A Literature Review of the Prevalence, Metabolism, and Usage Guidelines of Non-nutritive Sweeteners

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A Senior Thesis submitted in partial fulfillment
of the requirements for graduation
in the Honors Program
Liberty University
Spring 2022

Acceptance of Senior Honors Thesis

This Senior Honors Thesis is accepted in partial
fulfillment of the requirements for graduation from the
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Abstract

Due to their reputation for being a healthier option to traditional table sugar, non-nutritive sweeteners have garnered popularity, particularly with those affected by type II diabetes mellitus (DM2) or obesity. A literature review on the characteristics, metabolism, and optimal cooking guidelines of non-nutritive sweeteners was performed to establish more knowledge about these trending food additives. The literature review indicates that the presence of non-nutritive sweeteners (NNS) may influence glucose metabolism by binding T1R2/T1R3 sweetness receptors present throughout the gastrointestinal tract. However, not all studies showed positive correlations. Though inconclusive, the studies suggest a possible connection between excessive NNS consumption and impaired glucose metabolism, but moderate consumption appears to have no significant effect.

A Literature Review of the Prevalence, Metabolism, and Usage Guidelines of Non-nutritive Sweeteners

Introduction

Companies have responded to growing national health concern by manufacturing food and drink with sugar substitutes. These alternatives to sugar products have potential to reduce the negative health effects of traditional table sugar. This is because sugar alternatives can have few to no calories without sacrificing the enticingly sweet taste sugar offers. They have great potential in the management and prevention of obesity and diabetes. Therefore, these products are marketed as a healthier food choice for individuals attempting to lose weight and control their blood sugar levels.

Background

The first no calorie sweetener, saccharin, was discovered in the late 1800s. Since then, many more have been discovered or artificially manufactured (Sylvetsly & Rother, 2016). Although these alternative sweeteners have been around for over a century and are found in a wide variety of food, there is controversy over whether they influence metabolism or blood glucose levels. Some studies report correlations between sugar substitute consumption and increased blood sugar or increased BMI, while other studies find no correlation. The abundance of these no calorie sugars present in our food and these conflicting claims underscores the need for a thorough literature review to assess their effects. Addressing questions such as how these sugar substitutes are metabolized by the body, if they are a legitimate treatment approach for management of diabetes mellitus type II (DM2), and if they have the potential to prevent DM2

and obesity through weight management is necessary to address national health concerns (Nichol et al., 2019; Samuel et al., 2018).

In the United States today, sugar substitutes have garnered so much popularity that they are found not only in pre-packaged food and drink, but also in restaurants, which allow customers to choose which sugar substitute to use in sweetening their coffee. Sugar substitutes can also be found in virtually any supermarket. Moreover, an influx of recipes containing sugar substitutes are popping up on the internet, as bloggers and dieters attempt to control their weight without giving up sweet flavor. Because sugar substitutes have completely different chemical structures than traditional table sugar, they have different properties such as melting points and solubilities. Being unaware of these properties can result in kitchen disasters like unflavored cookies, icing the texture of milk, or entirely breaking down under heat. Therefore, cooking guidelines need to be established in addition to reviewing potential metabolic effects so the amateur chef can continue making safe and delicious food. The sugar substitutes discussed in this paper are non-nutritive sweeteners (NNSs), meaning they pass through the gastrointestinal tract largely untouched, contributing no energy production to the consumer, and thus have no calories (Kroger et al., 2006).

What Are They?

The United States Food and Drug Administration, USFDA, currently regulates NNSs as food additives and has approved six: aspartame, acesulfame potassium (ace-K), saccharin, sucralose, neotame, and advantame. Two others, *Stevia reabudiana* Bertoni and *Siraitia grosvenorii* (monk fruit), are generally recognized as safe. The preceding eight NNSs will be discussed in this literature review. Sugar alcohols are not classified as non-nutritive sweeteners,

but rather low-calorie sweeteners, and therefore will not be discussed (Center for Food Safety and Applied Nutrition, 2019).

Most non-nutritive sweeteners have two names: a lesser-known chemical name, and a more recognizable brand name. For example, the chemical aspartame is more widely known as NutraSweet or Equal, its brand names, and the chemical sucralose is more widely known as Splenda (Wilson et al., 2019). Each of these sugar substitutes are much sweeter than traditional table sugar and can generally be consumed in large quantities without exceeding the acceptable daily intake established by the FDA. Table 1 shows the NNSs and their brand names, relative sweetness to table sugar, and accepted daily intake.

Who Eats NNSs?

It was recently estimated that 41% of adults and 25% of children consume NNSs (Nichol et al., 2019). To assess the knowledge and use of NNSs among college students, a survey was given to 1,293 health science students at Winona State University. 493 students completed this survey with the results shown in Table 2. Particularly noteworthy findings from this survey revealed about one fifth of the health science college students were unaware whether NNSs were present in foods they eat, while another one fifth of survey respondents claimed they consumed NNSs daily. Not including the one fifth of respondents who were unsure of their NNS consumption, almost 60% of surveyed respondents consume NNSs at least once per week. These responses suggest that consumption of NNSs among this group occurs on a regular basis despite their limited knowledge about which foods contain NNSs (Wilson et al., 2019).

Table 1

Comparison of Characteristics of Non-nutritive Sweeteners to Sugar

Sweetener	**Brand Names**	**Sweetness as compared with sugar**	**Acceptable Daily Intake (maximum number of tabletop sweetener packets per day in 132 lb individual)**
Aspartame	Equal®, NutraSweet®, Sugar Twin®	200 times sweeter than sugar	75
Acesulfame-K	Sunett®, Sweet One®	200 times sweeter than sugar	23
Saccharin	Sweet'N Low®, Sweet Twin®, Necta Sweet®	200-700 times sweeter than sugar	45
Sucralose	Splenda®	600 times sweeter than sugar	23
Neotame	Newtame®	7,000-13,000 times sweeter than sugar	23
Advantame	No brand names	20,000 times sweeter than sugar	4920
***Stevia reabudiana* Bertoni**	TruVia®, Enliten®, PureVia®	200-400 times sweeter than sugar	9
Siraitia grosvenorii	Monk Fruit, PureLo®, Nectresse®	100-250 times sweeter than sugar	No data

Note. Adapted from https://www.fda.gov/food/food-additives-petitions/additional-information-about-high-intensity-sweeteners-permitted-use-food-united-states. Copyright 2018 by Federal Drug Administration.

Table 2

Survey Results of Frequency of NNS Consumption of College Students

Self-Described NNS Use:	**Percent (%)**
I do not know if I consume them	18.9
I never consume them	5.2
Once or more each day	21.1
Once or more each week	37.8
Once or more each month	10.2
Less than once each month	6.3

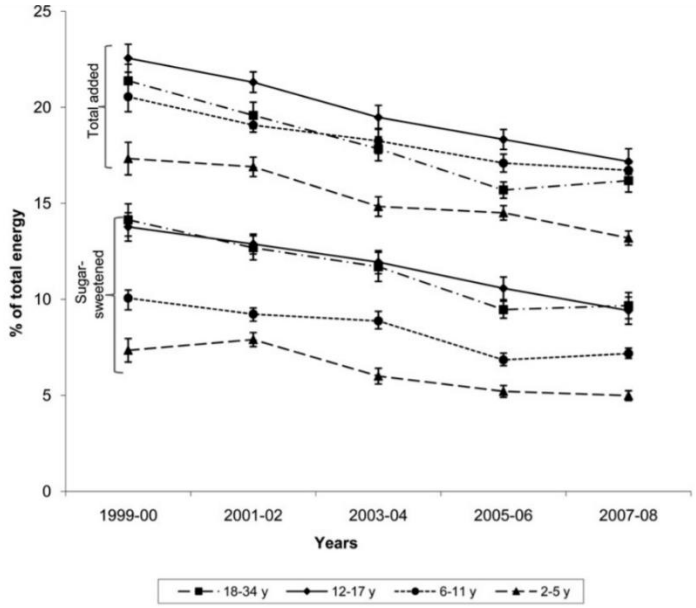
Note. Adapted from "Non-Nutritive (Artificial) Sweetener Knowledge among University Students" by Wilson, T., Murray, B., Price, T., Atherton, D., & Hooks, T, 2019, *Nutrients, 11*(9), 2201. http://dx.doi.org/10.3390/nu11092201

Although many studies have attempted to assess the true amount of NNS consumption in a population, all have their shortcomings. First diet assessments are generally performed through surveys and self-report forms which have their own limitations. Second, products containing NNSs are constantly being changed, added, and removed from the market. Third, the same product across various brands may be produced with a NNS in one brand and without a NNS in other brands. Because of this, individuals may be unaware that their brand contains NNSs. Difficulty in performing accurate diet assessments hinders researchers from establishing exact data on NNS consumption. The most effective way to minimize this sampling error is by increasing sample size (Sylvetsky & Rother, 2016).

The following study attempted to overcome the difficulty in performing accurate diet assessments by using a large sample size. This study consisted of 42,316 people in the United States over a ten-year period (1999-2008). The study found a decrease in NNS consumption among all age groups, with the most significant source of NNS consumption being through soda beverages. According to this study, the decrease in soda beverage consumption over the ten-year period was responsible for two thirds of the decrease of total NNS consumption. Interestingly, the consumption of all beverages sweetened with NNSs decreased over the ten-year period except for energy drinks. Figure 1 shows this trend (Welsh et. al., 2011).

Figure 1

Average Percent of Calories Consumed as Sugar-Sweetened Beverages and Total Added Sugars by Age Group from 1999-2008



Note. Reprinted with author permission from "Consumption of Added Sugars is Decreasing in the United States" by Welsh, J. A., Sharma, A. J., Grellinger, L., & Vos, M. B, 2011, *The American journal of clinical nutrition, 94*(3), p. 730. https://doi.org/10.3945/ajcn.111.018366

Normal Physiology of Sweetness Taste Receptors

NNSs function by binding to specific receptors on taste buds, resulting in a pleasant, sweet sensation. The sweetness receptor is a heterodimeric G-protein coupled receptor (GPCR) consisting of two subunits, T1R2 and T1R3 (taste type 1 receptor, member 2, and taste type 1 receptor, member 3). While sucralose binds both subunits, Ace-K and saccharin bind only the T1R3 subunit (Li et al., 2020; Rother et al., 2018). Upon binding, a signal transduction cascade begins with the release of α-gustducin. α-gustducin activates phospholipase C which cleaves phospholipids in the cell membrane. When phospholipase C cleaves a membrane phospholipid, inositol triphosphate (IP_3) is formed. IP_3 is transported to the endoplasmic reticulum of the cell where it opens ligand gated calcium channels of the endoplasmic reticulum. A rush of calcium ions flooding from the endoplasmic reticulum into the cytoplasm causes cell depolarization and the generation of an action potential. This action potential travels to a region of the brain that identifies this signal as sweet (Rother et al., 2018).

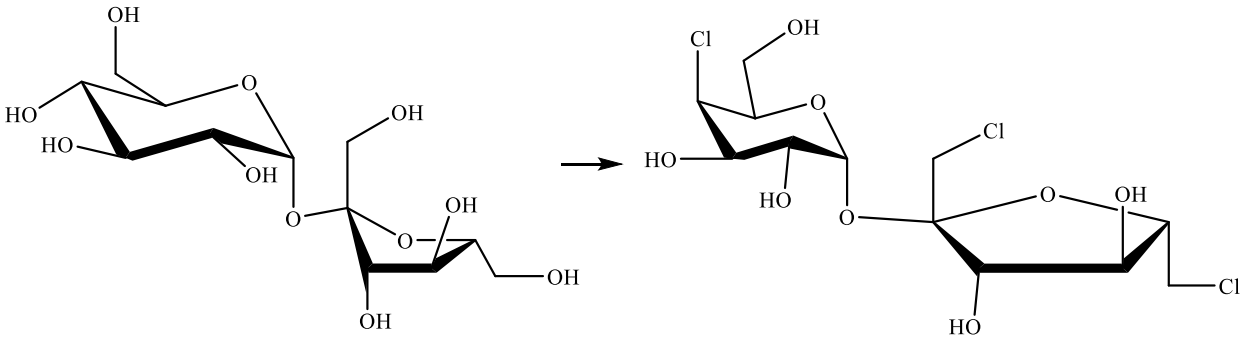
How Do NNSs Work?

Non-nutritive sweeteners are either discovered in nature or produced in a lab. Both *Stevia reabudiana* Bertoni and *Siraitia grosvenorii* were discovered in nature from the stevia plant and monk fruit respectively. The six USFDA approved NNSs, aspartame, ace-K, saccharin, sucralose, neotame, and advantame, were produced in a lab. A NNS can be made by altering the structure of a naturally occurring sugar to make it indigestible and therefore zero calories. However, the structure of the derivatized compound must maintain enough of its original structure to bind and activate the T1R2/T1R3 receptor. A molecule that is indigestible yet fails to activate the sweetness receptors will have no flavor, while a molecule that is not altered enough

yet maintains its ability to activate sweetness receptors will still contribute to caloric intake. For example, sucralose was discovered in 1976. Sucralose was made by altering the structure of sucrose, table sugar, by replacing three of its hydroxyl groups with three chlorine atoms. The chemistry of carbon four was also inverted (see Figure 2). These chemical changes to sucrose prevent the molecule from being broken down and absorbed in digestion, however its chemical structure remains similar enough to sucrose to activate the sweetness taste receptors so the consumer senses sweetness (Kroger et al., 2006).

Figure 2

Conversion of Sucrose to Sucralose



Sucrose Sucralose

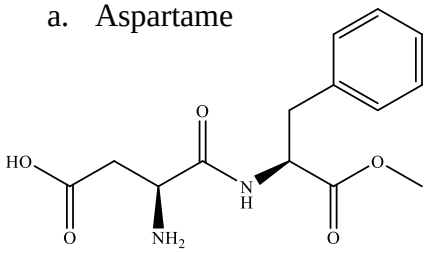
Whereas the disaccharide sucrose is enzymatically cleaved into two monosaccharides during digestion, glucose and fructose, sucralose is not. The substitution of three hydroxyl groups with the atom chlorine and inversion of chemistry at carbon four of sucrose prevent the sucrose enzyme from cleaving sucralose into monosaccharides. Since sucralose cannot be cleaved, it is not able to be absorbed by the body nor contribute energy (calories) to the consumer. However, the structure of sucralose is such that it still maintains enough specificity to bind its receptor (Grotz et. al., 2003).

The original chemical structures of the NNSs discussed in this review can be seen in Figure 3. Although none of these NNSs contribute to caloric intake, not all of them keep their original chemical structure throughout digestion. For example, one of the breakdown products of aspartame is phenylalanine (Newbould et al., 2021). Phenylalanine is not a health concern for most people and is generally recognized as safe. However, certain dietary situations such as Phenylketonuria (PKU) require affected individuals to pay special attention to phenylalanine consumption. This is because individuals affected by PKU lack the enzyme phenylalanine hydroxylase and are therefore unable to degrade phenylalanine. A buildup of phenylalanine is toxic to nervous cells and can result in impaired nervous function (Calorie Control Editorial Team, 2017). As a result, individuals affected by PKU must avoid ingesting aspartame to prevent toxic phenylalanine accumulation. Individuals without PKU do not have to monitor their phenylalanine intake as they have the enzyme phenylalanine hydroxylase to properly utilize phenylalanine. Due to conditions such as PKU, products containing aspartame are required to have warning the label: “Phenylketonurics: Contains Phenylalanine” (Calorie Control Editorial Team, 2017).

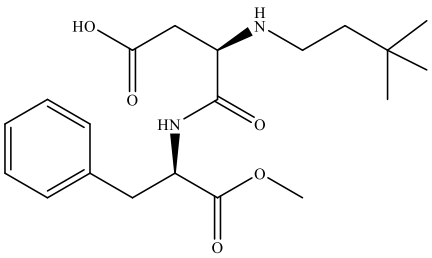
Figure 3

Molecular Structures of NNSs.

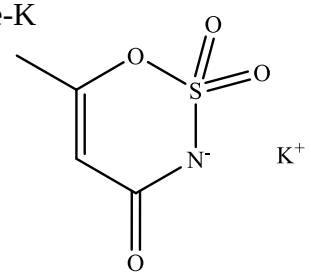
a. Aspartame



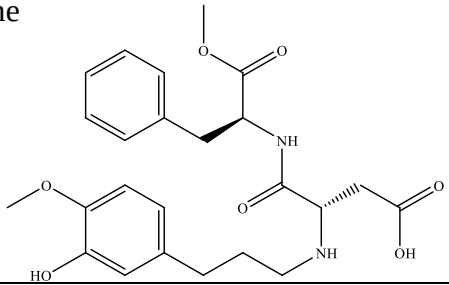
e. Neotame



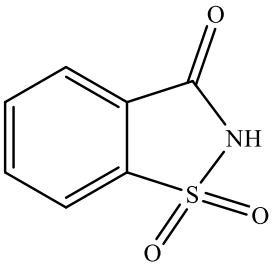
b. Acesulfame-K



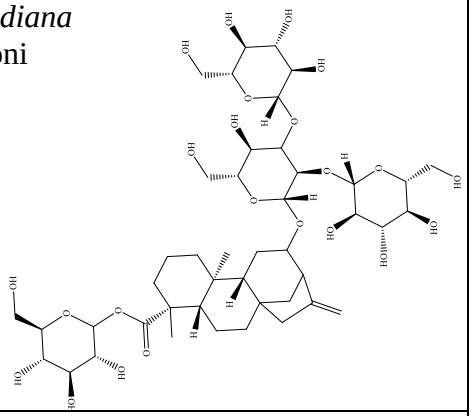
f. Advantame



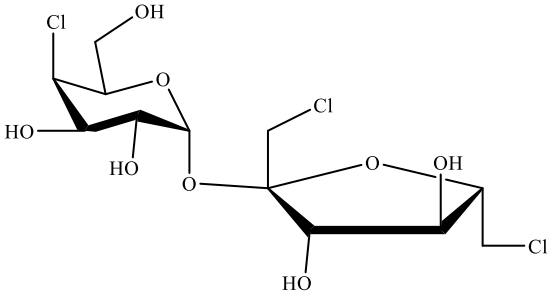
c. Saccharin



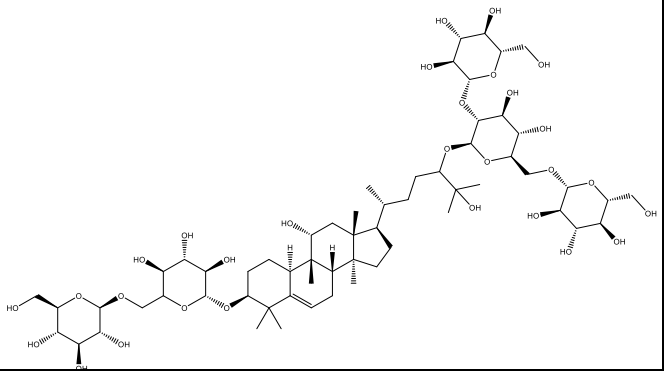
g. *Stevia reabudiana* (Bertoni) Bertoni



d. Sucralose



h. *Siraitia grosvenorii* (Mogroside V)



Note. Mogroside V is the molecule responsible for sweetness in *Siraitia grosvenorii*, monk fruit.

Do NNSs Have a Role in Glucose Metabolism?

The T1R2/T1R3 receptors responsible for sensation of sweetness in the mouth are found in not only the oral cavity, but also other tissues throughout the gastrointestinal tract. Since the structure of most NNSs is conserved throughout digestion, most maintain the chemical capabilities to bind the T1R2/T1R3 receptors in these tissues. As mentioned previously, binding T1R2/T1R3 receptors in the oral cavity results in an action potential sent to the brain interpreted as sweet (Nichol et al., 2019). It is well established that molecules' binding receptors in one tissue type can have a different effect in a different tissue. Determining the effect of T1R2/T1R3 receptor binding in endogenous tissue is foundational to determining the influence of NNSs, if any, on glucose metabolism and absorption. The answer to this question will provide insight into whether NNSs prove to be effective for prevention and management of DM2 and obesity (Nichol et al., 2019).

It was recently established that T1R2/T1R3 receptors are also found in human intestinal and pancreatic cells. Many studies have established that activation of T1R2/T1R3 receptors in enteroendocrine cells of the intestine results in increased glucose absorption through the intestinal epithelium (Mace et al., 2007; Margolskee et al., 2007; Stearns et al., 2010). In intestinal cells, glucose is absorbed by either the glucose transporter 2 pathway (GLUT2) or the sodium-glucose cotransporter (SGLT1). Both GLUT2 and SGLT1 are transmembrane proteins that transport glucose from outside the cell membrane into the cell. After a meal, the lumen of the intestines is high in glucose. This high glucose environment is the signal received by intestinal cells that causes an increased number of GLUT2 and SGLT1 proteins expressed in the intestinal cell membrane. Greater numbers of GLUT2 and SGLT1 membrane proteins result in

greater uptake of glucose, which can be metabolized and transported through intestinal cells into the bloodstream, raising an individual's blood sugar, and stimulating the release of insulin.

In a high glucose environment, for example after a meal, the GLUT2 pathway is utilized three to five times more than SGLT1 and functions by embedding more GLUT2 receptors into the cell membrane upon activation (Mace et al., 2007). One study investigated the effect of sucralose on these two glucose transporters in the intestine using *in vivo* rat jejunum. Since the presence of glucose affects the amount of GLUT2 in cell membranes, 20 mM glucose was given to rats as a control to establish initial GLUT2 membrane levels. After 30 minutes, 1 mM sucralose was added to the solution. After a short lull, the rate of glucose absorption doubled. However, when the rats were on a 20 mM glucose with 1 mM sucralose solution from the start, the amount of GLUT2 increased 3.2-fold within 5 to 20 minutes. The amount of GLUT2 that was expressed under 20 mM glucose and 1 mM sucralose is equivalent to the amount of GLUT2 that would result if 75 mM of pure glucose were given. These results indicate that sucralose consumption with glucose causes the amount of GLUT2 expressed in the cell membrane to increase, even though it is not getting broken down and digested by the body. Since GLUT2 is one of the two main pathways that transports glucose into the cell for metabolism, this experiment suggests that sucralose causes more rapid glucose uptake into cells. This study also suggests that the T1R2/T1R3 sweetness taste receptors may not only function to taste sweetness, but also act as glucose sensors (Mace et al., 2007; Stearns et al., 2010).

Regarding the SGLT1 pathway, NNSs were found to upregulate intestinal SGLT1 by increasing SGLT1 mRNA. Upregulation of SGLT1 would also cause more rapid uptake of glucose into cells. A proposed mechanism for this upregulation is α-gustducin and downstream

hormones released upon T1R2/T1R3 binding are responsible for increased production of SGLT1 mRNA. These studies also suggest that T1R2/T1R3 receptors may act as glucose sensors like the studies mentioned above. The proposed mechanism for T1R2/T1R3 receptors acting as glucose sensors is that the hormones gastric inhibitory polypeptide (G1P) and glucagon-like peptide 1 (GLP-1) are secreted from the cell and bind nearby cells. These neighboring cells then stimulate production of SGLT1 mRNA through a paracrine signal. G1P and GLP-1 are downstream hormones released as a result of T1R2/T1R3 binding (Margolskee et al., 2007). These studies indicate that when T1R2/T1R3 receptors are activated in the intestine, they cause the rate of glucose absorption into cells to increase (Mace et al., 2007; Margolskee et al., 2007; Stearns et al., 2010).

Application to the General Population

In conclusion, it is established that T1R2/T1R3 receptors are found not only in the oral cavity, but throughout the gastrointestinal tract namely the intestines and pancreas. As the structure of most NNSs is unchanged through digestion, NNSs are still capable of binding these receptors in other tissues. Multiple studies report that T1R2/T1R3 receptor binding in the intestines results in more rapid glucose absorption through embedding GLUT2 and SGLT1 into the cell membrane. Additionally, NNS consumption with glucose was reported to significantly increase the amount of GLUT2 present in cell membranes, and greatly increase the rate at which glucose is absorbed into cells.

Other studies indicate that stimulation of T1R2/T1R3 receptors found in β-cells of the pancreas results in insulin secretion (Nakagawa et al., 2009; Stearns et al., 2010). Pancreatic β-cells are the primary mode of glucose regulation in the body through secretion of insulin. In the

presence of glucose, sucralose was found to cause β-cells to secrete insulin. This was explained by an increase in activated cyclic AMP and calcium ion in β-cells, which by their signaling cascades cause insulin secretion. Additionally, the amount of insulin secretion was proportional to the dose of sucralose (Nakagawa et al., 2009).

Although these studies do not prove NNS consumption increases blood sugar, they do show a correlation between presence of NNSs outside a cell and increased GLUT2 and SGLT1 glucose transporters embedded in the membrane. This means that consumption of NNSs results in more rapid uptake of glucose. The studies also suggest that NNSs may cause an increase in insulin release when ingesting NNSs with glucose versus just glucose. This is because more rapid glucose absorption will lead to a transient spike in blood glucose.

Application to Diabetic Populations

Diabetes mellitus is the seventh leading cause of death in the United States, affecting roughly 9% of the world's population and claiming about 88,000 lives each year (Centers for Disease Control and Prevention, 2019; Efrat, 2019). Because obesity is the most prevalent and most important risk factor for type 2 diabetes mellitus (DM2), the combination of the two have earned their own name, "diabesity" (Toplak et al., 2016, p. 196). Additionally, some studies claim that DM2 is the most prominent risk factor for heart disease, the number one cause of death in the United States, claiming 660,000 lives each year (Centers for Disease Control and Prevention, 2019; De Schutter et al., 2014). The large number of people affected by these diseases, compounded with each disease's risk factors, make diabetes and obesity paramount health concerns in the United States. As a result, members of this population turn to NNSs in attempts to control their body's insulin response.

Regarding diabetic patients, it is demonstrated that sucralose consumption has no significant difference on plasma glucose nor serum C peptide levels. These findings were supported by analysis post meal with and without 1,000 mg of sucralose, as well as a thirteen-week study where sucralose was ingested at 7.5 mg/kg/day. This study is significant as it indicates regular consumption of sucralose does not result in higher blood sugar levels (Grotz et al., 2017; Grotz et al., 2003; Mezitis et al., 1996).

On the other hand, some studies claim that sucralose does affect blood sugar by decreasing the body's sensitivity to insulin. Since decreased insulin sensitivity leads to DM2, this indicates that sucralose consumption worsens DM2 in those already affected by the disorder (Pepino, 2018; Romo-Romo et al., 2018; Suez et al., 2014). A randomized clinical trial was performed in adults without diabetes, pre-diabetes, or on sugar-interfering drugs and a control group given placebo. Each individual chosen for the study had reported low consumption of NNSs on a regular basis. In the experiment, individuals consumed 15% of the ADI of sucralose through tabletop sweetener packets for fourteen days. Insulin sensitivity was measured through a variety of glucose variables. After fourteen days, individuals consuming 15% of the ADI of sucralose every day showed slightly decreased insulin sensitivity. This can be explained by the combination of increased GLUT2 and SGLT1 in the cell membrane and the release of GLP-1 and insulin. These factors contribute to a state of more rapid glucose uptake causing higher insulin release in habitual NNS consumers (Romo-Romo et al., 2018).

These studies indicate it is possible NNSs may decrease insulin sensitivity. Although there is conflicting data on whether NNSs alters blood glucose levels, NNSs still remain abundant in our food supply, and popular opinion seems to be in favor of them as dieting recipes

use them in abundance. However, different chemical structures cause NNSs to have very different properties than sugar, so specific cooking guidelines are needed to create the expected dish.

Cooking with Non-nutritive Sweeteners

Not only do individuals consume NNSs through pre-prepared food they purchase, but individuals are turning to NNS in their own recipes to create lower calorie dishes with the same sweet flavor traditional table sugar provides. This may be a great option for individuals looking to consume fewer calories without sacrificing sweet flavor or the palatability of food. Substituting NNSs in recipes can be tricky as each NNS has a different chemical structure from table sugar and from each other. This may cause different results than expected – even when keeping the rest of the recipe the same. Most NNSs can be found in the supermarket by alternative flours in the baking aisle. With many NNSs to choose from and different chemical structures of each, it is important to establish cooking guidelines to prepare a safe and delicious dish.

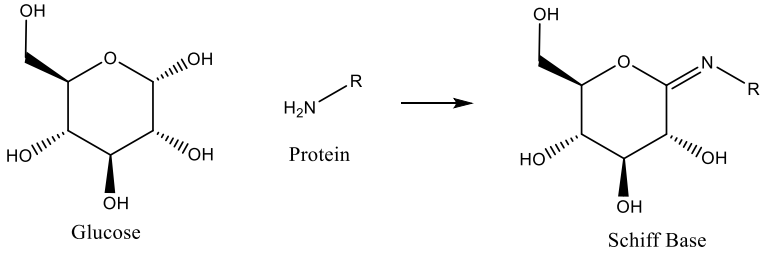
The chemical structure of NNSs cause them to behave differently than sugar and each other in cooking by affecting volume, texture, and color in the resulting dish. NNSs contribute little to no volume to the dish, may or may not be heat stable, and generally do not brown upon heating. For this reason, the right NNS must be chosen for the right dish. Simply substituting a NNS for sugar in a dish is bound to change the resulting texture. Generally, more fat or flour can be added to a dish to make up for the loss in volume, and the one chosen will depend on the desired texture (Webb, 2021). Additionally, NNSs will not give a dish the golden-brown color expected when baking, so the NNS combined with a small amount of sugar is recommended to

achieve the expected golden color. This coloring is the result of the Maillard reaction, the reaction responsible for the browning of breads and pastries (see Figure 4). Pyrolysis is a separate process that is responsible for sugar breaking down when melted over the stove (see Figure 5) (Webb, 2021).

When using table sugar, the reducing end of the hydroxyl group binds the amino group of the protein. This forms an unstable, Schiff base intermediate that goes onto more organic reactions including the Amadari rearrangement (Webb, 2021).

Figure 4

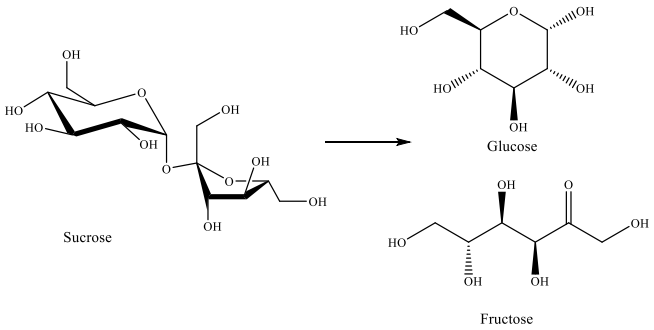
Maillard Reaction Between a Glucose Molecule and a Protein



In pyrolysis, the disaccharide sucrose breaks into two monosaccharides, glucose and fructose, which then form various other compounds (Webb, 2021).

Figure 5

Pyrolysis of Sucrose



Referring back to the NNS structures provided in Figure 3, it is evident that none of these chemicals are reducing agents, so they cannot participate in the Maillard reaction. If a NNS is heat stable and subsequently melted over the stove, pyrolysis will not occur. This is because none of the chemical structures of the NNSs break into glucose and fructose, the molecules that give caramelized sugar its taste and aroma (Webb, 2021). As sugar also contributes structure to foods, it is impractical to use a NNS for something like icing where the bulk of the structure comes from the sucrose (table sugar) molecules (Medline Plus, 2019).

One experiment was performed to determine the results of substituting sugar with various NNSs in cakes and biscuits. The control consisted of a cake and biscuit baked with table sugar (sucrose), while the experimental group consisted of the same recipe for cake and biscuit with the equivalent amount of NNS. This experiment identified the change in taste, texture, volume, and color when substituting sugar with a specific NNS. For example, ace-K, sucralose, and stevia substitutions resulted in significantly lower volumes than the control. Substituting aspartame resulted in an off-tasting product, while ace-K left a bitter aftertaste. Generally, NNS substitutions resulted in lighter crumb color and darker crust colors. This change in color can be explained by the Maillard reaction and pyrolysis that require table sugar (sucrose) to create the expected golden-brown color. The results are shown in Table 3 (Luo et. al., 2019).

Table 3

Reformulation Studies Examining the Feasibility of Using Non-nutritive Sweeteners in Baked Products

Non-nutritive Sweetener	Physiochemical Analysis	Sensory Analysis
Aspartame	+moisture + off flavor -cell hardness	No significant difference
Acesulfame-K	-volume -weight Lighter crust and crumb color	Higher acceptance than control Detectable bitter aftertaste
Sucralose	-volume	Darker crust color Lower acceptance Lower score than control biscuit Lower acceptance in all sensory aspects
***Stevia reabudiana* Bertoni**	Close to control cake Slightly decreased volume and diameter Lighter in crumb color	Close to control Lower color and appearance acceptance Darker crust color Lower texture acceptance

Note. "+" means significantly increased, "-" means significantly decreased. Adapted from "A Review of Food Reformulation of Baked Products to Reduce Added Sugar Intake" by Luo, X., Arcot, J., Gill, T., Louie, J. & Rangan, A, 2019, *Trends in Food Science & Technology*, *86*, p. 420. https://doi.org/10.1016/j.tifs.2019.02.051

Cooking Guidelines for Each NNS

Aspartame is not heat stable, so it is not a good choice in cooking or baked dishes. For this reason, it is mostly present in zero-calorie drinks which are the best type of food to use aspartame as a sugar substitute (Medline Plus, 2019). Although aspartame will eventually degrade when present in liquids for a lengthy amount of time, this is accounted for by the

expiration date stamped onto the commodity's packaging (Kroger et. al., 2006). Ace-K tastes most similarly to table sugar and is heat stable, making it a great substitution for table sugar. Although Ace-K tastes the most similarly to sugar, additional fat or flour is still necessary to maintain the desired texture for cooked dishes (Medline Plus, 2019).

Saccharin is not typically used in cooking or baking as people report it leaving a metallic or bitter aftertaste in the mouth. In the food industry, saccharin is mostly used in zero-calorie drinks (Medline Plus, 2019). It is one of the least costly NNSs, and as a result is one of the most widely consumed NNSs worldwide. (Sylvetsly & Rother, 2016; Kroger et. al., 2006). Between World War I and World War II, saccharin use in Europe greatly increased because of strict sugar rations. Although sugar rations are not present today, use of this NNS remains abundant (Kroger et. al., 2006).

Sucralose, advantame, and neotame are heat stable and can be used in cooking (Kroger et. al., 2006). Neotame is mostly commonly used as a tabletop sweetener (Medline Plus, 2019). Interestingly, this sweetener is approved for use in any food product except for poultry or meat. However, this disapproval did not fall under the USFDA, but rather the Food Safety and Inspection Service (FSIS). FSIS does not permit neotame in meat or poultry due to its established "identity regulations" outlining what can and cannot be added to meat and still be called meat (Kroger et. al., 2006).

Since stevia has a milder sweet flavor and a slightly bitter aftertaste, it is best used in dishes that have other strong flavors to mask it. For example, stevia can be a good sugar substitute in hot chocolate, smoothies, dressings, and sauces. *Siraitia grosvenorii*, monk fruit, is heat stable (Medline Plus, 2019). China has been using monk fruit to sweeten their food for a

thousand years by crushing up the fruit's flesh. A summary of these guidelines are provided in Table 4.

Table 4

Tastes and Melting Points of Various NNSs Discussed.

Sweetener	Melting point (*C)	Taste and Aftertaste
Aspartame	Decomposes before melting	A clean sweetness with a slight delay and moderate linger
Acesulfame-K	>200	A bitter and metallic off taste at high concentrations
Saccharin	>300	A bitter and metallic off taste without delay and linger
Sucralose	130	A slight delay in sweetness with moderate linger
Neotame	81-83	A delayed sweetness and linger
Advantame	n/a	A clean sweetness without off taste; with a linger
Stevia reabudiana	n/a	A clean, sweet taste (low concentration), Bitterness (high concentration), Metallic aftertaste, A bitter and licorice-like off taste, A slight delay and moderate linger sweetness
Siraitia grosvenorii	n/a	A delay of maximum sweetness and an aftertaste of liquorice and cooling effects, a delayed followed by a lingering and liquorice-like sweetness

Note. Adapted from "A Review of Food Reformulation of Baked Products to Reduce Added Sugar Intake" by Luo, X., Arcot, J., Gill, T., Louie, J. & Rangan, A, 2019, *Trends in Food Science & Technology*, *86*, p. 419. https://doi.org/10.1016/j.tifs.2019.02.051

Conclusion

At the end of the day, a good rule to live by is keep everything in moderation. Considering the most recent research on NNSs, there are studies that found a positive correlation between NNS consumption and upregulation of molecules related to glucose metabolism, while

other studies found no correlation. Certain populations such as those affected by phenylketonuria may need to avoid NNSs, while other populations may not need concern themselves with tracking these food additives. Whether or not NNSs affect the body like traditional table sugar, it is important to remember that NNSs have no nutritional value. Although NNSs taste good, they contribute no energy for bodily use. A diet high in NNSs likely lacks essential nutrients required for cellular function and consuming an insufficient number of calories comes with its own serious diseases. On the other hand, overconsumption of sugar can lead to insulin resistance, obesity, and DM2.

It is important to remember that sugar is not the enemy and it is incorrect to moralize food. Food is not inherently good or bad. Although generally inadvisable, consuming ice-cream for lunch does not make you bad, for the same reason that eating a salad for lunch does not make you good. There is no right or wrong food, there are just molecules that make up foods, that are chopped, mixed, and cooked together into a dish, which is then broken back down during digestion. The human body was built to run on essential biomolecules including carbohydrates. Food is fuel, and if that fuel is sweetened with NNSs as opposed to traditional table sugar, adequate carbohydrate consumption from elsewhere needs to be ensured for optimal bodily function.

Not only is food central to the United States today, but it is also a recurrent theme in the Bible. From Adam and Eve eating the forbidden fruit in the book of Genesis, celebrating with a feast upon the return of the prodigal son, Jesus’s providing wine at the wedding in Galilee as his first miracle, and communion during the Passover, food is central to expressing life, intimacy,

and fellowship. Though the act of eating is mundane, 1 Corinthians 10:31 and 1 Peter 4:4 reveal it ought to have the objective of bringing glory to God (*English Standard Version*, 2022).

In conclusion, some research on NNSs shows correlations between their consumption and a bodily response similar to what happens after consumption of sugar, while other research does not show a correlation. Consequently, there exists a need for further research on NNSs, especially since they remain prevalent in the United States' food supply. It is important to be conscious of the ingredients in foods and the way they are prepared to optimize health. For some this may include consuming NNSs on a regular basis instead of their sugar-sweetened counterparts, while other individuals may need to avoid NNSs as well as focus on implementing other aspects of health such as exercise. No matter how many NNSs are consumed, it is most important to consume adequate nutrition in type and amount to maintain optimal bodily function and help prevent disease.

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