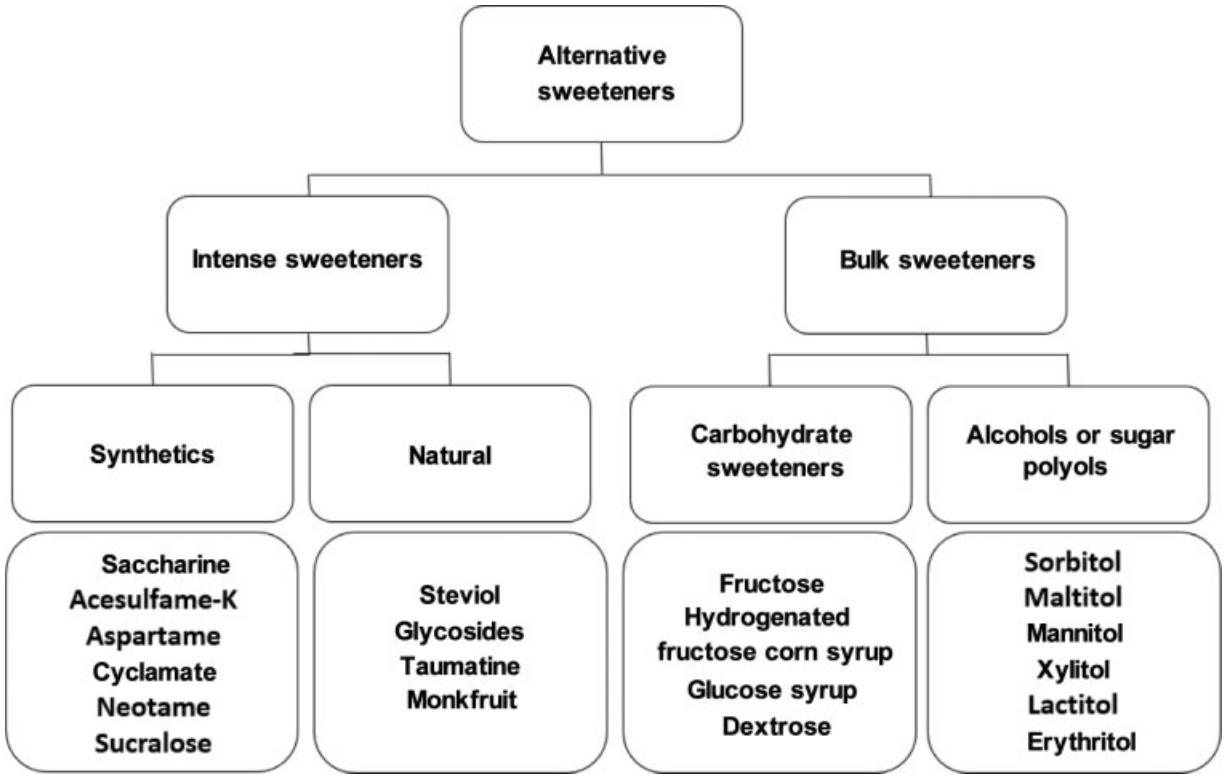

Fig. 1 Classificação de adocantes alternativos. Adapted from: Jain, T., & Grover, K. (2015). Sweeteners in human nutrition. *International Journal of Health Sciences and Research*, *5*(5), 439–451.[4] Adoçantes alternativos = Alternative sweeteners; Adoçantes intensos = Intense sweeteners; Adoçantes a granel = Bulk sweeteners; Sintéticos = Synthetics; Naturais = Natural; Adoçantes de carboidratos = Carbohydrate sweeteners; Álcoois ou polióis de açúcar = Alcohols or sugar polyols; Sacarina = Saccharine; Acesulfame-K = Acesulfame-K; Aspartame = Aspartame; Ciclamato = Cyclamate; Neotame = Neotame; Sucralose = Sucralose; Esteviol = Steviol; Glicosídeos = Glycosides; Taumatina = Taumatine; Fruta-dos-monges = Monkfruit; Frutose = Fructose; Xarope de milho de frutose hidrogenada = Hydrogenated fructose corn syrup; Xarope de glicose = Glucose syrup; Dextrose = Dextrose; Sorbitol = Sorbitol; Maltitol = Maltitol; Manitol = Mannitol; Xilitol = Xylitol; Lactitol = Lactitol; Eritritol = Erythritol.

Table 1 Relative sweetness and glycemic index of the polyols (adapted from[2,7])

Name	Chemical family	Caloric value (kcal/g)	Relative sweetness*	Glycemic index	Derived from
Erythritol	Monoscaride alcohol	0.2	0.63	1	Glucose
Xylitol	Monoscaride alcohol	3	0.97	12	D-xylose
Mannitol	Monoscaride alcohol	1.6	0.50	2	Fructose
Sorbitol	Monoscaride alcohol	2.6	0.58	4	Glucose
Isomalt	Dissaccharide alcohol	2	0.54	2	Sucrose
Lactitol	Dissaccharide alcohol	2	0.35	3	Lactose
Maltitol	Dissaccharide alcohol	3	0.87	35	Corn syrup with high maltose content

*in relation to sucrose.

Polyols are widely used in the food industry due to their low caloric content, although they have a lower sweetness than sucrose. For this reason, it is common to find on the market the association of a polyol with a high-potency sweetener to achieve the desired level of sweetness and flavor. In addition to providing a sweet taste, polyols (such as carbohydrates) also provide texture, moisture, contribute to preservation and give a refreshing sensation in the mouth, the latter characteristic being a consequence of the dissolution of the polyols representing an endothermic reaction. The property of enhancing the taste of food and beverages without causing a late bitter sensation (called "after taste") is described in erythritol studies.[2,6,7]

Another characteristic of polyols is their chemical property of stability at high temperatures, enabling its use in the preparation and cooking of various types of food. This applicability provides erythritol and xylitol, the main polyols used as table sweeteners, the increasing use as alternatives to sucrose, including for culinary purposes.[6]

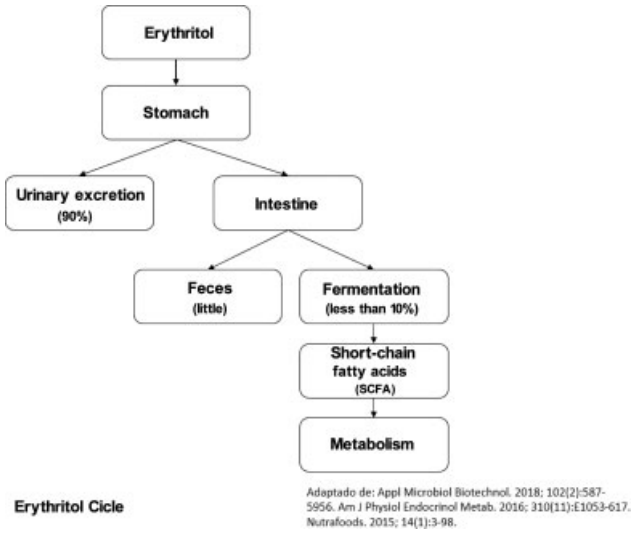

Fig. 2 Eritritol = Erythritol; Estômago = Stomach; Excreção urina (90%) = Urinary excretion (90%); Intestino = Intestine; Fezes (pouco) = Feces (little); Fermentação (menos de 10%) = Fermentation (less than 10%); Ácidos Graxos de cadeia curta (AGCC) = Short-chain fatty acids (SCFA); Metabolismo = Metabolism; Ciclo Eritritol = Erythritol Cicle.

Erythritol, or 1,2,3,4-Butanetretol, is a polyol that is present in some fruits (melons, peaches), vegetables, mushrooms, and fermented products such as wine, sake, beer, and soy sauce. Its individual consumption from natural sources is estimated between 25 mg/day in the United States to 106 mg/day in Japan.[6,8]

Erythritol is the only noncaloric polyol, which represents a great advantage for a sugar substitute. Due to its small molecular size, 90% of the erythritol consumed is absorbed into the small intestine. However, it is not metabolized and is excreted unchanged in the urine. The small fraction of nonabsorbable erythritol is eliminated unchanged in feces because, unlike other polyols, erythritol is not fermented by bacteria from the digestive tract (►**Fig. 2**). Thus, erythritol does not generate glycemic or insulinemic response, and the caloric contribution from by-products of fermentation is null, as there is no conversion of this polyol into substances such as volatile fatty acids, for example. Due to the absence of bacterial fermentation, erythritol is the polyol with better gastrointestinal tolerability and does not cause adverse events even when consumed in amounts two to four times greater than other polyols. The gastrointestinal tolerability of erythritol is also higher than that of fibers such as inulin and sugars such as lactose.[8]

Like other polyols, erythritol is not used as substrate for bacteria causing dental cavities, such as *Streptococcus mutans*. In fact, as will be discussed below, there is evidence that regular consumption of erythritol (and also xylitol) decreases plaque, thus contributing to the prevention of cavities.[9]

Xylitol is a five-carbon polyol produced from d-xylose that was discovered in 1891 and has been used as a sweetener since 1960. It can be found in nature in various fruits and vegetables, cereals, and mushrooms, and it is considered a habitual component of the human diet, although in amount $< 1\%$. Xylitol is the sweetest of polyols, the only one with sweetness equivalent to sucrose, but with a third of its calories, and without the residual taste of some of the synthetic sweeteners.[6,8]

Between 25 and 50% of the xylitol ingested is absorbed into the small intestine. When it reaches the portal circulation, xylitol is sequestered by the liver and metabolized in the pathway of pentoses-phosphate, a metabolism that does not depend on insulin.[6,8] About 50 to 75% of unabsorbed xylitol becomes substrate for bacterial fermentation in the large intestine, which means that this polyol has a prebiotic effect. The products of this fermentation are predominantly short-chain fatty acids (for example, acetate, propionate, butyrate) and small amounts of gases (H_2, CH_4 and CO_2). The gastrointestinal tolerability of xylitol is higher than that observed with sorbitol, and daily doses of 30 to 40 g per day do not usually cause adverse events such as flatulence or diarrhea.[8]

Erythritol and Xylitol in Oral Health

Dental cavities are a multifactorial disease in which host factors interact with pathogens and dietary factors; bacteria ferment carbohydrates from the diet (mainly sugars), forming acids (such as lactic acid and others) that lead to demineralization, initially micro, and then macroscopic, with progression and eventual cavitation.[8,10,11]

Thus, three conditions are necessary for the development of cavities: a cariogenic pathogen (*S. mutans*, *S. sanguis* and others), an environment that predisposes to the appearance of cavities (essentially by the presence of sugar in the diet) and a susceptible host (for example, one with lower salivary flow).[12]

The relationship between the consumption of foods with sugar and the incidence of dental cavities has been known for a long time and is supported by laboratory evidence and clinical evidence. The main acid-producing bacteria from the fermentation of sugars are from the genera *Streptococci* and *Lactobacilli*. While a high-sugar diet provides substrate for bacterial metabolization and local acid production, favoring cavity genesis, a diet low in sugars and other fermentable carbohydrates and rich in calcium favors the remineralization of teeth.[13]

Because they do not represent a substrate for oral bacterial fermentation, erythritol and xylitol are not cariogenic, a fact known for many years.[14,15] However, existing evidence on the relationship of these polyols with oral health goes beyond this neutral effect and suggest a cariostatic action.

Mäkinen et al.[9] conducted a 6-month-long study aimed at determining the effects of erythritol, xylitol, and sorbitol, administered in the amount of 7 g/day in the form of chewing gum, on the growth of dental plaque in healthy adolescents. The 136 participants were examined at the beginning of the study, and at 3 and 6 months, with dental evaluation and collection of saliva and dental plaque samples. Six months after the intervention, a statistically significant reduction was observed in the weight of the plate, in the number of plaques, and in the counts *of S. mutans* in the participants who received erythritol and xylitol, but not sorbitol.

The clinical result of these microbiological findings was demonstrated by several other authors, compiled in the systematic review of the literature published by Deshpande et al.[16] The authors specifically evaluated the cariostatic effects of xylitol, xylitol-sorbitol, sorbitol, and sorbitol-mannitol, always administered as a chewing gum. Preventive effects against cavities of the order of 58% (xylitol), 53% (xylitol-sorbitol), and 20% (sorbitol) were observed. For the association of sorbitol and mannitol, the observed reduction in the incidence of cavities was not statistically significant. A recent systematic review and meta-analysis, which included 12 interventional studies that evaluated the use of sugar-free chewing gum (containing polyols) in the incidence of cavities, confirmed these results, concluding by the protective effect of polyols, both in adults and in children (prevention fraction [PF], 28%; 95% confidence interval [CI]: 7–48%). In the 8 studies evaluating xylitol, the PF was of 33% (95%CI: 4–61%).[17]

The main finding of another systematic review that included 10 studies evaluating a total of 5,903 participants was that the use of a fluoride toothpaste containing 10% xylitol was associated with a 13% reduction in the incidence of cavities in children and in adults compared with fluoride toothpaste without xylitol (PF = -0 .13; 95%CI: - 0.18–- 0.08).[18]

Honkala et al.[19] conducted a randomized, double-blind, controlled 3-year study to assess the effects of daily consumption of 7.5 g of a polyol (erythritol, xylitol, or sorbitol) in the form of a bullet. At the end of the intervention period, the group receiving erythritol had a lower incidence of dentin cavities compared with the groups that received xylitol and sorbitol after 24 and 36 months. At the end of the intervention, the same participants discontinued the use of polyol and were followed for 3 additional years, at the end of which it was observed that the cavity stasis promoted by the consumption of erythritol was still maintained.[20]

The mechanism underlying the cariostatic effect of the polyols includes stimulating salivary flow, leading to the whitening of substances for cavity genesis of tooth surfaces; increased acid buffering and remineralization capacity; reduction of acid production due to the hypoacidifying nature of polyols; and inhibition of growth of *S. mutans*.[21] The increase of the concentration of polyols in the dental plate was accompanied by an increase in soluble calcium in it. It is postulated that this calcium acts as a contributing factor to the remineralization of incipient lesions in dental enamel.[22]

In addition, the consumption of xylitol for a prolonged time seems to select strains of *S. mutans* "resistant" to xylitol, which deplete more easily to saliva compared with the original strains, which results in a smaller number of bacteria in the plates.[23] There is also evidence that maternal consumption of xylitol is associated with a reduction in the transmission of cariogenic bacteria to children.[24–26]

Xylitol in the Prevention of Acute Otitis Media

Otitis media represents one of the most prevalent infectious diseases in childhood, with an additional impact represented by cases that progress to complications, such as preventable hearing loss.[27] The pathophysiology of acute otitis media includes a fundamental stage, which is the colonization of the upper airway mucosa by pathogenic bacteria, which invade the middle ear from the eustachian tube. Among the bacterial agents, *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most prevalent.[28]

In addition to the inhibiting effect on the growth of *S. mutans* already mentioned, it has been reported that xylitol, at concentrations of 1 and 5%, has significantly reduced the growth of α-hemolytic streptococci, including *S. pneumoniae* and *Streptococcus mitis*,[29] and that at a concentration of 5% reduced the adhesion of *S. pneumoniae* and *H. influenzae* to the epithelial cells of the oropharynx.[30]

Thus, several studies were conducted to evaluate whether regular xylitol consumption would be associated with protection against otitis media. Danhauer et al.[31] conducted a review of the literature in 2010, identifying 4 eligible randomized controlled trials ($n = 3.133$). The consumption of 2 g of xylitol 5 times a day (after meals and snacks) was associated with an average reduction in the risk of otitis of 32% (relative risk [RR] = 0.68; 95%CI = 0.57–0.83). The authors concluded that xylitol could be considered a form of prevention of otitis media, and that further studies would be needed, especially to evaluate other ways of administering the substance to children who are not yet able to chew a gum.

A systematic review and meta-analysis published by the Cochrane collaboration evaluated xylitol for the prevention of acute otitis media in children $\leq$ 12 years old; 5 clinical studies were included, totaling 3,405 individuals. Prophylactic administration of xylitol (in the form of chewing gum, tablets, or syrup) decreased by 25% the RR of acute otitis media in healthy children attending daycare ($n = 1,826$) compared with the control group (RR = 0.75; 95%CI = 0.65–0.88). There was also a 36% reduction in the use of antibiotics (RR = 0.64; 95%CI = 0.42–0.97), with no increase in the incidence of gastrointestinal adverse events compared with the control group. However, xylitol did not reduce the incidence of otitis media in children with active respiratory disease or in those predisposed to otitis media.[32]

Erythritol and Xylitol as Adjuvants in the Treatment of Obesity and Diabetes Mellitus

According to the most recent recommendations of the *American Diabetes Association* (ADA), the replacement of sugar by nonnutritive sweeteners can help reduce the consumption of carbohydrates and calories, which can lead to a reduction in blood glucose and weight, better by metabolic control.[33]

The evidences of benefits of polyols seem to transcend the simple reduction of caloric intake, and involve abdominal adipogenesis and metabolism of the enteroinsular axis; Amo et al. demonstrated that, in rats fed a high-fat diet, xylitol intake for 8 weeks was associated with a reduction in abdominal fat, in insulinemia and in insulin resistance.[34] Rahman et al.[35] added increasing amounts of xylitol to the diet of diabetic rats and observed, in animals receiving the highest dose (10% xylitol), lower body weight gain, reduced blood glucose levels, and improved morphology of pancreatic islets.

Human studies have also shown interesting results regarding the effects of polyols on enteric hormones. Wölnerhanssen et al.[36] conducted a study with 20 individuals (10 normal weight, 10 obese), and reported that both erythritol and xylitol increased concentrations of cholecystokinin (CCK) and glucacon-like peptide 1 (GLP-1), while blood glucose and insulinemia values did not change (erythritol) or were only mildly affected (xylitol). In addition, a delay in gastric emptying was observed. The study, however, was not able to observe reduced appetite or increased satiety, possibly due to its design (effect of acute consumption of high doses of polyols). Perhaps, long-term studies with lower doses can detect this effect, which is desirable for patients with type 2 diabetes mellitus (DM2) and obesity.

There is, however, no homogeneity in the findings. Overduin et al.[37] studied hunger/satiety and the response of intestinal and pancreatic peptides to meals containing sucrose or erythritol and observed that polyol consumption induced a blood glucose excursion and a lower plasma insulin response than sucrose-containing meals. However, the effects on intestinal hormones, including GLP-1, PYY, acute satiety, postprandial hunger, satiety 4 hour after meal, subsequent energy intake, and preference for sucrose showed no significant difference between isovolumetric meals containing erythritol or sucrose. Only in normal weight volunteers, hunger decreased significantly after consumption of an isocaloric meal containing erythritol when compared with the control meal containing sucrose.

Finally, an action that must be mentioned in relation to polyols, especially to erythritol, is its potential as an antioxidant. It has been shown that the elimination activity of the hydroxyl radical of erythritol is comparable to mannitol, recognized for its antioxidant properties. Erythritol inhibited hemolysis induced by oxidative stress in a concentration-dependent manner, which indicated that antioxidant properties also manifest in cellular systems. Additionally, the same authors demonstrated in vivo benefits, with improvement of endothelial function in the aorta of diabetic rats supplemented with erythritol.[38]

It is known that endothelial changes play a key role in vascular dysfunction associated with DM2.[39] Flint et al.,[40] studying the effects of erythritol on the endothelium, found that the acute consumption of 24 g of erythritol resulted in an improvement in endothelial function ($p = 0.005$), and chronic consumption caused a reduction in endothelium stiffness ($p = 0.02$). Endothelial function after acute erythritol intake compared with chronic consumption improved in relation to baseline, suggesting sustained improvement with chronic treatment.

Erythritol and Xylitol Safety Data

An extensive review presenting the risk assessment of sweeteners adopted by the European Union was published in 2006, including erythritol and xylitol. The approval of any substance as a food additive on that continent requires an extensive dossier that includes: (1) results of studies on absorption, distribution, and metabolism in experimental animals and humans; (2) in vitro and in vivo toxicological tests; (3) technical data regarding the identification of the substance, purity, stability, and potential degradation products; (4) description of the manufacturing process; (5) demonstration of the value generated for consumers; (6) description of the proposed applications and levels of use in different food categories; and (7) estimated exposure resulting from the proposed use.[41]

Xylitol was approved in the European Union for use as a sweetener in 1984, and a comprehensive toxicological assessment was considered for its approval, including studies on metabolism, acute and subchronic toxicity and chronic toxicity in rats and dogs, as well as a three-generation reproduction study conducted in rats, teratogenicity studies, effects of exposure through breastmilk, and results of various in vitro and in vivo mutagenicity tests. Data in humans on tolerability to xylitol administered orally were also reviewed. Xylitol was not genotoxic. Changes in metabolism and physiology associated with the ingestion of large amounts of polyols were also observed in long-term studies with xylitol. Data in humans do not suggest any problem related to the urinary excretion of oxalate, but consumption of ~ 50 g/day causes diarrhea.[42]

Nine years later, the European Union approved erythritol as a sweetener. Again, the approval was based on numerous studies conducted on animals and humans. The committee concluded that the effects observed in animal studies were attributable to physiological and adaptive responses to the rapid absorption and excretion of erythritol and the osmotic activity of the unabsorbed erythritol in the intestine. Erythritol had a laxative effect, but in high doses of other polyols (level without observable effect [NOEL] of ~ 0.5 g/kg of body weight for a single dose).[43] The safety of erythritol consumption has been confirmed by regulatory authorities worldwide; this polyol was approved as a food additive in Japan in 1990,[44] its safety was confirmed by the World Health Organization (WHO) in 2000,[45] and in 2001 the Food and Drug Administration (FDA) recognized erythritol as safe, with a last update and classification as GRAS in 2018.[46]

In line with the opinion issued by the European Union, the Joint Committee of the Food and Agriculture Organization (FAO)/WHO of Food Additives, after extensively evaluating preclinical and clinical toxicity data, concluded that it was not necessary to specify the daily intake of xylitol and erythritol. Thus, based on the available scientific data, the daily consumption of both substances does not pose a risk to human health.[45,47]

As important as the aforementioned data, which supported the approval of erythritol and xylitol as food additives, are the safety information from the meta-analyses of clinical studies that evaluated the use of polyol in their indications, in adults and in children, at the doses in which clinical benefit was observed.

In the systematic review and meta-analysis conducted by Riley et al.,[18] the authors aimed to evaluate the safety of xylitol use in the prevention of cavities in children and adults. Seven of the 10 studies included in the review provided safety data, and 4 of them reported that no adverse

Table 2 Summary of the main practical points of the present positioning

Polyol	Maximum doses recommended (41–46)	Safe for use during pregnancy and breastfeeding	Safe in regard to carcinogenicity/ mutagenicity	Safety studies with limits much higher than recommended doses (41–47)	Glycemic index (2,7)	Main benefits
Erythritol	40 g/day (1 g/kg in children)	Yes (48)	Yes	Yes	1	- Replaces saccharose with no cavity genesis effect (14, 15) - Dental plaque reduction, contributing to cavity prevention (9) - Potential metabolic benefits (34–40)
Xylitol	40 g/day (1 g/kg in children)	Yes (25, 26, 48)	Yes	Yes	12	- Replace saccharose with no cavity genesis effect (14, 15) - Dental plaque reduction, contributing to cavity prevention (9) - Reduction of risk of acute otitis media (31)

Summary box: Use recommendation and main scientific evidences of health benefits.

effects were observed with the use of xylitol. When reported, the adverse effects included: oral sores, cramps, constipation, flatulence, and diarrhea. In the meta-analysis performed by Newton et al.,[17] no adverse events were reported in any of the included studies. In the systematic review conducted by Danhauer et al.,[31] which included four studies, only one of them reported minimal adverse effects associated with xylitol use (gastrointestinal discomfort, flatulence, softened stools), which were similar in the experimental and control groups. Finally, in a study by Azarpazhooh et al.[32] study, no differences were found in the frequency of adverse events related to the gastrointestinal tract between the groups that received xylitol and the control group during the follow-up period of 1,826 healthy children (2 studies; RR 1.43; 95%CI: 0.74–2.75), 1,277 children with respiratory infection (1 study; RR 2.82; 95%CI: 0.61–13.00), and 326 children with predisposition to present with acute otitis media (1 study; RR 1.04; 95%CI: 0.92–1.16).

Polyols are naturally-occurring compounds and are detectable in fetal and maternal samples in normal pregnancies. For this reason, moderate consumption of this class of sweeteners is considered safe for use during pregnancy.[48] Studies conducted with the objective of evaluating the impact of maternal xylitol consumption on the colonization of newborns by *S. mutans* recruited women in the 6th month of gestation and followed them up until their children were 9 months old. No adverse outcomes to the maternal-fetal complex were reported with intrauterine exposure or through breast milk.[25,26]

Erythritol is a simple alcohol, which does not covalently bind to proteins. It is not a reactive compound and has no active metabolites. Thus, erythritol is unlikely to have an allergenic potential when consumed with food. No allergic reaction to erythritol was reported during clinical studies conducted with it. The allergenic potential of erythritol was investigated in rats and guinea pigs, with negative results in hypersensitivity reaction induction tests, increased production of IgE antibodies, active systemic anaphylaxis test, homologous passive skin test, late-type hypersensitivity test, and passive hemagglutination test.[43] Allergic reactions to erythritol have been reported rarely in the literature (all in Japanese patients), manifested as urticaria or anaphylaxis, without the underlying pathophysiological mechanism (mediated or not mediated by IgE) being elucidated.[49–53] According to one of the authors mentioned, the estimated prevalence of hypersensitivity to erythritol is < 1 per 1 million individuals.[49]

Like erythritol, xylitol is a low molecular weight substance with no reactive side chains that does not conjugate to macromolecules. Thus, the allergenic potential of xylitol is low. Reports of hypersensitivity reactions to xylitol are even rarer compared with erythritol. The case of a 2-year-old child with a previous history of cow milk allergy (with an episode of anaphylactic reaction) and egg allergy, who presented anaphylaxis after ingesting 400 mg of xylitol for the first time, was reported. The prick-test and the basophil activation test confirmed xylitol sensitization, the family was instructed not to offer polyol to the child, and she has remained asymptomatic ever since.[54]

A single case of xylitol contact dermatitis was reported in a 45-year-old Japanese individual who presented with oral lesions 5 months after starting consumption of a chewing gum containing polyol. The contact of chewing gum with the skin, after the product has been placed in the back pocket of the pants, led to the appearance of an erythematosus lesion. The patch test with xylitol confirmed that it was the causal agent of the reaction.[55] ►**Table 2**

Conclusion

The guidelines published by the WHO in 2015 on the consumption of sugars in adults and children recommend reducing the consumption of free sugars in the diet to $< 10\%$ of the total caloric intake, mainly due to the relationship between sugar consumption and body weight gain and tooth decay.[56] Polyols represent a class of sweeteners that is safe for human consumption and is approved globally.

In addition to being sugar substitutes with lower caloric content, some polyols, such as xylitol and erythritol, have health-beneficial properties, such as anticariogenic effect and prevention of the occurrence of otitis media; there is also the potential for beneficial effects for the metabolism of obese individuals and diabetes mellitus.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Taruno A, Nomura K, Kusakizako T, Ma Z, Nureki O, Foskett JK. Taste transduction and channel synapses in taste buds. Pflugers Arch 2021;473(01):3–13
2 Chéron J-B, Marchal A, Fiorucci S. Natural Sweeteners. Reference Module in Food Science 2018
3 Philippe RN, De Mey M, Anderson J, Ajikumar PK. Biotechnological production of natural zero-calorie sweeteners. Curr Opin Biotechnol 2014;26:155–161
4 Jain T, Grover K. Sweeteners in human nutrition. Int J Health Sci Res 2015;5(05):439–451 [4]
5 Saraiva A, Carrascosa C, Raheem D, Ramos F, Raposo A. Natural Sweeteners: The Relevance of Food Naturalness for Consumers, Food Security Aspects, Sustainability and Health Impacts. Int J Environ Res Public Health 2020;17(17):E6285
6 Grembecka M. Sugar alcohols—their role in the modern world of sweeteners: a review. Eur Food Res Technol 2015;241:1–14
7 *Sugar Alcohols (Polyols) and Polydextrose Used as Sweeteners in Foods - Food Safety - Health Canada*, H. Canada, Editor. 2005
8 O'Donnell K, Kearsley MW. Sweeteners and Sugar Alternatives in Food Technology. 2nd Edition ed. 2012UK: Wiley-Blackwell
9 Mäkinen KK, Saag M, Isotupa KP, et al. Similarity of the effects of erythritol and xylitol on some risk factors of dental caries. Caries Res 2005;39(03):207–215
10 Usha C, R S. Dental caries - A complete changeover (Part I). J Conserv Dent 2009;12(02):46–54
11 Rathee, M. and A. Sapra. Dental Cavities. 2020
12 Shaw JH. Causes and control of dental caries. N Engl J Med 1987; 317(16):996–1004
13 Touger-Decker R, van Loveren C. Sugars and dental caries. Am J Clin Nutr 2003;78(04):881S–892S
14 Kawanabe J, Hirasawa M, Takeuchi T, Oda T, Ikeda T. Noncariogenicity of erythritol as a substrate. Caries Res 1992;26(05): 358–362
15 Mäkinen KK, Bennett CA, Hujoel PP, et al. Xylitol chewing gums and caries rates: a 40-month cohort study. J Dent Res 1995;74 (12):1904–1913
16 Deshpande A, Jadad AR. The impact of polyol-containing chewing gums on dental caries: a systematic review of original randomized controlled trials and observational studies. J Am Dent Assoc 2008;139(12):1602–1614
17 Newton JT, Awojobi O, Nasseripour M, et al. A Systematic Review and Meta-Analysis of the Role of Sugar-Free Chewing Gum in Dental Caries. JDR Clin Trans Res 2020;5 (03):214–223
18 Riley P, Moore D, Ahmed F, Sharif MO, Worthington HV. Xylitol-containing products for preventing dental caries in children and adults. Cochrane Database Syst Rev 2015;(03):CD010743
19 Honkala S, Runnel R, Saag M, et al. Effect of erythritol and xylitol on dental caries prevention in children. Caries Res 2014;48(05): 482–490
20 Falony G, Honkala S, Runnel R, et al. Long-Term Effect of Erythritol on Dental Caries Development during Childhood: A Posttreatment Survival Analysis. Caries Res 2016;50(06):579–588
21 Van Loveren C. Sugar alcohols: what is the evidence for caries-preventive and caries-therapeutic effects? Caries Res 2004;38 (03):286–293
22 Steinberg LM, Odusola F, Mandel ID. Remineralizing potential, antiplaque and antigingivitis effects of xylitol and sorbitol sweetened chewing gum. Clin Prev Dent 1992;14(05):31–34
23 Gupta M. Sugar Substitutes: Mechanism, Availability, Current Use and Safety Concerns-An Update. Open Access Maced J Med Sci 2018;6(10):1888–1894
24 Burt BA. The use of sorbitol- and xylitol-sweetened chewing gum in caries control. J Am Dent Assoc 2006;137(02):190–196
25 Nakai Y, Shinga-Ishihara C, Kaji M, Moriya K, Murakami-Yamanaka K, Takimura M. Xylitol gum and maternal transmission of mutans streptococci. J Dent Res 2010;89(01):56–60
26 O'Connell AC. Use of xylitol chewing gum in mothers may delay transmission of mutans streptococci to their infants. J Evid Based Dent Pract 2011;11(01):62–64
27 Monasta L, Ronfani L, Marchetti F, et al. Burden of disease caused by otitis media: systematic review and global estimates. PLoS One 2012;7(04):e36226
28 Murphy TF. Otitis media, bacterial colonization, and the smoking parent. Clin Infect Dis 2006;42(07):904–906
29 Kontiokari T, Uhari M, Koskela M. Effect of xylitol on growth of nasopharyngeal bacteria in vitro. Antimicrob Agents Chemother 1995;39(08):1820–1823
30 Kontiokari T, Uhari M, Koskela M. Antiadhesive effects of xylitol on otopathogenic bacteria. J Antimicrob Chemother 1998;41(05): 563–565
31 Danhauer JL, Johnson CE, Corbin NE, Bruccheri KG. Xylitol as a prophylaxis for acute otitis media: systematic review. Int J Audiol 2010;49(10):754–761
32 Azarpazhooh A, Lawrence HP, Shah PS. Xylitol for preventing acute otitis media in children up to 12 years of age. Cochrane Database Syst Rev 2016;(08):CD007095
33 Evert AB, Dennison M, Gardner CD, et al. Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report. Diabetes Care 2019;42(05):731–754
34 Amo K, Arai H, Uebanso T, et al. Effects of xylitol on metabolic parameters and visceral fat accumulation. J Clin Biochem Nutr 2011;49(01):1–7
35 Rahman MA, Islam MS. Xylitol improves pancreatic islets morphology to ameliorate type 2 diabetes in rats: a dose response study. J Food Sci 2014;79(07):H1436–H1442
36 Wölnerhanssen BK, Cajacob L, Keller N, et al. Gut hormone secretion, gastric emptying, and glycemic responses to erythritol and xylitol in lean and obese subjects. Am J Physiol Endocrinol Metab 2016;310(11):E1053–E1061
37 Overduin J, Collet TH, Medic N, et al. Failure of sucrose replacement with the non-nutritive sweetener erythritol to alter GLP-1 or PYY release or test meal size in lean or obese people. Appetite 2016;107:596–603
38 den Hartog GJ, Boots AW, Adam-Perrot A, et al. Erythritol is a sweet antioxidant. Nutrition 2010;26(04):449–458
39 Tabit CE, Chung WB, Hamburg NM, Vita JA. Endothelial dysfunction in diabetes mellitus: molecular mechanisms and clinical implications. Rev Endocr Metab Disord 2010;11(01):61–74
40 Flint N, Hamburg NM, Holbrook M, et al. Effects of erythritol on endothelial function in patients with type 2 diabetes mellitus: a pilot study. Acta Diabetol 2014;51(03):513–516
41 Mortensen A. Sweeteners permitted in the European Union: safety aspects. Scandinavian Journal of Food and Nutrition 2006;50(03):104–116
42 Scientific Committee for Food. Sweeteners (opinion expressed on 14 September 1984). Reports of the Scientific Committee on Food (16th series). EUR 10210 EN. Luxembourg: Commission of the European Communities. Available from: http://ec.europa.eu/comm/food/fs/sc/scf/reports/scf_reports_16.pdf 1985
43 Scientific Committee for Food. Erythritol (opinion expressed on 5 March 2003. Available from: https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out175_en.pdf 2003
44 Boesten DMPHJ, et al. Health effects of erythritol. Nutrafoods 2015;14:3–9
45 Joint FAO/WHO Expert Committee on Food Additives (JECFA) – WHO Food Additives Series 44: Sweetening Agent – Erythritol - http://www.inchem.org/documents/jecfa/jecmono/v44jec03.htm 2000

46 GRAS Determination of Erythritol for use in Human Food. https://www.fda.gov/food/generally-recognized-safe-gras/gras-notice-inventory 2018
47 Joint FAO/WHO Expert Committee on Food Additives (JECFA) – WHO Food Additives Series 18: Sweetening Agent – Xylitol - http://www.inchem.org/documents/jecfa/jecmono/v18je16.htm 1983
48 Pope E, Koren G, Bozzo P. Sugar substitutes during pregnancy. Can Fam Physician 2014;60(11):1003–1005
49 Yunginger JW, Jones RT, Kita H, Saito K, Hefle SL, Taylor SL. Allergic reactions after ingestion of erythritol-containing foods and beverages. J Allergy Clin Immunol 2001;108(04):650
50 Hino H, Kasai S, Hattori N, Kenjo K. A case of allergic urticaria caused by erythritol. J Dermatol 2000;27(03):163–165
51 Shirao K, Inoue M, Tokuda R, et al. "Bitter sweet": a child case of erythritol-induced anaphylaxis. Allergol Int 2013;62(02): 269–271
52 Sugiura S, Kondo Y, Ito K, Hashiguchi A, Takeuchi M, Koyama N. A case of anaphylaxis to erythritol diagnosed by CD203c expression-based basophil activation test. Ann Allergy Asthma Immunol 2013;111(03):222–223
53 Kurihara K, Suzuki T, Unno A, Hatano M. [Case of 5 year-old boy with anaphylaxis due to erythritol with negative prick test and positive intradermal test]. Arerugi 2013;62(11):1534–1540
54 Okamoto K, Kagami M, Kawai M, et al. Anaphylaxis to xylitol diagnosed by skin prick test and basophil activation test. Allergol Int 2019;68(01):130–131
55 Hanakawa Y, Hanakawa Y, Tohyama M, Yamasaki K, Hashimoto K. Xylitol as a causative agent of oral erosive eczema. Br J Dermatol 2005;152(04):821–822
56 Guideline: Sugars intake for adults and children. Geneva: World Health Organization; 2015
57 Adoçantes calóricos e não calóricos. Food Ingredients Brazil. 2010;(15):22–35

