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Effect of Toothpaste Sweeteners on Glucose Homeostasis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: The oral mucosa, consisting of non-keratinized stratified squamous epithelium with lipids in the basal membrane, serves as a protective barrier. Its permeability can increase due to factors such as alcohol, stress, or chemicals. In this context, sweeteners, both synthetic and

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natural, could influence blood glucose levels, although further research is needed to understand their long-term effects. This study aims to evaluate the impact of high-Brix toothpastes on serum blood glucose levels.
Methods: A prospective study was conducted with 50 participants aged 18 to 25 years. Blood glucose levels were measured before and after brushing with different toothpastes, with three measurements taken at 15-minute intervals.
Results: The control group (without toothpaste) did not show a significant change in glucose level at a probability level (p= 0.5277). In contrast, the group using Arm & Hammer Truly Radiant toothpaste showed a significant difference (p= 0.0336), suggesting a potential effect on glucose level.
Conclusions: Sweeteners in toothpaste may alter blood glucose levels when exposed to a standardized brushing time of 3 minutes. Further studies are needed to confirm these findings and assess their clinical implications.

Keywords: Blood glucose; brix; sweetening agents; toothpastes.

1. INTRODUCTION

The mucosa of the oral cavity is composed of non-keratinized stratified squamous epithelium (Kitsukawa et al., 2024). At the basal membrane level, it contains lipids that are part of the lipid barrier, derived from the membrane surrounding the stratum spinosum granules in the epithelium. These lipids play a crucial role in protecting the mucosa. However, when exposed to various substances, they may dissolve or become altered, compromising the integrity of the lipid barrier and increasing epithelial permeability (Vilas et al., 2023).

The permeability of the oral mucosa is a key property regulating the entry and exit of various substances. The lipid barrier, which plays a fundamental role in this process, facilitates the passage of small lipophilic molecules. However, when this barrier is disrupted, whether by internal or external factors, the mucosal permeability increases, allowing the penetration of undesirable compounds and reducing its protective function for underlying tissues. In this context, while the oral mucosa relies on glycosylceramides to maintain its barrier function, its structure may be vulnerable to factors such as alcohol or stress (Casariego & Pérez, 2017; Nacucchio & Manzo, 2019 & Hidalgo et al., 2010).

Certain products, such as benzyl alcohol found in toothpaste, can disrupt the lipid barrier at high concentrations, increasing permeability and altering mucosal morphology, leading to changes like epithelial atrophy. Additionally, the thickness of the mucosa influences its ability to absorb substances: greater thickness reduces permeability to lipophilic compounds but does not similarly affect hydrophilic compounds (Albarracín-Vélez et al., 2018 & Pinelo-Cuevas & Rueda, 2012).

Sweeteners are substances used to mimic the sweet taste of sugar while providing little to no caloric intake. They can be classified as either synthetic or natural. One of the most common synthetic sweeteners is high-fructose corn syrup (HFCS), widely used in the food industry. HFCS is produced through an acid hydrolysis process of corn starch, converting starch into glucose, which is subsequently transformed into fructose by the enzyme glucose isomerase. HFCS is much sweeter than sucrose and is primarily used in soft drinks and processed foods. Although effective in reducing production costs, excessive consumption of HFCS has been associated with various health problems, including an increased risk of insulin resistance, metabolic syndrome, and obesity (Meneses et al., 2023).

Natural sweeteners, such as calorie-free options like stevia, sugar alcohols (erythritol, xylitol, sorbitol), and tagatose, are popular alternatives. These sweeteners provide no calories, making them attractive to individuals seeking to reduce caloric intake without sacrificing sweetness. Sugar alcohols, such as xylitol and erythritol, offer the added advantage of being incompletely absorbed in the small intestine, minimizing their impact on blood glucose levels.

Stevia, in particular, is renowned for its ability to lower blood glucose levels and has been investigated as a potential adjunct treatment for managing type 2 diabetes due to its hypoglycemic effect. Stevia activates sweet taste

receptors in the oral cavity (T1R2-T1R3 receptors) and stimulates the release of incretins—intestinal hormones that promote insulin secretion and enhance satiety. However, the long-term effects of natural sweeteners like stevia on metabolism require further study to confirm their safety and efficacy (Gutiérrez, 2024 & Vicuña et al., 2019).

2. MATERIALS AND METHODS

2.1 Study Design

Explanatory, prospective, analytical, descriptive, longitudinal, quasi-experimental, mixed, case-control, randomized, and risk-free study.

2.2 Sample Size

50 individuals aged 18 to 25 years.

2.3 Study Population

The study included various commercial toothpaste brands and serum glucose levels measured in 50 individuals divided into five groups of 10 participants each. Three blood glucose measurements were taken at 15-minute intervals.

2.4 Observation Units

The study compared the different sweeteners in toothpastes and used Brix degree measurements to determine the sugar content in the toothpaste. Serum glucose levels were assessed after a 3-minute oral exposure to the toothpaste.

2.5 Inclusion Criteria

Clinically healthy individuals, No family history of diabetes, Aged 18 to 25 years, Participants who arrived fasting and without brushing their teeth prior to the study at the Latino Laboratory facilities in Morelia.

2.6 Exclusion Criteria

Individuals who ate breakfast or brushed their teeth before the test, Participants with a family history of diabetes.

3. RESULTS

An evaluation was conducted on 48 commercially available toothpastes in the Morelia, Michoacán, Mexico, market at the facilities of the Centro Mexicano en Estomatología, Morelia campus. Despite the wide variety of both cosmetic and therapeutic toothpastes, not all could be analyzed due to their limited availability in stores.

To identify the toothpastes with the highest concentration of sugar substitutes, a Brix refractometer was used. A solution was prepared by diluting 1 g of toothpaste in 1 ml of distilled water, yielding a range of 12°–37.9° Bx. Additionally, the ingredient lists of the toothpastes were reviewed to catalog the sweeteners used. Most products combined multiple chemical compounds to enhance flavor, with sodium saccharin and sorbitol being the predominant sweeteners. Xylitol and stevia were used less frequently. Table 1.

Based on the collected data, three toothpastes with the highest Brix values were selected for further evaluation: Arm & Hammer Truly Radiant, Sensodyne Rápido Alivio, Colgate Sensitive Pro Alivio Inmediato. To perform this analysis, 50 participants (20 women and 30 men) aged 18 to 25 years were recruited. They were randomly assigned to five groups of ten participants each. These groups reported to the Latino Laboratory in Morelia, where their serum glucose levels were measured at three different intervals, with 15-minute gaps between each measurement.

The methodology included two control groups: First Control Group: Participants in this group were asked to arrive fasting and without brushing their teeth for 8 hours prior. Upon arrival, the first serum glucose sample was taken, followed by a second sample 15 minutes later, and a third sample after another 15 minutes. In most cases, glucose levels tended to decrease over time. The mean values were: First sample: 81.3 mg/dL, Second sample: 80.8 mg/dL, Third sample: 79.5 mg/dL. Second Control Group: This group also arrived fasting and without oral hygiene for 8 hours. The same sampling procedure was followed. After the first and second glucose measurements, participants were asked to brush their teeth using their usual technique, toothpaste, and rinse with tap water, if that was their routine at home. A third glucose sample was then taken 15 minutes after brushing. The mean glucose levels were: First sample: 81.3 mg/dL, Second sample: 86.8 mg/dL, Third sample: 86.3 mg/dL. Table 2.

Table 1. List of toothpastes ordered by descending brix levels and sweeteners identified in each dentifrice

Toothpaste	Sweetener	Brix
Arm & Hammer Truly Radiant	Sorbitol, Sodium Saccharin	37.9°Bx
Sensodyne Rapid Relief	Sodium Saccharin	37.2°Bx
Colgate Sensitive Pro Immediate Relief Gums	Sorbitol, Sodium Saccharin	36°Bx
Sensodyne Repair & Protect	Sodium Saccharin	36°Bx
Arm & Hammer Advance White Complete	Sodium Saccharin	36°Bx
Briden	Unspecified	34.8°Bx
Oral-B Gums Dentox	Sorbitol, Sodium Saccharin	34°Bx
Arm & Hammer Advance White Tartar Control	Sorbitol, Sodium Saccharin	34°Bx
Marvis Aquatic Mint	Sodium Saccharin	34°Bx
Colgate Sensitive Original	Sorbitol, Sodium Saccharin	34°Bx
Marvis Classic Strong Mint	Sodium Saccharin	33°Bx
Colgate Max Fresh	Sorbitol, Sodium Saccharin	32.2°Bx
Crest Complete Whitening + Scope	Sobitol, sodium Saccharin	32.2°Bx
Tom´s Antiplaque & Whitening	Xylitol	31°Bx
Oral-B Pro-Gums Sensitivity	Sorbitol, Sodium Saccharin	31°Bx
Colgate Total 12 Strengthened Gums	Sodium Saccharin	31°Bx
Colgate Total Active Prevention	Sorbitol, Sodium Saccharin	29.4°Bx
Colgate Sensitive Pro Relief	Sorbitol	29°Bx
Green Doctor Kids	Sorbitol, Stevia	28.2°Bx
Colgate Total 12 Clean Mint	Sodium Saccharin	28°Bx
Sensodyne Deep Clean	Sorbitol, Sodium Saccharin	28°Bx
Mitch Natural	Stevia	28°Bx
Colgate Total 12 Antitartar	Sodium Saccharin	28°Bx
Colgate Kids	Sodium Saccharin	27.8°Bx
Gum Original White	Sodium Saccharin	27°Bx
Colgate Total 12 Professional Whitening	Sodium Saccharin	26.9°Bx
Oral-B 3D White	Sorbitol, Sodium Saccharin	26.3°Bx
Colgate Activated Charcoal	Sodium Saccharin	26.3°Bx
Equate Extra Care	Sorbitol, Sodium Saccharin	25°Bx
Oral-B Kids	Sorbitol, Sodium Saccharin	24.2°Bx
Oral-B 100%	Sodium Saccharin	24°Bx
Colgate Luminous White	Sorbitol, Sodium Saccharin	23°Bx
Arm & Hammer Sensitive	Sorbitol, Sodium Saccharin	22°Bx
Pro Selection Sensitive Gums	Sorbitol, Sodium Saccharin	21.8°Bx
Dental Plus	Sorbitol, Sodium Saccharin	21.6°Bx
Gum Anti-Cavity Protection	Sorbitol, Sodium Saccharin	21.2°Bx
Crest Complete	Sorbitol, Sodium Saccharin	21°Bx
Mitch Activated Charcoal	Xylitol, Stevia	20.5°Bx
Colgate Maximum Protection	Sodium Saccharin	20°Bx
Crest Extra Whitening+Baking Soda	Sorbitol, Sodium Saccharin	19°Bx
Crest Antitartar	Sorbitol, Sodium Saccharin	18.8°Bx
Pro Selection Activated Charcoal	Sorbitol, Xylitol, Sodium Saccharin	18.3°Bx
Dentobac	Sorbitol, Sodium Saccharin	17°Bx
Colgate Max Clean	Sorbitol, Sodium Saccharin	16°Bx
Colgate Triple Action	Sorbitol, Sodium Saccharin	15.3°Bx
Colgate Triple Action Extra Whitening	Sodium Sacchrin	12°Bx
Crest Sugar Shield	Sorbitol, Sodium Saccharin	12°Bx

Table 2. Control Group 1: Blood glucose data from Control Group 1 shows a general trend of reduction; however, individual metabolism in certain cases results in an increase. Control Group 2: Glucose levels do not decrease in all cases, maintaining a balance in glucose metabolism after dental brushing

Control Group 1					
Time of First Sample	**Result mg/dl**	**Time of Second Sample**	**Result mg/dl**	**Time of Third Sample**	**Result mg/dl**
08:19 am	93	08:34 am	94	08:49 am	89
08:19 am	76	08:34 am	77	08:49 am	78
08:23 am	72	08:38 am	75	08:53 am	72
08:23 am	84	08:38 am	84	08:53 am	81
08:28 am	84	08:43 am	86	08:58 am	84
08:27 am	75	08:42 am	74	08:57 am	71
08:37 am	79	08:52 am	82	09:07 am	78
08:32 am	88	08:47 am	87	09:02 am	85
08:45 am	95	09:00 am	90	09:15 am	86
08:45 am	75	09:00 am	73	09:15 am	79
Average	*82.3*		*80.8*		*79.5*
Control Group 2					
Time of First Sample	**Result mg/dl**	**Time of Second Sample**	**Result mg/dl**	**Time of Third Sample**	**Result mg/dl**
07:30 am	87	07:45 am	84	08:10 am	87
07:45 am	85	08:00 am	85	08:23 am	85
08:10 am	70	08:25 am	77	08:46 am	79
08:12 am	79	08:27 am	85	08:49 am	85
08:16 am	92	08:31 am	97	08:51 am	99
08:20 am	73	08:35 am	88	08:57 am	88
08:35 am	98	08:50 am	105	09:28 am	100
10:00 am	86	10:15 am	85	10:35 am	84
10:12 am	78	10:27 am	87	10:47 am	86
08:40 am	75	08:54 am	81	09:24 am	80
Average	*81.3*		*86.8*		*86.3*

Three groups of ten participants each were formed, following the outlined procedure: Participants arrived fasting at the Latino Laboratory in Morelia, having refrained from brushing their teeth for at least 8 hours. Upon arrival, the first serum glucose sample was taken, after a 15-minute rest period, a second blood sample was collected, participants then brushed their teeth for 3 minutes using the assigned toothpaste. At the end of brushing, they were instructed not to rinse their mouths. A final blood sample was collected 15 minutes post-brushing.

An ANOVA test was performed to analyze glucose levels before and after toothpaste exposure. The results are summarized below: First Control Group: Mean glucose levels: 82.2 mg/dL (before), 80.3 mg/dL (after). Variance: 52.4 (before), 34.6 (after). F-statistic: 0.41, p-value: 0.5277, critical F-value: 4.41. Interpretation: No significant differences in glucose levels. Second Control Group: Mean glucose levels: 87.5 mg/dL (before), 88.0 mg/dL (after). Variance: 63.1 (before), 42.8 (after). F-statistic: 0.02, p-value: 0.8796, critical F-value: 4.41. Interpretation: No significant differences in glucose levels. Arm & Hammer Truly Radiant Group: Mean glucose levels: 80.4 mg/dL (before), 87.8 mg/dL (after). Variance: 55.3 (before), 48.1 (after). F-statistic: 5.28, p-value: 0.0336, critical F-value: 4.41. Interpretation: Significant differences in glucose levels, suggesting a potential effect of the toothpaste. Sensodyne Rápido Alivio Group: Mean glucose levels: 86.7 mg/dL (before), 87.2 mg/dL (after). Variance: 22.2 (before), 41.0 (after). F-statistic: 0.03, p-value: 0.8446, critical F-value: 4.41. Interpretation: No significant differences in glucose levels. Colgate Sensitive Pro Alivio Inmediato Group: Mean glucose levels: 78.8 mg/dL (before), 81.6 mg/dL (after). Variance: 127.9 (before), 51.6 (after). F-statistic: 0.43, p-value: 0.5171, critical F-value: 4.41. Interpretation: No significant differences in glucose levels. Fig. 1.

Table 3. In the Arm & Hammer Truly Radiant group, a progressive increase in glucose levels is observed across the three measurements. In the Sensodyne Rapid Relief group, results indicate that glucose levels remained relatively stable throughout the measurements, with a slight increase. For the Colgate Sensitive Pro Immediate Relief Gums group, a trend toward decreased glucose levels was noted

Arm & Hammer Truly Radiont					
Time of First Sample	**Result mg/dl**	**Time of Second Sample**	**Result mg/dl**	**Time of Third Sample**	**Result mg/dl**
09:25 am	77	09:40 am	86	10:07 am	87
08:40 am	76	08:55 am	68	09:41 am	82
09:28 am	72	09:43 am	80	10:18 am	85
09:32 am	83	09:47 am	90	10:21 am	98
09:50 am	70	10:05 am	82	10:48 am	91
09:36 am	90	09:51 am	87	10:23 am	93
10:06 am	82	10:21 am	71	11:00 am	92
10:24 am	70	10:39 am	74	10:05 am	79
10:34 am	79	10:49 am	79	11:23 am	77
10:39 am	87	10:54 am	87	11:29 am	94
Average	79.0		81.8		88.6
Sensodyne Rapid Relief					
Time of First Sample	**Result mg/dl**	**Time of Second Sample**	**Result mg/dl**	**Time of Third Sample**	**Result mg/dl**
07:23 am	81	07:38 am	84	08:04 am	87
07:52 am	88	08:07 am	83	08:36 am	86
08:05 am	91	08:20 am	97	08:46 am	98
08:13 am	82	08:28 am	85	08:51 am	81
08:25 am	71	08:40 am	82	09:10 am	78
08:30 am	95	08:45 am	87	09:16 am	87
08:36 am	80	08:51 am	84	09:16 am	86
08:37 am	92	08:52 am	86	09:17 am	84
08:50 am	95	09:05 am	93	09:20 am	98
09:14 am	84	09:29 am	86	09:52 am	87
Average	85.8		86.6		86.7
Colgate Sensitive Pro Immediate Relief Gums					
Time of First Sample	**Result mg/dl**	**Time of Second Sample**	**Result mg/dl**	**Time of Third Sample**	**Result mg/dl**
09:33 am	88	09:48 am	88	10:15 am	88
07:00 am	98	07:15 am	99	07:37 am	95
07:33 am	92	07:48 am	88	08:13 am	75
08:00 am	80	09:15 am	71	08:39 am	75
08:09 am	83	08:19 am	86	08:48 am	88
08:06 am	79	08:21 am	70	08:51 am	71
08:15 am	78	08:30 am	64	08:55 am	81
08:36 am	62	08:51 am	70	09:13 am	80
08:39 am	75	08:54 am	70	09:24 am	81
08:45 am	79	09:00 am	82	09:15 am	82
Average	80.2		78.8		78.4

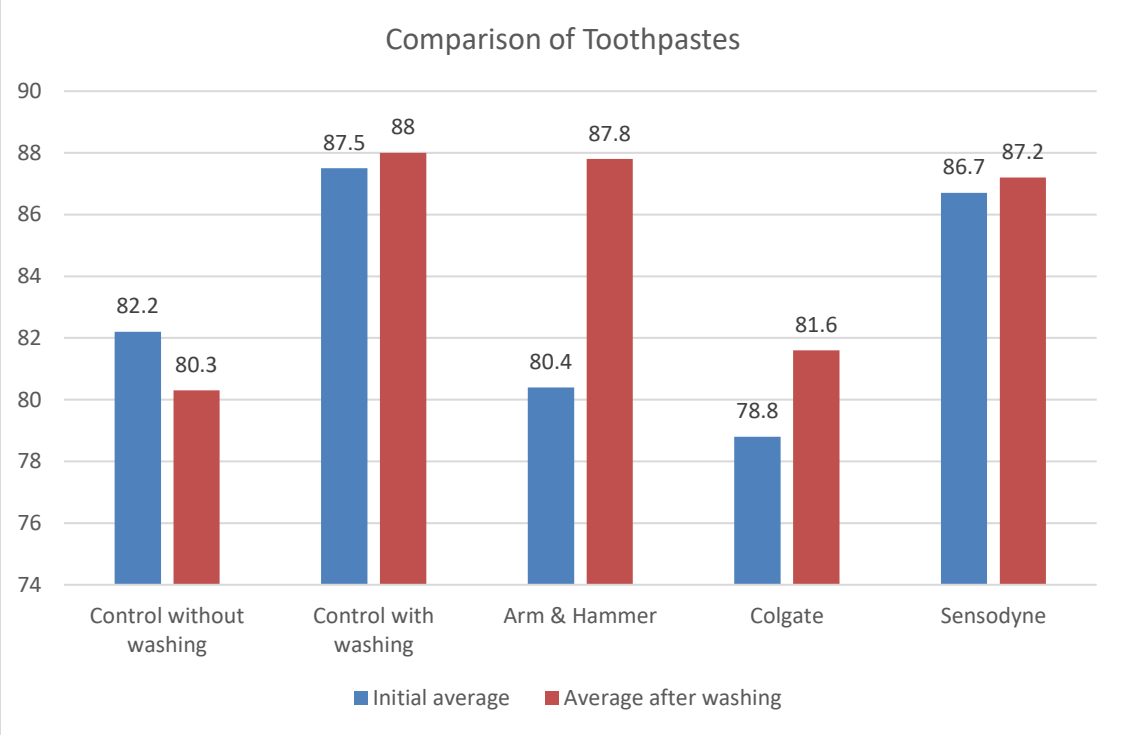

Fig. 1. The control group 1 "without washing" shows a decrease in the mean initial blood glucose from 82.2 mg/dl to 80.3 mg/dl. Meanwhile, the control group 2 "with washing" showed an increase in blood glucose after mouthwash from 87.5 mg/dl to 88 mg/dl. In contrast, the Arm & Hammer group increased from 80.4 mg/dl to 87.8 mg/dl, the Colgate group increased from 78.8 mg/dl to 81.6 mg/dl. The Sensodyne group showed a slight discrepancy, increasing from 86.7 mg/dl to 87.2 mg/dl

4. DISCUSSION

To date, no articles have been published in platforms such as Google Scholar, PubMed, Scielo, Elsevier, or ClinicalKey evaluating the Brix degrees of toothpaste or its effects on changes in glucose levels following toothbrushing.

In 2017, Casariego Z. and Pérez A. described factors that could influence the diffusion of substances across the oral mucosa, including age, delivery vehicles, stress, and alcohol. They noted that stress triggers continuous activation of the hypothalamus-pituitary-pancreas (HPP) axis, with glucocorticoids modulating the migration of leukocytes to protective tissues, including mucosal surfaces. Acute stress mediators, such as norepinephrine and epinephrine, spike immediately after a stressor but return to baseline levels once the stimulus is removed (Casariego, 2017).

In 2018, Albarracín-Vélez P.A., et al. demonstrated that variations in mucosal biotype significantly impact mucosal thickness, which ranged between 500 µm and 1000 µm, with an average of 736±110 µm. They concluded that these differences in thickness lead to variations in permeability. According to Fick's law of diffusion, the permeability of a membrane is inversely proportional to its thickness. Their studies indicated that as mucosal thickness increases, permeability to lipophilic substances decreases more than for hydrophilic substances Albarracín-Vélez et al., 2018).

In 2019, Vicuña H.I., et al. highlighted the potential metabolic implications of non-caloric sweeteners. Although these sweeteners are associated with reduced caloric intake and improved glycemic control, some studies suggest they might unexpectedly affect metabolism. For example, natural sweeteners such as stevia and tagatose have been linked to the secretion of incretins like GLP-1 and GIP, which could influence glucose homeostasis Vicuña et aol., 2019).

5. CONCLUSIONS

The sweeteners present in toothpastes can modify blood glucose levels when exposed to a standardized brushing time of 3 minutes. It is recommended that clinical laboratories and healthcare providers adopt a protocol for fasting blood glucose tests that excludes prior toothbrushing to avoid potential interference. Further research is necessary to replicate this study in patients with insulin resistance to determine if false positives occur in serum glucose testing.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT

As per international standards or university standards, Participants' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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