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Artificial Sweeteners and their effect of oral health

A Project Submitted to

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By

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Certification of the Supervisor

I certify that this project entitled " **Artificial Sweeteners and their effect of oral health**" was prepared by the fifth-year students **(Nour El Din Ali), (Zaid Hussein Radhi)** and under my supervision at the College of Dentistry/Ashur University in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

Supervisor's name: A.L. Tabarak Adel Rasool

Dedication

We would like to dedicate our humble effort to our supportive Father and Mother Their affection, love, encouragement and prays at day and night made us able to succee With passion and honor.

Nour El Din Ali & Zaid Hussein Radhi

Acknowledgment

I wish to thank my committee members who were more than generous with their expertise and precious time.

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Introduction

Sweeteners offer a sweet taste to food and can be classified as carbohydrate (caloric) and noncarbohydrate (noncaloric) sweeteners. Caloric sweeteners include sugar and sugaralcohols such as erythritol, sorbitol, mannitol, xylitol, maltitol, lactitol, and reducing starch syrup (Wilk, K et al., 2018). Noncaloric artificial sweeteners or non-nutritional sweeteners (NNSs) are a heterogeneous group of compounds with different chemical structures, which are popular substitutes for added sugars in foods and beverages due to their low caloric content and sweetness (Fleming-Milici et al., 2022). Non-nutritional sweeteners (NNSs) can be classified into artificial sweeteners (ASs) when chemically produced in the laboratory, and natural sweeteners (NSs) when directly extracted from plants. ASs include aspartame, saccharin, sucralose, neotame, acesulfame-k, and advantame, and NSs are mainly represented by stevia, made from bextracts of the intensely sweet plant S. Rebaudiana, but also include hoodia, agavis, and Luo Han Guo Monk fruit extracts (Liauchonak, I et al., 2019). Non-nutritional sweeteners (NNSs) were introduced into the market as food ingredients in the 19th century (Shah, S.I.A et al., 2023). Since then, NNSs have become extremely popular as sugar substitutes for weight control and prevention of obesity, especially during the past three decades, when the worldwide incidence of childhood and adulthood obesity has increased dramatically. From 1975 to 2016, a tenfold increase in the number of obese children and adolescents, aged 5–19 years, worldwide was reported recently [5]. Specifically, using body mass index (BMI), obesity rates among children and adolescents globally increased from less than 1% (i.e., five million girls and six million boys) in 1975 to approximately 6% in girls (i.e., 50 million) and 8% in boys (i.e., 74 million) in 2016 (NCD Risk Factor Collaboration., 2017). Apart from the common use of sweeteners for weight loss, diabetes management, and the prevention of dental caries (Wilk, K et al., 2022)(Patil, S et al., 2023), they are also added in pharmaceutical and other healthcare products, such as toothpaste and food supplements 8. (Serra-Majem, L et al., 2018).

Artificial sweeteners are used worldwide as sugar substitutes in remarkable amounts in food, beverages, and also in drugs and sanitary products, such as mouthwashes. They provide no or negligible energy and thus are ingredients of dietary products (Kroger M et al., 2006).

Sweeteners have been classified as natural sweeteners and artificial sweeteners. These artificial sweeteners further classified as nutritive and non-nutritive sweeteners depending on whether they are a source of calories. The nutritive sweeteners include the monosaccharide polyols (e.g., sorbitol, mannitol, and xylitol) and the disaccharide polyols (e.g., maltitol and lactitol). The non-nutritive sweeteners are better to known as artificial sweeteners (Christina R Whitehouse et al., 2008).

The main reasons for using artificial sweeteners are weight loss, dental care, diabetes mellitus, reactive hypoglycemia and low cost (Christina R Whitehouse et al., 2008). Dental caries is also known as teeth decay or cavities. Breakdown of teeth due to activities of bacteria. This occurs due to acid made from sugar on the tooth surfaces. Simple sugars in foods are the primary energy source of these bacteria (Richard J. Lamont et al., 2015) Reactive hypoglycemia refers to low blood sugar that occurs after a meal usually within 4 hours after eating. This can occur in both people with and without diabetes and is thought to be more common in overweight individuals. Reactive hypoglycemia is known as the result of too much insulin being produced and released by the pancreas following a large sugar or carbohydrate-based meals (Johnson DD et al., 1980) To reduce these activities, most of the people are using artificial sweeteners.

In rats, saccharin, sucralose, and aspartame consumption may increase the proportions of Bacteroides spp. and Clostridiales (Suez et al., 2014).

Low dose aspartame consumption (60 mg/L drinking water) in rats may increase total bacteria abundance including Clostridium leptum and Enterobacteriaceae (Palmnas et al., 2014).Neotame, mainly found in carbonated soft drinks, yogurts, cakes, drink powders, and bubble gums could increase the abundance in Bacteroidetes and reduce that of Firmicutes in the mice model (Chi et al., 2015).

Acesulfame-K is another artificial sweetener commonly found in frozen desserts, candies, and beverages. In human volunteers, bacterial diversity differed across acesulfame-K consumers and non-acesulfame-K consumers (Frankenfeld et al., 2015).
Overall, artificial sweeteners, including also aspartame, sucralose, and cyclamate could cause gut dysbiosis (Cao et al., 2020) and consequently impact host functions such as metabolism. Artificial sweeteners consumption could increase insulin resistance and glucose intolerance as well as natural sugar (Suez et al., 2014; Palmnäs et al., 2014; Bian et al., 2017) and induce elevated inflammation as evaluated in the mouse model (Bian et al., 2017).

Aim of the Study

This project aims to conduct a Comparison between the types of artificial sweeteners and their effect on oral health and their effect on bacteria that cause decay and whether they are better than natural sugars in terms of preventive measures.

Review of literature

Artificial sweeteners comprise carbohydrate substitutes that replace natural sweeteners in beverages and food due to their very low or no energy value and cost-effective availability with higher sweetening value than natural sweeteners.

Artificial sweeteners are many times sweeter than table sugar. Smaller amounts are needed to create the same level of sweetness, and which are either not metabolized in the human body or do not significantly contribute to the energy content of foods and beverages. Those provide the sweeteners of sugar without the calories and produce a low glycemic response. The main reasons for using artificial sweeteners are weight loss, dental care, diabetes mellitus, reactive hypoglycemia and low cost. Consumers and food manufacturers have long been interested in dietary sweeteners to replace sucrose in foods (Christina R Whitehouse et al., 2008). These sweeteners are widely used in baked goods, carbonated beverages, powdered drink mixtures, jams, jellies and dairy products (Findikli Z et al., 2014).

History of Artificial Sweeteners

Artificial sweeteners first entered the food industry in the 1800s. However, since the 2000s, there has been an explosive increase in their consumption. In the United States, AS consumption is estimated to have increased by ~200% in children/adolescents and 54% in adults between 1999 and 2000, with ~25% of children and 41% of adults consuming AS at least once daily between 2009 and 2012 (Sylvetsky AC et al., 2017). Consumption of AS may, however, be more widespread because of their presence in “lower-calorie” food products as well as medications to improve palatability.

The use of AS-altered diets is even listed in guidelines for the medical management of patients with inflammatory bowel disease (IBD) (Lamb CA et al., 2019) Specifically, the British Society of Gastroenterology consensus guidelines recommend the use of Crusha flavoring, which has AS. Such additions to food and medications seem unjustified owing to rising evidence that AS affect inflammation pathways. AS have also been shown to exert physiological effects on glucose metabolism, appetite stimulation, and metabolic disease (e.g., type 2 diabetes; T2DM, metabolic syndrome, obesity) (Suez J et al., 2014; Ruiz-Ojeda FJ et al., 2019; Malik VS et al., 2019) .

Possible Health Benefits of Artificial Sweeteners

1-Weight Control

One of the most annealing aspects of artificial sweeteners is that they are non-caloric. Although they are not a 'silver bullet', low calorie sweeteners can help people reduce their calorie intakes. Long-term trials consistently indicate that the use of low-calorie sweeteners results in slightly lower energy intakes and that if low calorie sweeteners are used as substitutes for higher energy-yielding sweeteners, they have the potential to aid in weight management (Halldorsson et al., 2010).

2-Diabetes

People with diabetes have difficulty in regulating their blood sugar levels. Low calorie sweeteners offer people with diabetes broader food choices by providing the pleasure of the sweet taste without raising blood glucose. As low-calorie sweeteners have no impact on insulin and blood sugar levels and do not provide calories, they can also have a role in weight loss and weight control for people with type II diabetes (Negro et al., 1994).

3-Dental Cavities

When sugar-sweetened foods and drinks are consumed, the bacteria present in the mouth converts the sugar to acid. If this acid is not removed by teeth cleaning, it can wear away the surface enamel, eventually causing cavities to form. Low calorie sweeteners are not fermentable and do not contribute to tooth decay. By improving palatability, low calorie sweeteners can also encourage the use of toothpastes, mouthwashes and fluoride supplements that assist dental hygiene (Roberts, HJ., 2007).

Possible Health Concern of Artificial Sweeteners

1-Preterm Delivery

A prospective cohort analysis of 59,334 women from the Danish National Birth Cohort (1996-2002) concluded that daily intake of artificially sweetened soft drinks increased the risk of preterm delivery (Fowler et al., 2008).

2-Hepatoxicity

A case study of the hepatotoxicity of saccharin was published in 1994. A patient presented with elevated serum concentrations of liver enzymes after the oral administration of three different drugs, of which saccharin was the only common constituent (Blum et al., 2005).

3-Thrombocytopenia

Additionally, a case report in 2007 revealed four individuals with thrombocytopenia attributed to products containing aspartame (Ansari A et al., 2015).

4-Weight reduction

Although artificial sweeteners became popular, they can help reduce weight but epidemiologic data suggest an association between artificial sweetener use and weight gain. A prospective cohort study on drinkers of artificially sweetened beverages consistently had higher body mass index (BMIs) at the follow-up, with dose dependence on the amount of consumption. Average BMI gain was +1.01 kg/m2 for control and 1.78 kg/m2 for people in the third quartile for artificially sweetened beverage consumption. Similar observations have been reported in children, wherein a two-year diet soda consumption was associated with higher BMI Z-scores indicating weight gain (DuBois GE et al., 2012).

The Impact of Artificial Sweeteners on Body Weight Control and Glucose Homeostasis

Obesity and its associated metabolic disorders, including T2DM, cardiovascular disease, and fatty liver disease, are preventable. Many strategies exist to achieve successful weight loss by improving dietary habits and energy balance. However, even more challenging than achieving weight loss is the maintenance of body weight after weight loss (van Baak M et al., 2019). The intake of sugar contributes to the overall energy density of diets, thereby promoting obesity (Khan T et al., 2016; Blaak E., 2016). In particular the consumption of sugar-sweetened beverages has been associated with cardiometabolic complications, driven by an increased energy intake and obesity(Richelsen B et al., 2013).Therefore, one common approach to improve energy balance is to refrain from sugars by replacing them with artificial sweeteners. Although the World Health Organization (WHO) recommends free sugar intake of <10% of total energy intake, preferably <5% of total energy intake as a conditional recommendation, a large proportion of the European population appears to exceed this threshold, especially children) (Azaïs-Braesco V et al., 2017).

As artificial sweeteners offer a sweeter taste without calories, the replacement of sugars with these sweeteners seems promising in reducing sugar and energy intake. Meta-analyses of Randomized Controlled Trials (RCTs) have shown that daily energy intake (after 4 or 10 weeks) and sugar intake (after 4 weeks) were lower in healthy, overweight, and obese individuals receiving artificial sweeteners as a replacements of sugars in the diet (Toews I et al., 2019).

Sweetener

A sweetener is a natural or synthetic substance that gives sweet taste to foods and beverages (Carlson J,. et al 2016). Depending on their caloric value, sweeteners can be classified as nutritive or non-nutritive (NNSs) (Figure 1).

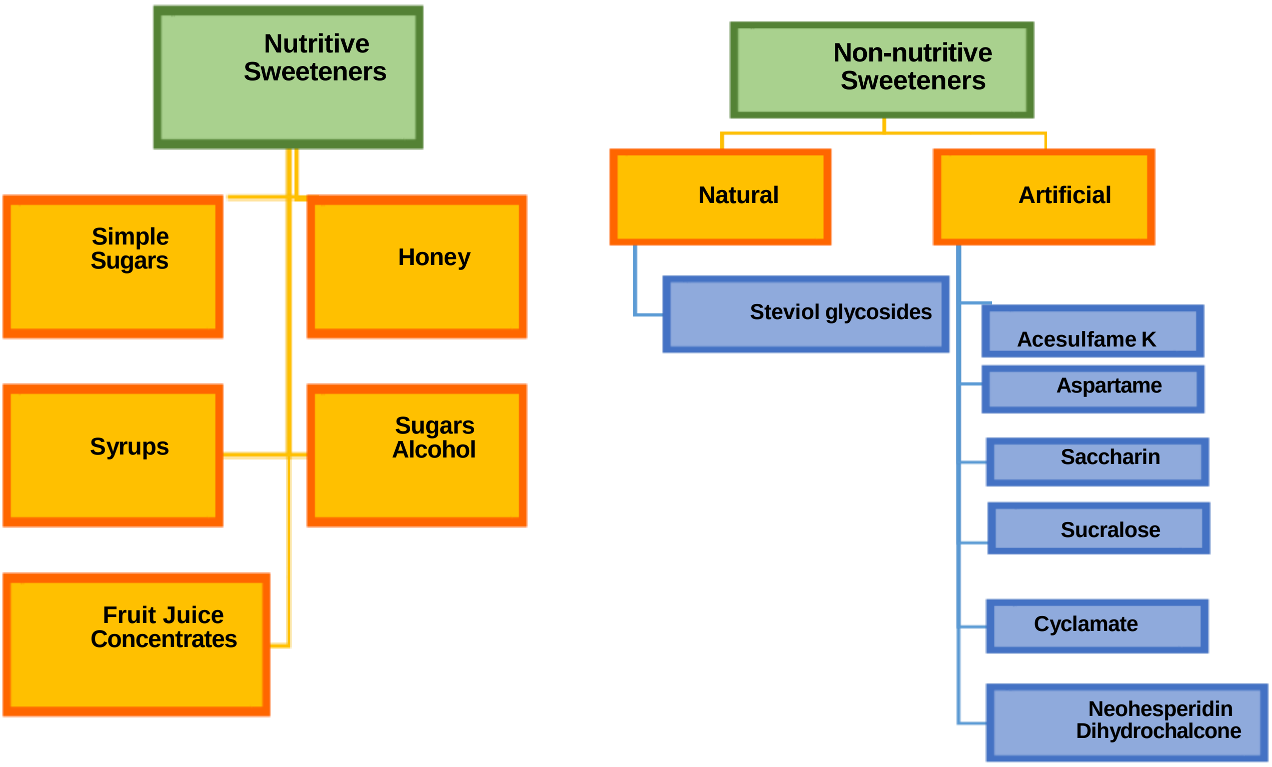

Figure 1. Classification of the most common sweeteners used in foods.

1.1 Structural requirements for sweetness

The generally accepted theory for the phenomenon of sweetness was developed by Shallenberger and Acree. According to this theory, a molecular system of a proton donor and proton acceptor is necessary. Changes in the distance between groups, as well as changes in electronic structure influence the occurrence of the sweet taste and may change the general taste perception, sometimes eliminating sweetness totally, or changing it to bitterness (L. B. Kier., 1972).

1.2 General Uses

1.2.1 Foods and Beverages

Foods and beverages are the most important fields of application of artificial sweeteners, with calorie reduction being the main goal. Single sweeteners or combinations with other sweet substances. Artificial sweeteners can be used in diabetic foods and beverages; depending on the type of product, either as single sweetening agents or combined with bulk sugar substitutes suitable for diabetic consumption. Beverage uses of artificial sweeteners account for more than 50% of human consumption; sugar replacement by artificial sweeteners is simple, as carbohydrates do not play any important functional role in beverages. Other important applications are fruit flavored dairy products and desserts (Vom RymonLipinski., 2000).

1.2.2 Pharmaceuticals

Artificial sweeteners are used to mask undesired flavors and tastes of active pharmaceutical ingredients, e.g., bitterness, whenever the pharmaceuticals are intended for use by diabetics. Sweeteners are used in syrups, and soluble tablets and powders.

1.2.3 Cosmetics

Several types of cosmetics, especially oral hygiene products, are sweetened to make them more pleasant for consumers. For oral hygiene products (e.g., toothpaste, mouthwash, etc.), non-cariogenic ingredients have to be used. The desired sweetness level is adjusted with an additional quantity of artificial sweetener.

1.2.4 Tabletop sweeteners

For household use, artificial sweeteners are formulated into table-top sweeteners, such as sweetener tablets, powders and spoon-by-spoon products, and liquids.

The main five sugar substitutes for use in a variety of foods are saccharin, acesulfame potassium, aspartame, neotame and sucralose.

Types of artificial sweeteners

1. Aspartame

Aspartame is a white, odorless powder that is two hundred times sweeter than sucrose and readily dissolves in water.Aspartame is one of the most debated sweeteners. It has been used in 6000 different products. The Food and Drug Administration (FDA) approved that the Acceptable daily intake (ADI) of aspartame is 50 mg/kg/day (Rencuzojullari et al., 2004).

Equal **NutraSwee**

Figure 2. Aspartame containing products

Aspartame's relationship with tooth decay

Aspartame an artificial intense sweetener, was tested for its cariogenicity alone and in the presence of sucrose. Sprague-DawleyTM rat pups (Charles River Laboratories, Bloomington, MA) inoculated with Streptococcus mutans were fed basal diet with one of the following added:50% sucrose;30% sucrose;30% sucrose + 0.15% aspartame; 0.30% aspartame; 0.15% aspartame and no addition. Animals were sacrificed after eight weeks. Caries was evaluated using "Keyes" technique.The technique includes: Microscopic examination of the plaque. Cleaning the teeth and gums with a mixture of salt, baking soda and peroxide. It was found that the addition of 0.15% aspartame to 30% sucrose diet significantly reduced caries in comparison to rats fed only 30% sucrose diet. In animals fed aspartame only, there was no caries.

S. mutans counts were high in the animals receiving sucrose diets with and without aspartame. The animals receiving only aspartame had very low S. mutans counts. (Pediatr Dent., 1991).

Aspartame relationship with diabetes

Since the FDA of the United States Department of Health and Human Services recognized aspartame as safe for use human consumption, it has gained popularity as an alternative to sucrose (Azima HSM et al., 2018).

Aspartame is a white, odorless powder that is two hundred times sweeter than sucrose and readily dissolves in water. Although it is a low caloric sweetener and has no effect on glycemic control, diabetic patients are advised to consume only minimal quantity as studies have shown that aspartame has both harmful and beneficial effects on the lifestyle and metabolism of diabetic patients who depend on it (Rencuzogullari et al., 2004) Particularly, aspartame has been linked to the exacerbation of diabetes, headache, seizures, depression, arthritis and other medical conditions (Carlson J., 2016).

Uses

Under the trade names Equal, NutraSweet and Candee, aspartame is an ingredient in approximately 6,000 consumer foods and beverages sold worldwide, including diet sodas and other soft drinks, instant breakfast, breath mints, cereals, sugar-free chewing gums, coca mixes, frozen dessert, gelatin dessert, juices, chewable vitamin solemnest, milk drinks, pharmaceutical drugs and solemnest, shake mixes, tabletop sweeteners, teas, instant coffees, wine colors and yogurt. Aspartame is less suitable for baking than other sweeteners because it breaks down when heated and loses much of its sweetness (Struck et al., 2014).

Metabolism and Health aspects

Upon ingestion, aspartame breaks down into natural residual components, including aspartic acid, phenylalanine, methanol and further break down products including formaldehyde, formic acid and diketone piperazine (George et al., 2010; Troche et al., 1998). Each of which then metabolized just as it would be if derived from other dietary sources and are safe as consumed in normal diets. People with phenylketonuria (PKU) must also avoid food products that contain aspartame, as it's converted into phenylalanine in the body.As a result, this amino acid can build up to toxic levels in the blood and other tissues.

2. Saccharin

Saccharin is the first and oldest artificial sweetener that has been used for over a century to sweeten foods and beverages without adding calories. Saccharin has been approved by FDA for use in more than 100 countries. Saccharin is an artificial sweetener that has been widely accepted as a sugar substitute. It is three hundred to five hundred times sweeter than sucrose and is the most important and widely used sweetener, especially for diabetic patients, as it goes directly through the human digestive system without being digested (Amin et al., 2016; Spillane et al., 1996).

Sweet'N Low **Sodium Saccharin**

Saccharin

Figure 3. Saccharin Containing Products

Saccharin's relationship with tooth decay

Saccharin was first developed in 1878; oldest approved artificial sweetener. It is 300 times as sweet as sucrose by weight, non-cariogenic and non-caloric but can have a slightly bitter or metallic taste.6 Saccharin, when used as a supplement to a cariogenic diet significantly, reduced both fissure and smooth surface caries in rats, apparently interfering with the growth of Streptococcus mutans (Bukhamseen F et al., 2015).

Saccharin relationship with diabetes

Saccharin is an artificial sweetener that has been widely accepted as a sugar substitute. It is three hundred to five hundred times sweeter than sucrose and is the most important and widely used sweetener, especially for diabetic patients, as it goes directly through the human digestive system without being digested (Amin et al., 2016; Spillane WJ et al., 1996). Although, saccharin has been extensively investigated, most of research has produced conflicting reports. Studies have shown that consumption of larger amounts of saccharin results in reduced hyperinsulinemia, a decrease in the resistance of insulin and improvement in the overall control of blood sugar in mice subjects compared to control subjects (Bailey CJ et al., 1997).

Suez et al. also report that at the FDA recommended dose of 5 mg/kg (Miller R., 2015). saccharine showed the highest level of alteration in glucose intolerance in both lean and obese mice when compared with control models (Suez J et al., 2015).

Metabolism

After ingestion, saccharin is not absorbed or metabolized. Instead, it is excreted, unchanged via the kidneys.

Uses of Saccharin

Important fields of application are soft drinks, tabletop sweeteners, and desserts. For taste reasons, blends with other artificial sweeteners, or combinations with reduced sugar levels are preferred wherever such blends are approved. In oral hygiene products, saccharin masks undesired tastes of other ingredients. In starter feed for livestock, saccharin is used to avoid reduced feed intake after weaning. Besides its applications as an artificial sweetener, saccharin is used in electrolytic nickel deposition. Addition of saccharin to the nickel salt solutions increases the hardness and brightness of the nickel plate. This effect is apparently specific to saccharin (L. Kreutzig et al., 1991).

3. Neotame

Neotame is the newest sweetener and a derivative of aspartame. At-butyl group is added to the free amine group of aspartic acid. This could be a super sweet deal for food and beverage manufacturers, all the sweetness of sugar without a metallic after-taste plusata fraction of the amount of sweetener needed compared to other sugar substitutes. The neotame was approved in 2002 as a general-purpose sweetener, excluding in meat and poultry by FDA (Christina et al., 2008).

Figure 4. Neotame containing products

Neotame's relationship with tooth decay

Neotame is a derivative of aspartic acid and phenylalanine. It is approximately 7,000 - 8,000 times sweeter than sugar, although some report a sweetening power of up to 13,000 times that of sugar. Neotame was approved by FDI in July 2002 as a general-purpose sweetener. Because of extraordinary sweetness, neotame is consumed in small amounts and produces reduced level of phenylalanine in bloodstream which is clinically insignificant. It is not fermentable by oral microbiota and possesses a crisp and sweet taste (Bukhamseen F et al., 2015).

Metabolism and health aspect

Neotame is rapidly metabolized, completely eliminated and does not accumulate in the body. The major metabolic pathway of neotame is hydrolysis of the methyl ester by esterase which is present throughout the body. This yields de esterifies neotame, the major metabolite and a significant amount of methanol. Due to the presence of the 3-3-di-methylbutyl group, peptidases which would typically break the peptide bond between the aspartic acid and phenylalanine moieties are essentially blocked, thus reducing the availability of phenylalanine. The amount of methanol derived from neotame is exceedingly small (Bert Fraser-Reid., 2014). Neotame was approved by the U.S. Food and Drug Administration (USFDA) as a general-purpose sweetener in July 2002 (Knight I 1993). It has also been favorably evaluated by JECFA (Patel et al., 2006) which established an ADI of 2mg/kg body weight/day. The ADI for neotame in the US is18mg/person/day (USFDA., 2009).

Uses

Neotame is stable at high temperatures. It is a general all-purpose sweetener that has both cooking and baking applications. Neotame is used in baked goods, beverages, candies, chewing gum, dairy products, frozen desserts, puddings, and yogurt-type products and as a tabletop sweetener (USFDA., 2006).

In Drinks

Neotame's sweetness can be kept in cola carbonated drinks as long as 4-5 months, it can be applied in juice, vegetable juice and low alcohol wine, improve the taste and flavor of drinks, can also be applied in solid powdered beverage like lemon tea and milk powder.

In Starch, protein foods

Neotame can be mixed with other nutrition and non-nutrition sweeteners. It can resist starch's deceasing, prolong the products' duration. Also, can resist protein denaturation and keep good flavor in rich protein foods.

In Savory food

Neotame can be applied in high temperature short time (HTST) products including popcorn, cookie and cakes, because of the heating time is very little, and neotame concentration merely changes.

4. Sucralose

This non-nutritive sweetener is made from sucrose by a process that substitutes 3 chloride atoms for 3 hydroxyl groups on the sucrose molecule (FDA., 2006). Sucralose is 450–650 times sweeter than sucrose, has a pleasant sweet taste and its quality and time intensity profile is very close to that of sucrose (Arora S et al., 2009). It has a moderate synergy with other nutritive and non-nutritive sweeteners (Beyts P K et al., 1995). It is very much soluble in water and is stable over a wide range of pH and temperature. It does liberate HCl when stored at high temperature and produce some kind of discoloration (Beyts P K et al., 1995).

Figure 5. Sucralose Containing Products

Sucralose relationship with tooth decay

Sprague Dawley rats infected with Streptococcus mutans were given sucrose or sucralose along with a diet that contained no extra sucrose. Following thirty-five days, the level of infection of S. mutans was determined and the sulcal caries scored. Rats fed sucralose had same number of total viable flora; however, the level of S. mutans of the total viable flora was reduced by up to twenty-fold in contrast with the sucrose control. Sucralose fed rats had less than fifty percent of the sulcal caries evident in the sucrose control. Rats were desalivated and inoculated with S. mutans and Actinomyces viscosus and fed diets that contained either fifty six percent sucrose or sucralose at 93 mg/100 g. The number of coronal lesions did not vary significantly among groups, but the severity of the lesions was comparatively lower following thirty-five days of feeding the sucralose diet compared with the sucrose control. Substitution of sucralose for sucrose brought about substantially fewer lingual and proximal lesions. Although comparable levels of root surface exposures were accomplished in the test and control diet, only rats fed sucralose stayed free of root surface caries. These results shows that sucralose is non cariogenic (Bukhamseen F et al., 2015).

Sucralose relationship with diabetes

Sucralose is a derivative of sucrose and is a high intensity sweetener (Grice HC et al., 2000). Various studies have been done to investigatethe safety of sucralose and the results of these studies demonstrate the safety of sucralose for human consumption (Grice HC et al., 2000). Of note, a study investigated the effect of daily sucralose consumption on glycemic control in patients with type 2 diabetics. This study found no significant difference in hemoglobin A1c (HbA1c) - a measure of blood sugar/glucose that is attached to hemoglobin, fasting plasma glucose, or fasting serum C-peptide changes from baseline between the study group and control group (Grotz V et al., 2003). Furthermore, they reported a decrease in blood glucose and HbA1C were reported to have decreased during the study period in the sucralose group (Ferguson MC et al., 2013).

Metabolism and health aspect

Metabolism and health aspect although sucralose is made from sugar, the human body does not recognize it as a sugar and does not metabolize it therefore it provides no calories. The bulk of sucralose ingested does not leave the gastrointestinal tract and is directly excreted in the feces while 11–27% of it is absorbed (Knight I., 1993). The amount that is absorbed from the gastro intestinal tract is largely removed from the blood stream by the kidneys and eliminated in the urine. As it is an organo chloride and some of which are known to have significant toxicity (Patel RM et al., 2006) but sucralose is not known to be toxic.

Uses

Sucralose is used in many food and beverage products because it is a no-calorie sweetener, does not promote dental cavities are safe for consumption by diabetics and nondiabetics (Findikli et al., 2014; Christina et al., 2008) and does not affect insulin level, although the powdered form of sucralose-based sweetener product Splenda (as most other powdered sucralose products) contains 95% (by volume) bulking agent's dextrose and maltodextrin that do affect insulin levels. Sucralose is a general-purpose sweetener that can be found in a variety of foods including baked goods, beverages, chewing gum, gelatins, and frozen dairy desserts. It is heat stable, meaning that it stays sweet even when used at high temperatures during baking, making it suitable as a sugar substitute in baked goods (Sonders et al., 1986).

5. Acesulfame potassium

This is a general-purpose sweetener, white crystalline structure, high-intensity, non-nutritive sweetener, non-carcinogenic Acesulfame-K is not metabolized by the body and is not stored in the body. It is quickly absorbed and excreted in urine without undergoing any modification. And stable under high temperatures. So, it does not break down in heat, therefore often used in baked products. It is used in over 4,000 products in approximately 90 countries. The "K" refers to the mineral potassium, which is naturally found in our bodies (Sonders et al., 1986).

Acesulfame K is about two hundred times sweeter than of a three percent sucrose solution. Its sweetness intensity decreases with increasing sucrose concentrations to values from hundred and thirty to hundred times the sucrose value It has identical sweetness as aspartame, about half as sweet as sodium saccharin, and four to five times sweeter than sodium cyclamate.

Figure 6. Acesulfame contain product

Acesulfame potassium relationship with tooth decay

Hoechst (1967), found that compounds with the dihydro - oxthiazinone dioxide ring system had a sweet taste. In terms of sweetness, Acesulfame - K is about 130 times as sweet as sucrose. It is stable in high temperature, low pH and storage range that is likely to be encountered in foods and beverages (Bukhamseen F et al., 2015). It is not cariogenic, but no active cariostatic properties have been reported aside from a positive synergistic effect on inhibition of acid production by oral microorganisms when combined with cyclamate and saccharine (Bukhamseen F et al., 2015).

Acesulfame potassium relationship with diabetes

Acesulfame potassium is an artificial sweetener that is two hundred times sweeter than sucrose and it was accepted by the FDA as an all-purpose sweetener in 2003 (Shwide-Slavin C et al., 2012). Acesulfame potassium has no glycemic effects by itself and is widely available commercially under brand names such as sweet and safe and Sunett. It is not metabolized in the body and therefore, it is excreted by the kidney unchanged (Shwide-Slavin C et al., 2012).

Uses

Acesulfame K is used in all fields of applications of artificial sweeteners. Common applications are tabletop sweeteners; beverages; foods, such as dairy products, desserts, bakery products, confectionery, chewing gum, pickles, and marinated fish; oral hygiene products and pharmaceuticals.

Owing to its synergistic characteristics, acesulfame K is often used in sweetener blends, and in combination with bulk sweeteners in products requiring good stability, e.g., confectionery or bakery products (McKetta et al., 1996). Ace-K is stable in dry preparation such as powdered beverages, desserts and tablet, as well as in products that have a low-water content, including hard candy or chewing gum. Ace-K is stable under the normal heating condition during food processing including: Production of fermented milk products, Spray-drying, form-mat drying and drying in a fluidized bed, Baking (Mattes et al., 2009).

Metabolism and health aspect

examined the influence of acesulfame-K on the composition and metabolism of gut microbiota in CD-1 mice. After four weeks' acesulfame-K intervention, the disturbance of metabolic pathways and intestinal flora was significantly induced in a gender-dependent manner. In male mice, the body weight was significantly increased, functional bacterial genes associated with carbohydrate or energy metabolism were enhanced, and the relative abundance of Bacteroides, *Sutterella* and *Anaerostipes* was significantly increased. In female mice, there was no significant change in body weight, but several bacterial metabolites such as 2-oleotriglyceride, succinic acid and d-lactic acid decreased (Bian et al., 2017).

6. Sodium cyclamate

Sodium cyclamate is not one of the sweetest artificial sweeteners as it is only 30 times sweeter than sucrose. Moreover, its taste when used alone is bitter, but it has a good synergistic effect with saccharin as already mentioned (Bellisle et al., 2007). Their use in mix has the advantage of better taste and quality of products (Bert Fraser-Reid., 2014)

To understand whether their use is safe or not, the FDA studied the presence of these compounds in foods and found low levels of cyclohexylamine. Since their levels did not increase after four months at room temperature in cola beverages, so they concluded that cyclamate sweeteners are quite stable for use in various foods such as beverages, bakery goods and confectionery (Mattes et al., 2009; Bellisle et al.,2007)

Figure 7. Dairy products of sodium cyclamate

Sodium cyclamate relationship with tooth decay

Cyclamate are 30 times sweeter than sucrose and is freely soluble in water. It is not fermented by oral microorganisms, consequently non – acidogenic in plaque pH measurements in vivo and thus possesses no cariogenicity.Cyclamates as 1% dietary levels produce a minimal laxative effect and are tumour promoters rather than true carcinogens (Bukhamseen F et al., 2015).

Uses

Sodium Cyclamate is widely used as sweetener in food production. As sweetener: in cakes, baked foods, candied fruits and Pickles to improve sweetness. As sweetener: in soft drinks, juices and ice creams to improve sweetness. Table-top sweeteners in the tablet, powder or liquid form.

Conclusions and Suggestion

Artificial sweeteners provide some of the health benefits. However, commonly these sweeteners are toxic at high concentrations in the long term. Their consumption has been shown to cause mild to serious side effects ranging from headaches to life-threatening brain damages.

Artificial sweeteners are widely used in food products. Many people use them to reduce calorie intake without concern of possible negative side-effects. Even though nutritional agencies attest to their safety, there is an increasing number of reports about the potential impact of these substances on elevated risks of cancer, cardiovascular diseases, obesity, and type 2 diabetes. There are also suspicions that by affecting gut microbiota, artificial sweeteners might contribute to various metabolic disorders. Given the current state of knowledge, it is challenging to determine whether the impact of artificial sweeteners on health is beneficial, neutral, or negative.

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