SWEETENERS AND METABOLIC DISEASES: XYLITOL AS A NEW PLAYER

RĂZVAN VASILESCU[1], ANA MARIA IONESCU[2], ANDRADA MIHAI[3], SIMONA CARNICIU [3] and CONSTANTIN IONESCU-TÎRGOVIŞTE[3]

[1] Clinical Hospital Colentina – Department of Diabetes, Nutrition and Metabolic Diseases, Stefan Cel Mare str.19-21, Bucharest
[2] Emergency Hospital Floreasca, Floreasca 8, Bucharest
[3] National Institute of Diabetes, Nutrition and Metabolic Diseases "N.C. Paulescu", Bucharest, Romania

Received July 26, 2011

Sweeteners are divided by their sources into natural and synthetic and by their nutritional values into nutritive and non-nutritive. Xylitol is a five carbon natural sweetener found in fibrous vegetables and fruit, which offers many health benefits to human. On oral health xylitol prevents dental caries, retards demineralization of tooth enamel, promotes remineralization of tooth enamel, increases saliva production, relieves dry mouth, protects salivary proteins, improves breath odor, reduces infections in the mouth and nasopharynx. Xylitol is a low glycaemic sweetener, which does not cause the sharp increase in blood sugar level usually seen following consumption of other carbohydrates. Thus, xylitol can be recommended as a sugar-free sweetener suitable for diabetics as well as for the general population seeking a healthier lifestyle. The reduced caloric value of xylitol, 40% fewer calories in comparison with ordinary sugar, is consistent with the objective of weight control. In conclusion, xylitol could be the ideal sweetener.

Key words: sweeteners; xylitol; obesity; diabetes.

INTRODUCTION

Sweet taste is apart salt, bitter and sour, one of the four fundamental and appreciated tastes. Sugar is a symbol of the refined food and possibly the most powerful in several negative effects. In fact, sugar is not a food but more a chemical compound (sacharosse – a bi-molecule formed by a molecule of glucose and the other of fructose) which in small amounts (~ 15g in 100 g in sugar beet) could be a useful nutrient component. Unfortunately, in some developed countries, the sugar consumption per capita is sometimes more than 70 kg/year. For that, in USA is considered by some nutritionist a "true white poison". In fact, humans were not designed to eat a large amount of sugar, white or brown, corn syrup, sucrose, dextrose, glucose fructose, lactose, maltose, barley malt, honey, rice syrup and maple syrup[1].

A sweetener is any natural and/or artificial substance that provides a sweet taste in food and beverages. It is known that sugar can induce weight gain and reactive hypoglycemia, both in children and adults. It raises triglycerides and LDL-cholesterol, acting as cardiovascular risk factor. In children, more than in adults, the consumption of sugar can act as an addiction, stimulating the increase intake along the time. That is why the replacement of sugar with non-nutritive and nutritive sweeteners is a strategy had in view over the world[2].

Natural and chemical sweeteners

Sweeteners are divided in *natural* (sugar, fructose, sorbitol, xylitol) and synthetic (saccharine, cyclamate, aspartame). In addition to their sweetening power, they are used during food preparation for fermentation, baking, food browning and caramelization. Sugar and other natural sweeteners such as honey and corn syrup have server as a main

sweetening agent for most food products. However, these sweeteners have some side effects being linked with health problems such as tooth decay, obesity and diabetes.

Nutritive sweeteners act both to provide a sweet taste and to be a source of calories or energy, whereas non-nutritive sweeteners (such as cyclamate, saccharine, aspartame) are sweet without the added calories. Nutritive sweeteners include refined sugar, honey, high fructose, corn syrup, dextrose and several sugar alcohols (sorbital, for instance). Sucrose (formed by two molecules one of glucose and one of fructose) is known as table sugar. Its caloric power is of 4.1 kcal/g. Fructose (known as "fruit sugar", because is present in fruits) also produces 4 kcal/g. A group of related compounds includes corn sugar (glucose or dextrose), milk sugar (lactose) and malt sugar (maltose). All this molecules contains 6 atoms of carbon. Xylitol release 2 kcal/g *vs* 4kcal/g for glucose. Otherwise, xylitol has been routinely used in infusion therapy as a source of energy[2,3]. This is based on the non-involvement of insulin in the initial metabolism of administrated xylitol. That is why the glycemic index of xylitol is very low *vs*. glucose or other carbohydrates sources. For that, xylitol has been proposed as a preventive compound both in type 2 diabetes and obesity. The multifaceted nature of xylitol is related to its chemical profile. Xylitol is a substance that can produce abundant NADH and NADPH. These molecules can affect the cellular redox potential. Finally, this altered redox potential can regulate the level of coenzymes and hormones[4]. According to Makinen, xylitol could be looked as a reservoir of "extra" hydrogen atoms, which can be enzymatically deposited onto other molecules, eventually generating reduced forms of several coenzymes. In addition, the metal-complexing[5] and water displacing capacity[6] of xylitol are specific properties which must be explored in future studies.

Non-nutritive artificial sweeteners

Currently there are seven non-nutritive or low calorie sweeteners used in various countries:

– **Saccharin** is a non-caloric sweetener. A tablet contains 25 mg and is oldest synthetic sweetener used in our country. Because it crosses the placenta, its use in pregnancy is questionable, even though it has been remove of potential carcinogens (effect observed at very high doses in some animal models). Children may be particularly susceptible to developing diarrhea from ingestion of as little as 0.5 g/kg body weight of polyols. Polyols should not be used to treat hypoglycemia.

– **Aspartame** (from amino acid class) has a 200 times sweeter power than sugar. Is a dipeptide formed by two amino acids (one of them phenylalanine) and it is counter indicated in people with phenylketonuria. Although aspartame contains 4 kcal per gram, it is consumed in very small amounts, contributing negligible energy.

– **Cyclamates** are sodium or calcium salt of cyclamic acid. Are 30 times sweeter than sugar. A tablet of natrium cyclamates contains 100 mg and maximum doses is 2.5 mg/kg per day. Due to some same side effects they have been removed from the market several decades ago.

– **Sucralose** is an only low calorie sweetener made from sugar. It is 600 times sweeter than sugar, contains no calories and is highly stable under a variety of processing conditions.

– **Acesulfame potassium** did not influence the blood glucose in diabetic patients.

– **Alitame** (and **neotame)** is about 8000 times sweeter than sugar and was approved by FDA (Food and Drug Administration) in 2000, but is not yet on the market.

– **Tagatose**, knownd as D-tagatose is a low caloric sweetener derived from lactose.

A sweet alternative: xylitol

Xylose is a compound discovered in XIX century by two groups of researchers, one in Germany, leaded by Fischer [7] and the second, independently in France, by Bertrand, in 1891, so that the "discovery" of xylitol must be credited to two groups of researchers.

Xylose and xylitol and his pathway derive from the glycolise (Fig.1). The interest for industrial production of xylitol sharply increased in England in the 2nd World War, when sugar was difficult to find on the market. Using a technology of extraction from various hardwood trees like birch has been obtained a crystalline sweet product, which was used till today as sweetener in preparation of various cafeteria products.

Xylitol is a white, crystalline, natural carbohydrate that is classically included amount the sugars. Otherwise, *xyl* in Greek means wood. It is found not only in fibrous vegetables (wood scraps), but also in fruits, and mainly in corn crops, from where is now regularly extracted.

By the mid-1950, Touster and his coworkers concluded that xylitol is formed in the human body[8]. This discovery was related with the

investigation of L-xylulose, a characteristic urinary sugar in essential pentosuria. This is a rare, recessive genetic defect.

Xylitol is a pentose which appears during the metabolisation of glucose, among the various pentoses, such as rybulose-5 phosphate or xylulose-5 phosphate. It is produces by human body during a normal metabolism at to 15 g per day. Chemically xylitol is included among the polyols as sugar alcohols, of course without inebriating effects. Polyols possess functional hydroxyl groups. It is important to note that xylitol differs from other polyols like sorbitol: xylitol is a 5-carbon pentatol, whereas sorbitol is a 5 carbon hexitol. That is important because sorbitol can support the growth of cariogenic bacteria in the mouse. However, this bacteria is unable to utilize xylitol for growth, so that they prevent a cavity-causing pathology. For that it is said that xylitol is a friend of teeth, having antibacterial qualities[9,10].

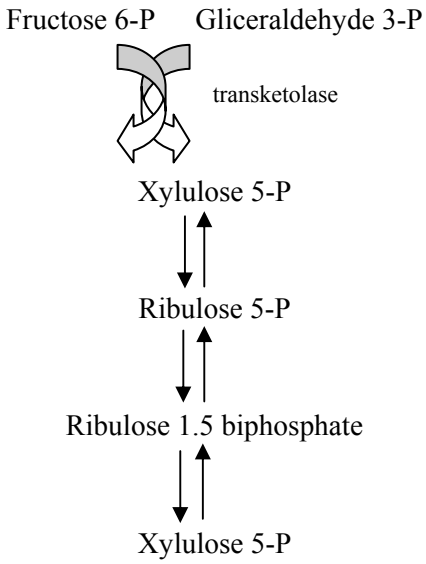

Fig. 1. The xylitol pathway derives from glycolises.

Xylitol is tolerated well even in large servings. Very sensitive individuals may need to adapt to tolerate higher intakes. An adaptative increase in the activity levels of an enzyme (a polyol dehydrogenase) greatly increases the rate of xylitol absorption in a few days. This is not the case with xylitol. Xylitol is slowly absorbed and metabolized, resulting in minimal changes of insulin. In comparison with ordinary sugar has 40% fewer calories (Table 1).

Xylitol binds with calcium and other polyvalent cations, contributing to remineralization of enamel. The calcium-xylitol complexes facilitate calcium absorbtion through the gut wall. This suggests xylitol may play a role in preventing osteoporosis. This hypothesis has been tested in experimental animals.

Xylitol also reduces the incidence of perio-dontal diseases.

Advantages of using xylitol to improve blood sugar control are presented in Table 2.

Table 1

Clinically proved effects of xylitol (ref. 5, 11, 12, 13)

Inhibits plaque and dental cavities by 80%
Retards demineralization of tooth enamel
Promotes remineralization of tooth enamel
Increases saliva production
Relieves dry mouth (xerostomia)
Protects salivary proteins, has a protein-stabilizing effect
Improves breath odor
Reduces infections in the mouth and nasopharynx

Table 2

Positive effects of xylitol on carbohydrate metabolism

Excellent taste, versatility and equivalent sweetness
Low calorie
Very low glycemic index
Minimal effect on blood sugar and insulin levels
Slow, steady release of energy
Antiketogenic – lowers serum free fatty acid levels and improves peripheral glucose utilization
Increases absorption of B vitamins and calcium
Improve dental health
Inhibits yeast, including Candida albicans
Decreases glycation of proteins, reduces AGEs
Reduces carbohydrate cravings and binge eating

Xylitol slows stomach-emptying and its low glycemic index and mostly insulin-dependent metabolism makes it ideal for maintaining steady levels of insulin and blood sugar. This increases satiety and reduces bingeing. Xylitol is incomepletely absorbed, and only a portion of what is absorbed slowly converts glucose. An important effect of xylitol metabolism is the activation of the glutathione antioxidant system which helps to squelch free radicals generated by heavy exercise, thereby reducing oxidative damage. Because xylitol is efficiently and steadily converted to glucose and glycogen it may be useful when coupled with other carbohydrates for recovery after heavy exercise. Likewise, it may be valuable for carbohydrate loading by packing glycogen after a depletion phase.

Xylitol used between meals maintains a steady trickle of energy. Unabsorbed xylitol acts like dietary fiber, helping to maintain healthy gut function. Partial bacterial fermentation here produces volatile short chain fatty acids that utilized existing insulin-dependent energy pathways.

Xylitol is a sweet-tasting sugar substitute that has been approved for use in more than 35 countries. Consumption of xylitol is associated with a significant reduction in tooth decay, resulting in fewer cavities and resolution of periodontal disease. Xylitol has been shown to contribute to increased bone density, weight loss, stabilization of blood sugar and lowering of insulin levels. Additional benefits include the dates from Table 3.

Table 3

Benefits of Xylitol

Increases energy by enhancing ATP production
Increase utilization of fat
Replenishes glycogen
Anabolic – keeps biosynthetic pathways open
Anticatabolic – helps maintain lean muscle mass
Antioxidant – generates NADPH, keeping glutathione in an active state
Increases endurance
Reduces free radical and oxidative damage

CONCLUSION

In conclusion, by its chemical structure, xylitol could be the ideal sweetener because its high sweetening capacity and very low caloric content. For that, it is useful both in prevention of obesity and in diabetic patients due to its very low glycemic index.

In addition, because xylose can not be used by various bacteria present in oral cavity, its role in prevention of paradontopathy and dental caries it is of great importance.

REFERENCES

1. Sellman S., *Xylitol: Our Sweet Salvation?* The SPECTRUM vol. 4, No. 8, February **2003**, p. 23.
2. Carr CJ, Krantz JC., *Metabolism of the sugar alcohols and their derivatives*. Adv Carbohydr Chem **1943**; 1:115-192
3. Georgieff M., Moldawer LL, Bistrian BR, Blackburn GL., *Xylitol an energy source for Intravenous nutrition after trauma.* J parenter Enteral Nutr **1985**; 9:199-209.
4. Mäkinen K., *The Rocky Road of Xylitol to its Clinical Application* J Dent Res **2000;** 79(6):1352-1355.
5. Angyal SJ, Greeves D., Mills JA., *Complexes of carbohydrates with metal cat ions. III Conformations of aditols in aqueous solutions.* Aust J Chem **1974**; 27:1447-1456.
6. Lewin S., *Displacement of water and its control of biochemical reactions.* Chapters 1 and 2. London and New York: Academic Press, **1974**.
7. Fischer E., Stahel R., *Zur Kenntniss der Xylose***.** Ber Dtsch Chem Ges **1891**; 24:528-539.
8. Touster O, Shaw DRD., *Biochemistry of the acyclic polyols.* Physiol Rev **1962**; 42:181-225.
9. Birkhed D., *Cariologic aspects of xylitol and its use in chewing gum: a review.* Acta Odontol Scand **1994**; 52:116-127.
10. Edgar WM., *Sugar substitutes, chewing gum and dental caries – a review.* Br Dent J **1998**; 184:29-3.