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A REVIEW ON THE SUGAR ALTERNATES

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ABSTRACT: Background: Due to the rise of diabetes as the primary health issue nowadays, there is a need for a sweetener, which apart from fulfilling the role of a sweetener, also complies with the normal body metabolism. **Objectives:** To review the literature available on the different sugar alternates present globally. **Methods:** A literature search has been done on the various substitutes of sugar present, belonging to various categories such as artificial sweeteners, natural sweeteners, novel sweeteners, and sugar alcohols. **Results:** A vast variety of sugar substitutes are available, which are suitable in one or more ways. The main matter of concern is the selection of the right sweetener according to the requirement. **Conclusion:** Apart from being of low calorie, these sweeteners provide multiple advantages; therefore by choice of right alternate, consumers are benefitted with the sweet taste, thereby complying with the normal body metabolism.

INTRODUCTION: Today the primary goal of diabetes management is to keep the blood glucose level under control. Today consumers have a free choice of food products. They must choose the right food to comply with dietary recommendations, and at the same time, the food industry can contribute to this change by providing a variety of adapted food products. There is a need for a sweetener, which apart from fulfilling the role of a sweetener, also complies with the normal body metabolism. This has directed the food industry to discover several forms of intense alternative sweeteners, which have made possible to offer the consumer the sweet taste without the calories [1]. The sensory properties of food are highly influenced by the sensory properties like taste, smell, texture, and appearance.

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A sweetener is a food additive, which mimics the effect of sugar on taste. Therefore, they are called sugar substitutes. Consumers often select those foods, which are composed of low-calorie sweetener because they want the taste of sweetness without added calories. The dietary option that such product provides may be especially helpful in the management of obesity or diabetes mellitus [2]. A sugar substitute is a food additive that mimics the taste of sugar but usually has less food energy. These are both natural and synthetic. The synthetic-based ones are referred to as artificial sweeteners [3]. These artificial sweeteners also called non-nutritive or low-calorie sweeteners. These are intense sweeteners, providing no or a few calories per gram. They are used in beverages, dietary products, medicines, *etc.* [4] Artificial sweeteners have gained attention as nutritional tools that provide a sweet taste without the extra energy derived from foods and drinks containing caloric sugars and thus may assist in weight-loss plan adherence [5]. They play an important role in the treatment of diabetes mellitus and obesity as well as in the maintenance of dental care.

They are cost effective and have a longer shelf life [6]. Some people choose to limit their food energy intake by replacing high energy sugar or corn syrup with other sweeteners having little or no food energy. This allows them to eat the same foods they normally would [7]. This review article deals with a detailed outlook on some of the sugar substitutes available.

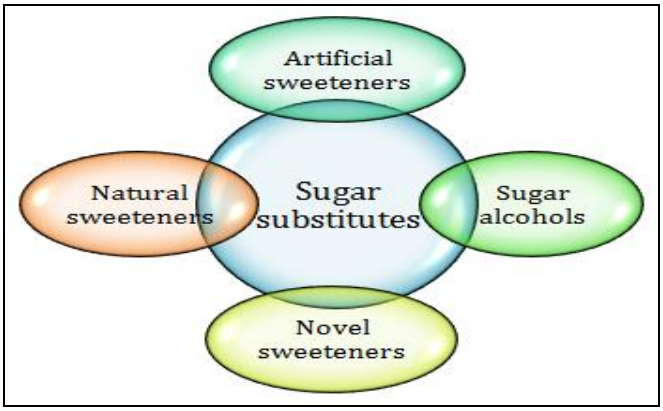

FIG. 1: SUGAR SUBSTITUTES

Sugar substitutes are basically of four types as mentioned in **Fig. 1**, which can be mainly by their origin as follows:

- Artificial sweeteners
- Natural sweeteners
- Novel sweeteners
- Sugar alcohols [8]

Artificial sweeteners are chemically synthesized, are low in calories. Some of them are discussed as following as shown in **Fig. 2**.

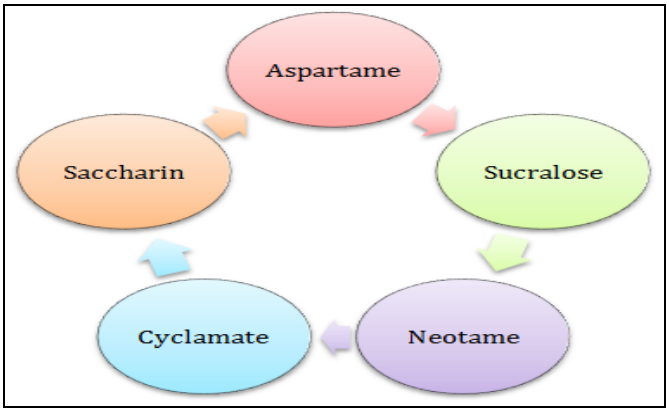

FIG. 2: ARTIFICIAL SWEETENERS

Aspartame: It was discovered by James Schlatter, a chemist in 1965. It is chemically-(L-*α*-Aspartyl)-L-phenylalanine, 1-methyl ester. It is an artificial, non-saccharide sweetener. It is a formed by the combination of the amino acids aspartic acid and phenylalanine as shown in **Fig. 3**. [9] Aspartame is used to sweeten a variety of low and reduced calorie foods and beverages including tabletop sweetener, also sweetens gum, breakfast cereal, and other dry products. Aspartame provides energy of 4 calories per gram. Aspartame is unstable if subjected to prolonged heating and therefore cannot be used in baking or cooking. It also decomposes in liquids during storage. Upon ingestion, aspartame splits into its natural residual components, such as aspartic acid, phenylalanine, methanol, which further break into formaldehyde, formic acid and diketopiperazine [10, 11].

We eat about 5 g aspartame annually, equivalent to another kg of sucrose, whose 4000 kcal (16 740 kJ) could generate 0.5 kg gain in weight. But evidence that aspartame prevents weight gain or obesity is generally inconclusive. One of the most significant advantages of aspartame is that people who have diabetes or are on a low-calorie diet can enjoy a variety of desserts that are low in fat and calories but are still enjoyable. They reduce the levels of blood sugar, which is excellent for people who have diabetes. Moreover, products that are made with aspartame are much lower in calories, than foods and beverages that contain sugar.

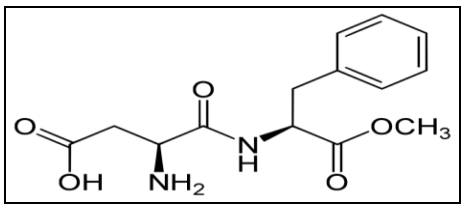

FIG. 3: ASPARTAME

The disadvantages of it are effects on gums, headaches, rashes on the skin. Two Japanese companies have reported one formation route to produce aspartame directly by incubating micro-organisms with L-aspartic acid and the methyl ester of phenylalanine [12, 13].

Saccharine: It was originally listed as GRAS, in 1996, the ban imposed on it earlier was withdrawn due to the reasonable certainty of no harm from Saccharin. It is an excellent low-calorie sugar-free product [14]. Saccharin, which is chemically 1,1-dioxo-1,2-benzothiazole-3-one, as shown in figure 4 is 300 times sweeter than sucrose. It is heat stable and is not metabolized in the body. Apart from

being used as a tabletop sweetener, it is also used to sweeten soft drinks, baked goods, jams, canned fruit, candy, salad dressings, dessert toppings, and chewing gum. Consumption of saccharin-sweetened products can benefit people with diabetes as the substance goes directly through the human digestive system without being digested.

To monitor the risk factors as headaches, breathing difficulties, diarrhea and skin problems associated with the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives had established an acceptable daily intake of 5 mg/kg body weight for saccharin [15]. One animal study has shown that consumption of products containing saccharin may lead to increased body weight and obesity [16, 17].

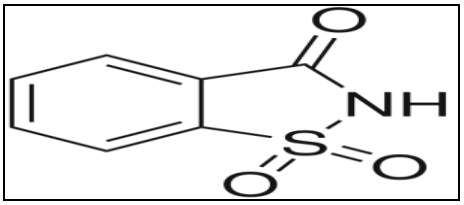

FIG. 4: SACCHARINE

Sucralose: This organochlorine sweetener is a synthetic disaccharide which is chemically1, 6-dichloro-1, 6-dideoxy -*β* -D -fructofuranosyl -4-chloro- 4-deoxy-α-D-galactopyranoside, as shown in figure 5, provides 3.3 cal/gm. Its sweetness potency is approximately 385 to 650 fold higher than sucrose.

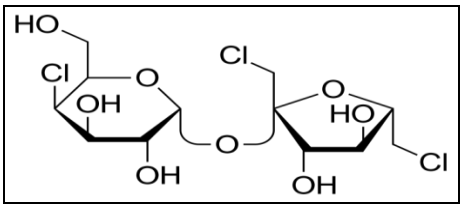

FIG. 5: SUCRALOSE

In 1998, the U.S. Food and Drug Administration approved sucralose for use in various categories that included water-based as well as fat-based products either in foods or in beverages, *e.g.*, frozen dairy desserts, baked goods, confectionaries, puddings, chewing gum, etc. It is made from sugar, so tastes like sugar [18]. GLP-1 was elevated in human subjects (both in healthy volunteers and in individuals with type 1 diabetes) who drank a caffeine-free diet soda sweetened with sucralose and ace-K when compared with carbonated water control. The advantages of it are many as it mixes well, has a longer shelf life with no bitter after taste. The disadvantages of it are digestion, causing diarrhea, gas, and bloating [19].

Cyclamate: Cyclamate was discovered in 1937 by graduate student Michael Sveda, while working in the lab he put his cigarette down on the lab bench, tasted sweet on later use led to the discovery of sweet taste of cyclamate. It is sodium or calcium salt of cyclamic acid or cyclohexane sulfamic acid, as shown in **Fig. 6**.

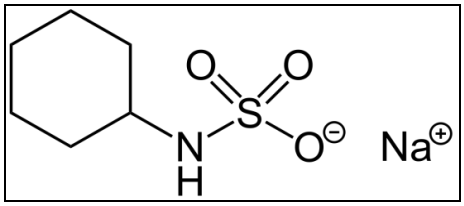

FIG. 6: CYCLAMATE

It is 30-50 times sweeter than sucrose. But it is least potent of all the commercially used artificial sweeteners. It is often used in combination with other artificial sweeteners, especially saccharin; the mixture of 10 parts cyclamate to 1 part saccharin is commonly used for various purposes. It is cheap and is stable under heating. Cyclamate is available in the market in tablet form as well as in the way of liquid by the diabetics. As it is stable to heat, therefore suitable for use in cooking and baking [20]. Sodium cyclamate is used as a non-nutritive sweetener and the analogous calcium salt used mainly in low sodium diets. Cyclamate offers advantages to people with diabetic diets to satisfy their taste for sweets without affecting blood sugar, which gives them flexibility in meal planning with the resulting variety of diabetic foods available and is less expensive as well. The main disadvantages are its carcinogenic effects on bladder [21].

Neotame: Neotame is a derivative of a dipeptide compound of the amino acids - aspartic acid and phenylalanine. Chemically it is (3S) -3 -(3, 3-Dimethylbutylamino)-4-[[(2S)-1-methoxy-1-oxo-3-phenylpropan-2-yl]amino]-4-oxobutanoic acid, as shown in **Fig. 7**. It provides zero calories per gram. Neotame has been developed as a sweetener with a high degree of sweetness and is obtained by N-alkylating aspartame. Its degree of sweetness varies according to the kind of food and blend composition. It is 7000 to 13,000 times and about

30 to 60 times sweeter than sugar and aspartame respectively. Its advantages are that it has zero calories per serving as well as zero glycemic indexes. This makes it suitable as part of a diabetic diet. It doesn't show any significant toxicity and is non-carcinogenic. The disadvantage of it is the toxicity exerted by it more severe than aspartame. Neotame is quickly metabolized and eliminated, without getting accumulated in the body. The hydrolysis of methyl ester metabolizes it by esterase which is present throughout the body [22]. The degree of sweetness varies according to the kind of food and blend composition[23]. Neotame is a highly potent sweetener that can be used to modify and enhance the flavor of foods and beverages [24].

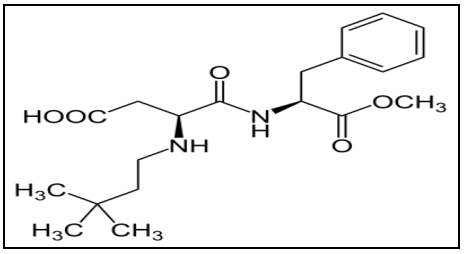

FIG. 7: NEOTAME

Natural Sweeteners: These are found in nature, occur mostly in the form of fruits. They carry a nutrition value and are non-carcinogenic as compared to synthetic sweeteners. They have larger sweetening powers even in smaller concentrations. They have low calorific value and are thermostable as well. Some important ones are as follows:

- Honey
- Stevia
- Liquorice
- Hesperidin
- Thaumatin

Honey: Honey is a naturally occurring product, having numerous beneficial effects. It has been reported to contain about 200 substances. It consists of mainly fructose and glucose, along with fructooligosaccharides and many amino acids, vitamins, minerals, and enzymes. It contains flavonoids such as kaempferol, quercetin, ferulic acid, and ascorbic acid. Sugar accounts for 95-99% of honey dry matter. One oz. of honey contains 86 calories. The essential carbohydrates of honey are constituted by fructose ranging from 32.56 to 38.2% and glucose ranging from 28.54 to 31.3 %, which represents 85-95% of total sugars [25].

Almost all natural honey contains flavonoids such as apigenin, pinocembrin, kaempferol, quercetin, galangin, chrysin and hesperetin, phenolic acids such as ellagic, caffeic, p-coumaric and ferulic acids. Ascorbic acid, tocopherols, catalase (CAT), superoxide dismutase (SOD), reduced glutathione (GSH), Millard reaction products and peptides. Most of those compound work together to provide a synergistic antioxidant effect. The disadvantage is that the glycemic index of honey is higher than sugar; therefore it raises blood sugar levels more quickly. This is because of its higher fructose content, and the absence of trace minerals. The advantage of honey is that it has slightly more calories than sugar, although it is sweeter, so less amount may be required [26, 27, 28, 29, 30].

***Stevia*:** Being native of South America, *Stevia* is a green, leafy plant has been used for therapeutic purposes for many centuries. The plant is cultivated for its strong, sweet flavor. There are more than 100 species of the stevia plant, but most important of all- *Stevia rebaudiana* is excellent as a sweetener, due to the compound rebaudioside A, the sweetest-flavored component of the *Stevia leaf*. Rebaudioside A is a steviol glycoside, having aglycone in the form of steviol that is 200 times sweeter than sugar. It provides zero calories per gram. The glycoside contains only glucose as its monosaccharide moieties. It includes four glucose molecules in total with the mean glucose of the triplet connected to the main steviol structure at its hydroxyl group, and the remaining glucose at its carboxyl group forming an ester bond.

The glucosyltransferase UGT76G1 from *Stevia rebaudiana* is a chameleon enzyme in the targeted biosynthesis of the next-generation premium stevia sweeteners, rebaudioside D (Reb D) and rebaudioside M (Reb M). *Stevia* offers advantages to diabetics in the suppression of plasma glucose levels and significantly increases glucose tolerance, resulting in stabilization of blood sugar levels. The disadvantages of it are that people with sensitivity to sugar alcohol may experience bloating, abdominal cramps, nausea, and diarrhea, though one type of sugar alcohol, erythritol, poses less risk of symptoms than others [31, 32, 33, 34, 35].

Liquorice: Glycyrrhizin is found in liquorice root of a small leguminous shrub, *Glycyrrhiza glabra* L.

from Europe and Central Asia. Glycyrrhizin or 20-*β*-carboxy-11-oxo-30-norolean-12-en-3*β*-yl-2-O-β-d-glucopyranosyl-α-d-glucopyranosiduronic acid is a triterpenoid glycosides. Glycyrrhizin is 50-100 times sweeter than sucrose and has a slow onset of sweetness followed by a lingering licorice-like aftertaste. It has a sweet woody flavor, which limits its use as a sweetener in pure or crude form.

Glycyrrhizin helps to enhance food flavors, masks bitter flavors, and increases the perceived sweetness level of sucrose. It provides zero calories per gram. The advantages of it are that liquorice root also contains substances with an anti-diabetic effect. These amorfrutins not only reduce blood sugar; they are also anti-inflammatory and are very well tolerated. The disadvantages of consuming liquorice daily for several weeks or longer can cause severe side effects including high blood pressure, low potassium levels, weakness, paralysis, and occasionally brain damage in otherwise healthy people. Many manufacturing companies use it as a sweetener for many products to mask the bitter taste [36, 37, 38, 39, 40, 41, 42, 43].

Recently one compound named mono ammonium glycyrrhizin was known as MAG has gained popularity in Europe. Recently in 2018 the research team of a startup named Diabport Healthcare Private Limited, operating in North India, came up with a particular combination of mono-ammonium glycyrrhizin and *Stevia* which has shown tremendous publicity among diabetic patients as it produced effects which do not cause aftertaste as with other artificial sweeteners. The mentioned formulation is readily available and is recommended by physicians and healthcare professionals.

Hesperidin: is a flavonoid glycoside as shown in figure 8 present in citrus fruits, mainly belonging to the Rutaceae family. Its aglycone form is called hesperetin, which is a form of flavonoid. Its name is derived from the word "hesperidium", for fruit produced by citrus trees. Hesperidin was first isolated by French chemist Lebreton 1828, from the white inner layer of citrus peels. The advantage of it is that it prevents diabetic retinopathy in people with diabetes whereas its disadvantage is that it causes stomach pain and upset, diarrhea, and headache [44].

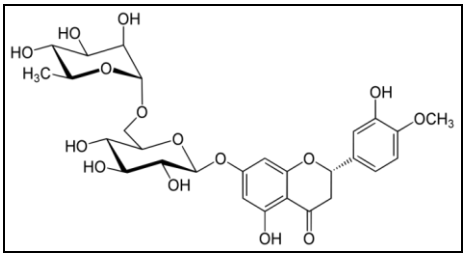

FIG. 8: HESPERIDIN

Thaumatin: *Thaumatococcus daniellii* is indigenous to Africa, is the natural source of thaumatin, which is an intensely sweet protein, commonly used as a sweetener. The aril of it is rich in thaumatin, which is at least 3000 times as sweet as sucrose. It provides 4 cal/gm. In West Africa, the aril is traditionally used for sweetening bread, wines and sour food. Seeds on consumption, even after one hour, the sweet taste is retained, that even sour materials are taken also taste very sweet. Since the mid-1990s, the food and confectionery industry uses it as sweetener and flavor enhancer. It is used as a non-caloric natural sweetener. The advantage of it is that because of not being a carbohydrate, is too good for consumption for people with diabetes. The disadvantages of it are the induction of heart disease, metabolic syndrome, and strokes [45-49].

Novel Sweeteners: Novel sweeteners or sweetening materials not previously known or used in the food materials as food additives and as such would generally be reviewed within existing regulations which deal with food additives [24]. Novel sweeteners are hard to fit into any particular category because of their manufacturing process. For example, despite being promoted as natural sweeteners, highly-processed *Stevia* preparations along with other additives have been approved by the FDA, but whole-leaf *Stevia* and crude *Stevia* extract have been not. Besides from being calorie-free, *Stevia rebaudiana*, the plant from which the popular *Stevia* sweetener is made, has been linked to various health benefits.

Novel sweeteners include:

- Stevia extract,
- Tagatose,
- Trehalose [50, 51]

***Stevia*:** is obtained from the leaves of the plant species *Stevia rebaudiana*. It is used as a sweetener as well as a sugar substitute. The active compounds

of *Stevia* are steviol glycosides mainly stevioside and rebaudioside, which have up to 150 times the sweetness of sugar. It provides zero calories per gram. These are heat-stable, pH-stable, and not fermentable. Some of its extracts have a bitter or liquorice-like aftertaste at high concentrations. Its taste has a slower onset and longer duration than that of sugar [52, 53]. *Stevia* and other derivatives are small, herbaceous shrub of the Asteraceae family. *Stevia* leaves contain a complex mixture of sweet diterpene glycosides, including stevioside, steviolbiosides, rebaudioside (A, B, C, D, E, and F), and dulcoside A. Dry leaves of *Stevia* are sweeter approximately 10-15 times than sucrose. The use of sweeteners containing stevia or steviol glycosides is recommended for diabetics and obese persons, as they are non-toxic and non-addictive, and can be cooked or baked.

However, very little attention has been directed towards the safety of these sweeteners in bakery products and their role in the formation of heat-induced compounds. It has been reported that substituting sucrose with *Stevia* decreased the acrylamide level eight times. Replacing reducing saccharides with polyols in the dough formulation led to a decrease in the extent of browning reactions because the formation of HMF was limited during the baking process. Similar behavior has been described for acrylamide. Meanwhile, there are no data in the recent literature on the influence of sugar replacers on the formation of 3-MCPD, which is 3-monochloropropane-1,2-diol or 3-chloropropane-1,2-diol and its esters [54, 55, 57, 57, 58].

Trehalose: Trehalose, also known as mycose or tremalose, is a natural alpha-linked disaccharide, containing an α,α-1,1-glucoside bond between two α-glucose units. Chemically it is(2R,3S,4S,5R,6R)-2-(Hydroxymethyl)-6-[(2R, 3R, 4S, 5S, 6R)-3, 4, 5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyoxane-3,4,5-triolas shown in **Fig. 9**. In 1832, H.A.L. Wiggers discovered trehalose from ergot of rye. In 1859, Marcellin Berthelot isolated it from trehala manna and named it trehalose. It provides 4 cal/gm. Microbes can synthesize it like bacteria, fungi, plants, and invertebrate animals. It is a non-reducing sugar. It is implicated in the anhydrobiosis-the ability of plants and animals to withstand prolonged periods of desiccation. It has high water retention capabilities. It is used in various food and cosmetics. Trehalose offers advantages to diabetics as it triggers only a small increase in blood insulin levels. It is safer and non-toxic in use. The disadvantage of it is that any undigested trehalose passes to the large intestine where normal bacteria break it down to gases and irritant substances that can cause abdominal bloating or diarrhea [59, 60, 61, 62, 63].

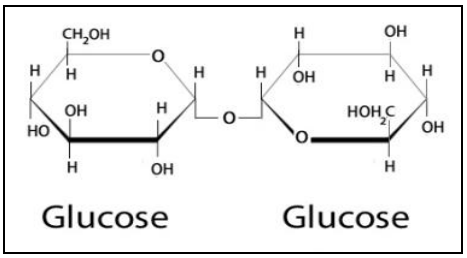

FIG. 9: TREHALOSE

Tagatose: is a natural sweetener found in traces in fruits, cacao, and dairy products. It provides 1.5 kcal/gm. Chemically it is (3S, 4S, 5R)-1, 3, 4, 5, 6-Pentahydroxy-hexane-2-one as shown in figure 9. It can be commercially obtained from galactose through an enzymatic conversion. Initializing with lactose which is hydrolyzed to glucose and galactose. D-Tagatose was introduced as a sweetener by G. Levin. He patented a cheap method to make tagatose in 1988. The low food calorie contents are due to its resemblance to L-fructose. D-tagatose provides an advantage as glycemic and lipoprotein control through the certain mechanism of action, unlike any agent that is currently available in the market. The disadvantage of it is gastrointestinal disturbances [64, 65, 66].

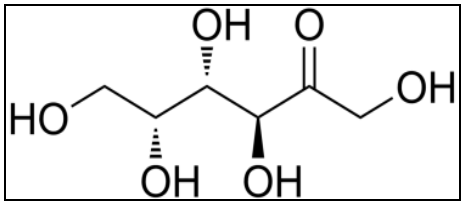

FIG. 10: TAGATOSE

Sugar Alcohols: The sugar alcohols commonly found in foods are:

- Sorbitol,
- Mannitol,
- Xylitol,
- Isomalt, and hydrogenated starch hydrolysates.

Sugar alcohols are obtained from plant products such as fruits and berries. These sugar substitutes provide somewhat fewer calories than sucrose, mainly because they are not well absorbed and may even have a small laxative effect [67]. Polyols are naturally present in smaller quantities in fruits and certain kinds of vegetables or mushrooms; they are regulated as generally recognized as safe, or as food additives. Among polyols, erythritol ((2S,3R)-butane-1,2,3,4-tetrol), xylitol (2S,4R)-pentane-1,2,3,4,5-pentol), and maltitol ((2S,3R,4R,5R)-4-[(2R, 3R, 4S, 5S, 6R)-3, 4, 5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyhexane-1, 2, 3, 5, 6-pentol) are the most recognised polyols used in bakery industry [68, 69, 70]. They provide good stability during baking with acceptable textural and sensory properties, low glycemic index and their sweetness are roughly comparable with this obtained from sugar (erythritol: 70%, xylitol: 100%, maltitol: 90% of the sucrose sweetness [71, 72, 73].

Sorbitol: Sorbitol is a sugar substitute. Chemically it is (2S, 3R, 4R, 5R)-Hexane-1,2,3,4,5,6-hexol as shown in **Fig. 11**. Sorbitol is about 60% as sweet as sucrose. Sorbitolprovides dietary energy in the form of 2.6 kilocalories per gram. It is often used to sweeten diet foods as mints, cough syrups and is used to make sugar-free chewing gum. The advantages of sorbitol is that it has lesser effects on blood sugar levels than sugar, which can benefit people at risk of developing diabetes. When eaten, sorbitol has a mouth-cooling sensation, with virtually no aftertaste. Sorbitol offers disadvantages in the intestine by causing water retention, resulting in diarrhoea [74, 75, 76].

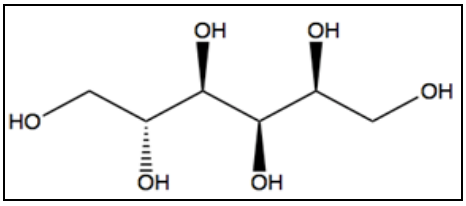

FIG. 11: SORBITOL

Mannitol: Mannitol is classified as a sugar alcohol, as shown in **Fig. 12**, that is, it can be derived from a sugar called mannose by reduction. Other sugar alcohols include xylitol and sorbitol. Mannitol and sorbitol are isomers, the only difference being the orientation of the hydroxyl group on carbon 2. It is a reduced-calorie sweetener with only 1.6 calories per gram. It is non -hygroscopic. It provides sweetness, with a cool and refreshing taste. It can be used as an alternative sweetener for people with diabetes. Mannitol is slowly absorbed from the intestinal tract. Therefore, when mannitol is used, the rise in blood glucose and demand for insulin is much less than compared to that of sucrose. It also controls caloric intake and body weight in people with diabetes. Mannitol offers advantages as the body only partially absorbs it and it significantly reduces the rise in blood glucose and insulin levels that occur following the ingestion of glucose. Mannitol does not promote dental caries. Mannitol has a shallow glycemic index. This combined with its low-calorie value (1.6 kcal/g), which is very beneficial for weight control, makes mannitol a useful alternative sweetener for people with diabetes. Products sweetened with mannitol in place of sugar help provide diabetics with a broader range of low-calorie and sugar-free options. The disadvantages of it are abdominal pain, excessive gas (flatulence), loose stools or diarrhea [77, 78].

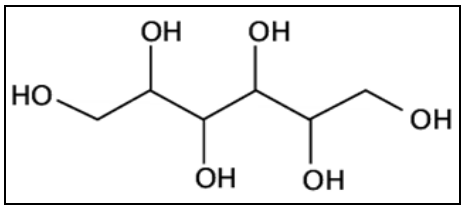

FIG. 12: MANNITOL

Xylitol: xylitol is achiral, unlike other sugar alcohols as shown in **Fig. 13**. It is produced on the industrial basis from xylan, which is hemicellulose, extracted from hardwoods or corncobs. It can be hydrolyzed into xylose, which is catalytically hydrogenated into xylitol. The conversion changes the sugar xylose, which is an aldehyde into xylitol, primary alcohol. One gram of xylitol contains 2.43 kilocalories. The disadvantages of xylitol are like gas, bloating and diarrhea [79, 80, 81].

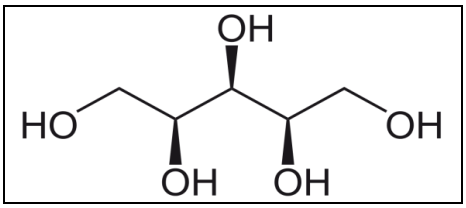

FIG. 13: XYLITOL

Oligosaccharide Based Sweeteners: They differ in their nature of monomeric sugars and are named so. They have varied sources of origin and differ in their benefits imparted to the consumer. The most

popular oligosaccharides are FOS, galacto-oligosaccharides (GOS), lactulose derived galactooligosaccharides (LDGOS), xylooligo-saccharides (XOS), arabino-oligosaccharides (AOS), algae-derived marine oligosaccharides (ADMO). Other oligosaccharides occurring in nature are pectin-derived acidic oligosaccharides (pAOS), maltooligosaccharides (MOS), cyclodextrins (CD) and human milk oligo-saccharides (HMO) with specific acknowledged benefits. Fructooligosaccharides have been claimed to lower fasting glycemia and serum total cholesterol concentrations, possibly via effects of short-chain fatty acids produced during fermentation. Compared to sugars, they are more slowly absorbed because the chains have to be split before being absorbed. The presence of oligosaccharides in the glucose syrup we use provides an additional advantage to the products [82, 83].

CONCLUSION: Sugar alternates are being used in various food and beverages are very popular in most of the countries. Six low-calorie sweeteners have been currently approved for use in foods in the U.S. and Europe such as *Stevia*, acesulfame-K, aspartame, neotame, saccharin, and sucralose. Some studies have been carried out to confirm the safety of artificial sweeteners. Some studies have also shown the adverse effects as well as safety parameters of the artificial sweeteners. But most of the studies have limitations such as effects shown only in animals, not in human, small sample size, high doses, statistically non-significant or borderline significant, *etc*. The sugar substitutes have been tested on safety parameters and then approved by different regulatory authorities like the USFDA *etc*. In spite of the demand for rare sugars, their commercial availability, application, and usefulness are negligible as they are expensive to prepare and unavailable.

So research is required to make natural sugars having the desired quantities of sweetness, low caloric value, and least observed physiological effects. Products containing *Stevia* and Mono ammonium glycyrrhizin should be encouraged as besides carrying the goodness of natural ingredients, it is free from the hazardous effects of other chemical based alternates. MAG (Mono ammonium glycyrrhizin) enhances the flavor of cocoa and chocolate-flavored products, flavors and sweetens candy, confectionery, and beverages, and masks the bitter taste of pharmaceuticals [84].

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REFERENCES:

1. Gray A: Nutritional recommendations for individuals with Diabetes. In: Feingold KR, Anawalt B, Boyce A: Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc; 2000. Available from: http://www.ncbi.nlm.nih.gov/books/NBK279012/
2. Chattopadhyay S, Raychaudhuri U and Chakraborty R: Artificial sweeteners-A review. J Food Sci Technol 2014; 51(4): 611-21.
3. FDA No Calories. Sweet! [Last accessed on 2011 Feb 1]. Available from: http://www.fda.gov/fdac/features/2006/406_sweeteners.html.
4. Lange F, Scheurer M and Brauch H: Artificial sweeteners-A recently recognized a class of emerging environmental contaminants: A review. Anal Bioanal Chem 2012; 403: 2503-18.
5. Brown R, Banate M and Rother K: Artificial Sweeteners: A systematic review of metabolic effects in youth. Int J Pediatr Obes 2010; 5(4): 305-12.
6. Sugar substitute, cited from From Wikipedia, the free encyclopedia, available on https://en.wikipedia.org/wiki/Sugar_substitute.
7. Bellisle F and Drewnowski A: Intense sweeteners, energy intake and the control of body weight. Eur J Clin Nutr 2007; 61: 691-700.
8. Healthy Lifestyle Nutrition and healthy eating available on https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/artificial-sweeteners/art-20046936.
9. Mazur R, Goldkamp A, James P and Schlatter J: Structure-taste relationships of aspartic acid amides. J Med Chem 1970; 6: 1217-21.
10. George V, Arora S, Wadhwa B and Singh A: Analysis of multiple sweeteners and their degradation products in lassi by HPLC and HPTLC plates. J Food Sci Technol 2010; 47: 408-413.
11. Trocho C, Pardo R, Rafecas I, Virgili J, Remesar X and Fernandez J: Formaldehyde derived from dietary aspartame binds to tissue components *in-vivo*. Life Sci 1998; 63: 337-49
12. Tordoff MG and Alleva AM: Effect of drinking soda sweetened with aspartame or high fructose corn syrup on food intake and body weight. Amer J Clin Nutr 1990; 51: 963-9.
13. Drewnowski A: Review: intense sweeteners and energy density of foods: implications for weight control. Eur J Clin Nutr 1999; 53: 757-63.
14. Renwick AG: The intake of intense sweeteners-An updated review. Food Addit Contam 2006; 23(4): 327-338.
15. Anonymous: Joint FAO/WHO Expert Committee of Food Additives. Evaluation of Certain Food Additives and

Contaminants: Saccharin. World Health Organization, 1993: 17-19.
16. Hampton T: Sugar substitutes linked to weight gain. JAMA 2008; 299: 2137-8.
17. Anonymous: Joint FAO/WHO Expert Committee of Food Additives. Evaluation of Certain Food Additives and Contaminants: Saccharin. World Health Organization, 1993: 17-19.
18. Schiffman S and Rother K: Sucralose, a synthetic organochlorine sweetener: Overview of biological issues. J Toxicol Environ Health B Crit Rev 2013; 16(7): 399-451.
19. Brown AW, Bohan Brown MM, Onken KL and Beitz DC: Short-term consumption of sucralose, a nonnutritive sweetener, is similar to water with regard to select markers of hunger signaling and short-term glucose homeostasis in women. Nutr Res 2011; 31: 882-888.
20. Smith J and Hong-Shum L: Food Additives Data Book. John Wiley & Sons, 2008: 960. ISBN: 978-1-405-17543-0.
21. Bopp BA, Sonders RC and Kesterson JW: Toxicological aspects of cyclamate and cyclohexylamine. Crit Rev Toxicol 1986; 16: 2130306.
22. Neotame: Stability overview (2002) http://www.neotame.com/pdf/neotame_stability_overview_US.pdf. Accessed 27 February 2009.
23. Prakash I: Synthesis of N-[N-(3,3-dimethyl butyl)-L-α-aspartyl]-L-phenylalanine 1-methyl ester using 3,3-dimethyl butyraldehyde precursors, 2007 Ip.com US Patent 7288670.http://ip.com/patent/US7288670. Accessed 2 June 2010.
24. Satyavathi K, Raju PB, Bupesh KV and Kiran TNR: Neotame: High-intensity low caloric sweetener. Asian Journal of Chemistry 2010; 22(7): 5792-5796.
25. Eteraf-Oskouei T, Najafi M, Alvarez-Suarez JM, Tulipani S, Romandini S, Bertoli E and Battino M: Contribution of honey in nutrition and human health: a review. Mediterr J Nutr Metab 2010; 3: 15-23.
26. Johnston JE, Sepe HA, Miano CL, Brannan RG and Alderton AL: Honey inhibits lipid oxidation in ready-to-eat ground beef patties. Meat Sci 2005; 70: 627-631. [PubMed]
27. Turkmen N, Sari F, Poyrazoglu ES and Velioglu YS: Effects of prolonged heating on antioxidant activity and color of honey. Food Chem 2006; 95: 653-657.
28. Rakha MK, Nabil ZI and Hussein AA: Cardioactive and vasoactive effects of natural wild honey against cardiac malperformance induced by hyperadrenergic activity. J Med Food 2008; 11: 91-98. [PubMed]
29. Al-Mamary M, Al-Meeri A and Al-Habori M: Antioxidant activities and total phenolics of different types of honey. Nutr Res 2002; 22: 1041-1047.
30. Venkata SD, Srisailam K and Veeresham C: Natural sweetening agents from plants, Journal of Medicinal and Aromatic Plant Sciences 2002; 24: 468-477.
31. Sweeteners MBA Glória, in Encyclopedia of Food Sciences and Nutrition (Second Edition). Academic press 2003.
32. Stevia: British & World English. Oxforddictionaries.com. 7 February 2013. Retrieved 13 February 2013.
33. Stevia: US English. Oxforddictionaries.com. 7 February 2013. Retrieved 13 February 2013.
34. Goyal S, Samsher and Goyal R: Stevia (*S. rebaudiana*) a bio-sweetener: A review. Int J Food Sci Nutr 2010; 61(1): 1-10.
35. Gupta S, Purwar S, Sundaram S and Rai G: Nutritional and therapeutic values of *Stevia rebaudiana*: A review. Journal of Medicinal Plants Research 2013; 7(46): 3343-3353.
36. Seki H, Ohyama K, Sawai S, Mizutani M, Ohnishi T, Sudo H, Akashi T, Aoki T, Saito K and Muranaka T: Licorice *ß*-amyrin 11-oxidase, a cytochrome P450 with a key role in the biosynthesis of the triterpene sweetener glycyrrhizin. Proc Natl Acad Sci USA 2008; 105: 14204-14209.
37. Kitagawa I: Liquorice root. A natural sweetener and an important ingredient in Chinese medicine. Pure Appl Chem 2002; 74: 1189-1198.
38. Omar H: Licorice abuse: time to send a warning message. Ther Adv Endocrinol Metab 2012; 3(4): 125-138.
39. Rao K: A review on liquorice. Anc Sci Life 1993; 13(1-2): 57-88.
40. Kalsi S, Verma S, Neha and Kaur A: A review on *Glycyrrhiza glabra* (liquorice) and its pharmacological activities. International Journal of Pharmaceutics & Drug Analysis 2016; 4(5): 234-239.
41. Dastagir G and Rizvi M: Review - *Glycyrrhiza glabra* L. (Liquorice). Pakistan Journal of Pharmaceutical Sciences 2016; 29(5): 1727-1733.
42. Anil K and Jyotsna D: Review on *Glycyrrhiza glabra* (Liquorice). JPSI 2012; 1-2: 1-4.
43. Bahmani M: A review of the health effects and uses of drugs of plant licorice (*Glycyrrhiza glabra* L.) in Iran. Asian Pacific Journal of Tropical Disease 2014: 4(2): 847-49.
44. Hesperidin cited from https://en.wikipedia.org/wiki/Hesperidin.
45. Garg A, Garg S, Zaneveld L and Singla A: Chemistry and pharmacology of the citrus bioflavonoid hesperidin. Phytotherapy Research 2001; 15(8): 655-69.
46. Faus I and Sisniega H: Biopolymers. Wiley-VCH, Weinheim, Edition 1st, 2003: 203-210.
47. De Vos AM, Hatadat M, Van Der Wel H, Krabbendam H, Peerdeman AF and Kimt SH: Three-dimensional structure of thaumatin I, an intensely sweet protein. Proc Natl Acad Sci USA 1985; 82: 1406-1409.
48. Kaneko R and Kiyabatake N: Sweetness of sweet protein thaumatin is more resistant under acid conditions than under neutral or alkaline conditions. Biosci Biotechnol Biochem 2001; 65: 409-413
49. Nova Sep- High purity NaturlThaumatin. Available from URL:http://www.novasep.com/upload/pdf/THAUMATIN.pdf Pages 655-669
50. Natural and Artificial Sweeteners safety *vs.* Sweetness Published on 05/20/2014 by Pasha Gurevich. Labdoor magazine. Available from: http://labdoor.com/article/natural and artificial sweerener safety vs sweetness
51. Novel Sweeteners, Regulatory Issues and Implications, S. W. Gunner, Food Directorate, Health Protection Branch, Health and Welfare Canada Tunney's Pasture, Ottawa, Ontario K1A 0L2, Canada Sweeteners 2007: Chapter 23, 302-312
52. Stevia from Wikipedia, the free encyclopedia available from: https://en.wikipedia.org/wiki/Stevia.
53. Stevia green green stevia available from:https://www.greengreenstevia.com/blogs/news/17890401-stevia.
54. Marcinek K and Krejpcio Z: *Stevia rebaudianabertoni*-chemical composition and functional properties. Acta Sci Pol Technol Aliment 2015; 14: 145-152.
55. Raymond KW: General Organic and Biological Chemistry. John Wiley and Sons, USA, Vol. 516, 2010: 364-368.
56. Kulthe AA: Development of high protein and low-calorie cookies. J Food Sci Technol 2014; 51: 153-157.

57. Garcia-Serna E: Use of coffee silverskin and stevia to improve the formulation of shortbread. Pol J Food Nutr Sci 2014; 64: 243-251.
58. Delgado-Andrade C, Rufián-Henares JA and Morales FJ: Hydroxymethylfurfural in commercial shortbread marketed in Spain. J Food Nutr Res 2009; 48: 14-19.
59. Streeter JG: Accumulation of α,α-trehalose by Rhizobium bacteria and bacteroids. J Bacteriol 1985; 164(1): 78-84.
60. Tillequin F: Trehala, a meeting point between zoology, botany, chemistry, and biochemistry. Revue d'histoire de la pharmacie 2009; 57(362): 163-72.
61. Richards A: Trehalose: a review of properties, history of use and human tolerance, and results of multiple safety studies. Food and Chemical Toxicology 2002; 40(7): 871-898.
62. Ohtake S and Wang J: Trehalose: Current use and future applications. JPS 2011; 100(6): 2020-53. Available from: http://doi.org/10.1002/jps.22458.
63. Trehalose.Nutrients review.com, available from: http:// www.nutrientsreview.com/carbs/disaccharides-trehalose. html.
64. Espinosa I and Fogelfeld L: Tagatose: from a sweetener to a new diabetic medication? Expert Opin Investig Drugs 2010; 19(2): 285-94.
65. Wyss M, Agüero S and Dávila L: D-Tagatose is a promising sweetener to control glycaemia: A new functional food. Bio Med Research International 2018; 7.
66. Levin G: Tagatose, the new GRAS sweetener, and health product. Journal of Medicinal Food 2002; 5(1): 23-36.
67. Struck S: Sugar replacement in sweetened bakery goods. Int J Food Sci Technol 2014; 49: 1963-1976.
68. Zoulias EI, Oreopoulou V and Kounalaki E: Effect of fat and sugar replacement on cookie properties. J Sci Food Agric 2002; 82: 1637-1644.
69. Lin SD: Effect of erythritol on quality characteristics of reduced-calorie Danish cookies. J Food Qual 2010; 33: 14-26.
70. Grembecka M: Sugar alcohols-their role in the modern world of sweeteners: a review. Eur Food Res Technol 2015; 241: 1-14.
71. http://www.joslin.org/info/what_are_sugar_alcohols.html.Joslin Diabetes Center.
72. Hayes C: The effect of non-cariogenic sweeteners on the prevention of dental caries: a review of the evidence. Journal of Dental Education 2001; 65(10): 1106-1109.
73. Guillaume NG and Marc LC: *Streptococcus mutans* and oral *Streptococci* in dental plaque. Canadian Journal of Microbiology 2011; 57(1): 1-20.
74. Kearsley MW and Deis RC: "Sorbitol and Mannitol", in sweeteners and sugar alternatives in food technology. Wiley-Blackwell 2006: 249-261.
75. Adcock L and Gray C: The metabolism of sorbitol in the human subject. Biochem J 1957; 65(3): 554-560.
76. Lee J: Sorbitol, Rubus fruit, and misconception. Food Chemistry 2015; 166: 616-622.
77. https://caloriecontrol.org/mannitol/ available from Calorie control council.
78. Shawkat H: Mannitol: a review of its clinical uses. Continuing Education in Anaesthesia Critical Care & Pain 2012; 12(2): 82-85.
79. Sheet B, Artik N, Ayed M and Abdulaziz O: Some alternative sweeteners (Xylitol, Sorbitol, Sucralose, and Stevia): Review. Karaelmas Science and Engineering Journal 2014; 4(1): 63-70.
80. Nigam P and Singh D: Processes for fermentative production of xylitol-A sugar substitute. Process Bio-0chemistry 1995; 30: 117-124.
81. Atillio C, Patrizia P andManuel DJ: "Xylitol production from hardwood hemicellulose hydrolysates. Applied Biochemistry and Biotechnology 1999; 82: 141-151.
82. Crittenden RG and Playne MJ: Production, properties, and applications of food-grade oligosaccharides. Trends Food Sci Technol 1996; 71: 353-361.
83. Prapulla SG, Subhaprada V and Karanth NG: Microbial production of oligosaccharides: A review. Adv Appl Microbiol 2000; 47: 299-343.
84. M.B.A. Glória, Sweeteners in Encyclopedia of Food Sciences and Nutrition (Second Edition) 2003: 42-47.

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