EVALUATING SUCRALOSE'S INTERACTION EFFECTS ON DNA AND RNA NITROGENOUS BASES THROUGH QUANTUM CHEMICAL METHODS

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ABSTRACT

Sucralose (Sc) is a non-nutritive sweetener derived from sucrose. This sweetener has gained great popularity in the food industry. The objective of this work was to analyze the effect of Sc (Splenda) interactions on Nitrogenous bases (NB) (DNA and RNA). We started the investigation with the Sc molecule. The structure was taken from the PubChem page. Then it was designed in the hyperchem simulator. These interactions are studied in two groups. A) As pure substances. We found that Sc has a very high ETC and for that reason is very unstable. Due to this instability of the Sc, it can attack any NB. B) As substances in crossed bands. HOMO of substance one vs. LUMO of substance two. We found interactions of high probability and high stability and chemical affinity between the Sc as an oxidizing agent and the NBs: C, G, and A. These interactions are hazardous for human health.

INTRODUCTION

Sc is a non-nutritive sweetener derived from sucrose (table sugar). This sweetener has gained great popularity in the food industry; It has a sweet taste quality and very similar to sucrose. It has also been determined that Sc is 600 times sweeter than sucrose and is synthesized by selective halogenation of sucrose. This synthesis of the Sc is carried out by replacing the three hydroxyl groups of the molecule with three chlorine atoms to obtain 4-chloro-4-deoxy-α-D-galactopyranoside from 1, 6-dichloro-1,6-dideoxy- β-D-fructofuranosyl or C12H19Cl3O8. [1]

Sc is a synthetic organochlorine sweetener and is a common ingredient in the world's food supply. This substance interacts with the chemo-sensors in the alimentary tract that play a role in the sensation of sweet taste and the secretion of hormones. [2]

Most of the Sc ingested is not absorbed in the gastrointestinal tract but is excreted directly in the feces, but between 11 and 27% is absorbed. [3] Research has shown that Sc is highly soluble in water and does not bind to plasma proteins. Besides, Sc is eliminated by the kidneys without dechlorination within 24 hours of its consumption and without any osmotic effect. [4]

The tremendous potential value of non-nutritive sweeteners reduces the caloric intake of foods, and with them, reduce the incidence of obesity because the amount absorbed cannot be metabolized for energy purposes. [5]

Some researchers have reported that the artificial sweetener, Sc, stimulates the absorption of glucose in rodents by improving the apical availability of the GLUT2 transporter. These investigators report that it was evaluated whether exposure of the small bowel proximal to Sc affects glucose uptake and glycemic response to an intraduodenal (ID) glucose infusion in healthy human subjects. They conclude that Sc does not appear to modify the rate of glucose uptake or the glycemic or incretin response to glucose infusion in the ID when administered acutely in healthy human subjects. Both human and rodent studies showed that Sc could alter levels of glucose, insulin and glucagon-like peptide (GLP-1). Taken together, these findings indicate that Sc is not a biologically inert compound. In their investigations, these authors demonstrate that the consumption of Sc in the presence of a carbohydrate rapidly alters the metabolism of glucose and may contribute to the increase of DT2. In contrast, other researchers report that laboratory rats prefer solutions with Sc in water than solutions prepared with aspartame. Swithers and Davidson, in 2008, published a study in rodents where they suggest the consumption of these products, contrary to their original purpose. Could induce weight gain in the subject due to poorly understood mechanisms to date.

On the other hand, other researchers concluded that Sc, administered by intragastric infusion, does not stimulate the release of insulin, GLP-1 or GIP or slow gastric emptying in healthy humans. (glucagon-like peptide-1), (glucose-dependent insulinotropic polypeptide). Recently it has been demonstrated that the artificial sweetener Sc is a generalized pollutant of wastewater, surface water, and groundwater.

In addition, it has been reported that the artificial sweetener, Sc, stimulates the absorption of glucose in rodents by improving the apical availability of the GLUT2 transporter. We evaluated whether exposure of the small intestine proximal to Sc affects glucose uptake and glycemic response to an intraduodenal (ID) glucose infusion in healthy human subjects. In conclusion, Sc does not appear to modify the rate of glucose uptake or the glycemic or incretin response to glucose infusion in the ID when administered acutely in healthy human subjects. Consistent with the above, both human and rodent studies demonstrated that Sc could alter glucose, insulin and glucagon-like peptide levels (GLP-1). Taken together, these findings indicate that Sc is not a biologically inert compound. [6-8]

The objective of this work was to analyze the effect of Sc (Splenda) interactions on NB (DNA and RNA).

MATERIALS AND METHODS

We started the investigation with the Sc molecule. The structure was taken from the PubChem page (figure 1). [9] Then it was designed in the hyperchem simulator.

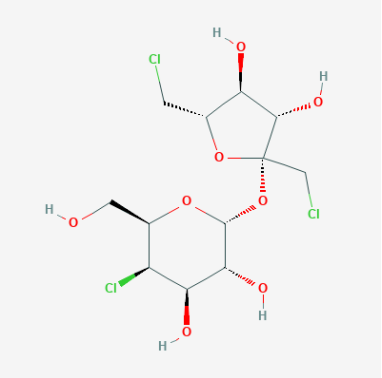

Figure 1. Sc. (2R,3R,4R,5R,6R)-2-[(2R,3S,4S,5S)-2,5-bis(chloromethyl)-3,4-dihydroxyoxolan-2-yl]oxy-5-chloro-6-(hydroxymethyl)oxane-3,4-diol. PubChem.

The parameterization of the use of the Hyperchem simulator is described below (tables 1, 2). The parameters of other investigations made by the director of our project are taken so that the results are compared with the same criterion. [10-14]

SE-PM3 is a program for molecular modeling used by scientists to analyze the quantum composition of molecules for HOMO-LUMO, BG, EP, and other properties. [15-18] These data are used to form the table where is the ETC´s of the interaction between the Sc and the NB. El Software Hyperchem Professional performs Molecular modeling and analysis of the Sc and the NB. (Hyperchem, hypercube, Multi in for Windows, series 12-800-1501800080.) (Multi in South 1236-301 Tlacoquemecatl Insurgentes Col. del Valle, Benito Juárez, CDMX, Mexico C.P. 03200).

Table 1. Parameters used for quantum computing molecular orbitals-HUMO and LUMO

Parameter	Value	Parameter	Value
Total charge	0	Polarizability	Not
Spin Multiplicity	1	Geometry Optimization algorithm	Polak-Ribiere (Conjugate Gradient)
Spin Pairing	RHF	Termination condition RMS gradient of	0.1 Kcal/Amol
State Lowest Convergent Limit	0.01	Termination condition or	1000 maximum cycles
Interaction Limit	50	Termination condition or	In vacuo
Accelerate Convergence	Yes	Screen refresh period	1 cycle

Table 2. Parameters used for visualize the map of the electrostatic potential of the molecules

Parameter	Value	Parameter	Value
Molecular Property	Property Electrostatic	Contour Grid increment	0.05

	Potential		
Representation	3D Mapped Isosurface	Mapped Function Options	Default
Isosurface Grid: Grid Mesh Size	Coarse	Transparency level	A criteria
Isosurface Grid: Grid Layout	Default	Isosurface Rendering: Total charge density contour value	0.015
Contour Grid: Starting Value	Default	Rendering Wire Mesh	

RESULTS AND DISCUSSION

Interaction of pure substances

Table 3 shows the calculation of the ETCs of the six NBs and the Sc. The NBs include the two tautomers of the U. It can be seen that the base with the highest ETC is the Sc. This observation indicates that the Sc can attack all the NBs in their pure state. We can also observe that the most robust interaction is G: G, that is, this is the most stable interaction.

Table 3. ETCs of the NBs and the Sc

No.	Reducing agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
*1	Sc	Sc	-9.472	0.194	9.666	-0.115	0.185	0.300	32.220
2	U1	U1	-9.710	-0.511	9.200	-0.126	0.171	0.297	30.975
3	T	T	-9.441	-0.475	8.966	-0.123	0.169	0.292	30.707
4	A	A	-8.654	-0.213	8.441	-0.140	0.156	0.296	28.518
5	U2	U2	-9.910	-0.415	9.495	-0.147	0.202	0.349	27.208
6	C	C	-9.142	-0.344	8.799	-0.174	0.161	0.335	26.265
7	G	G	-8.537	-0.206	8.331	-0.150	0.172	0.322	25.872

**Sweetener*

Interaction of substances on crossband

Table 4 shows a mixture of pure substance interactions and cross-band interactions. The pure Sc is the interaction four that has much energy to attack all the interactions of less value of ETC.

The interactions 5, 6, 7, 8, 11, 12, 14, 17 and 18 compete with the allowed molecular bonds of the NBs of DNA and RNA. The Sc in these interactions acts as an oxidizing agent or reducing agent (antioxidant) for good or for ill.

Table 4. ETCs of the NBs and the Sc on cross band.

No.	Reducing agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
1	Sc	A	-9.472	-0.213	9.259	-0.115	0.156	0.271	34.165
2	Sc	C	-9.472	-0.344	9.128	-0.115	0.161	0.276	33.071
3	Sc	G	-9.472	-0.206	9.266	-0.115	0.172	0.287	32.285
4*	Sc	Sc	-9.472	0.194	9.666	-0.115	0.185	0.300	32.220
5	U1	Sc	-9.710	0.194	9.904	-0.126	0.185	0.311	31.846
6	Sc	T	-9.472	-0.475	8.997	-0.115	0.169	0.284	31.678
7	Sc	U1	-9.472	-0.511	8.961	-0.115	0.171	0.286	31.331
8	T	Sc	-9.441	0.194	9.635	-0.123	0.185	0.308	31.283
9	U1	U1	-9.710	-0.511	9.200	-0.126	0.171	0.297	30.975
10	T	T	-9.441	-0.475	8.966	-0.123	0.169	0.292	30.707
11	U2	Sc	-9.910	0.194	10.104	-0.147	0.185	0.332	30.434
12	Sc	U2	-9.472	-0.415	9.057	-0.115	0.202	0.317	28.570
13	A	A	-8.654	-0.213	8.441	-0.140	0.156	0.296	28.518
14	A	Sc	-8.654	0.194	8.848	-0.140	0.185	0.325	27.225
15	U2	U2	-9.910	-0.415	9.495	-0.147	0.202	0.349	27.208
16	C	C	-9.142	-0.344	8.799	-0.174	0.161	0.335	26.265
17	G	Sc	-8.537	0.194	8.731	-0.150	0.185	0.335	26.063

18	C	Sc	-9.142	0.194	9.336	-0.174	0.185	0.359	26.006
19	G	G	-8.537	-0.206	8.331	-0.150	0.172	0.322	25.872

**Interaction 4. Sweetener*

Interaction of allowed NBs of DNA and RNA

Table 5 shows the Sc with its interactions exclusively oxidants. Interactions 12 and 13 (contaminant) compete with a high probability affinity with the allowed pair C: G (10, 14). Interactions 5, 6, 7, and, 8 (contaminant) compete with allowed pair A: T, A: U1, A: U29, (9, 11, 15).

Table 5. Comparison between the allowed interactions of the NBs in the DNA and RNA and the sweetener.

No.	Reducing agent	Oxidizing agent	ETC	Observation
1	U1	A	33.679	Allowed interaction
2	T	A	33.076	Allowed interaction
3	Sc	Sc	32.220	Sweetener
4	U2	A	32.004	Allowed interaction
**5	U1	Sc	31.846	Polluting interaction
**6	T	Sc	31.283	Polluting interaction
**7	U2	Sc	30.434	Polluting interaction
**8	A	Sc	27.225	Polluting interaction
*9	A	T	26.471	Allowed interaction
10	G	C	26.345	Allowed interaction
*11	A	U1	26.185	Allowed interaction
**12	G	Sc	26.063	Polluting interaction
**13	C	Sc	26.006	Polluting interaction
*14	C	G	25.827	Allowed interaction
*15	A	U2	24.092	Allowed interaction

**Most likely allowed interaction of the two interactions listed as oxidizing agent and reducing agent.*
***Pollutant interactions of the sweetener and NBs.*

Quantum wells

To better clarify the logic of the research, quantum wells were designed (figure 2). The solid lines represent the limits of pure substances, and the points represent the value of the ETCs of the crossed bands of the pure substances. The continuous lines of the quantum wells have been omitted for better visualization. It can be seen that the red dot is the deepest bottom of the wells. This depth tells us that it is the most likely interaction. On the other hand, the red line is the limit between the medium probability zone and the high probability zone from top to bottom, respectively.

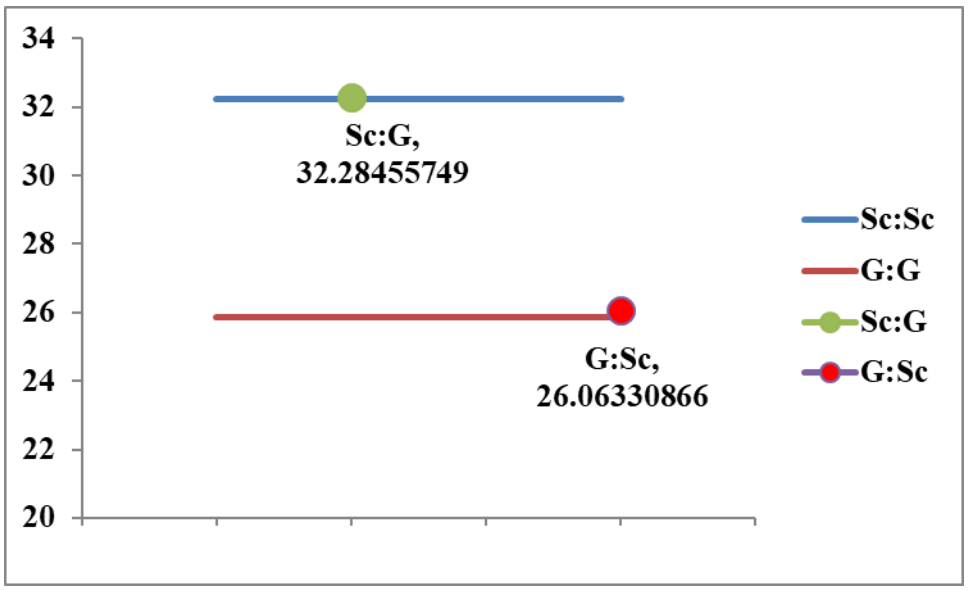

Figure 2. Graphical representation of the quantum well. The red dot shows the Sc as an oxidizing agent; the green dot shows the Sc as a reducing agent (antioxidant) vs. G

The interaction C: Sc is presented in figure 3 and the interaction A: Sc in figure 4; they show a pattern similar to the G: Sc interaction (figure 2). The difference is only observed in the values of their ETCs respectively.

Another significant difference is observed in the quantum well of the interaction A: Sc. This oxidation is the most probable of all in that it is located separates from the red line, deep in its quantum well.

The oxidation interactions 5, 6 and 7 of Table 5 present a different pattern in the zone of average probability located within the two continuous lines.

The remaining interactions are shown in Tables 4 and 5. They present a pattern of reduction and average probability.

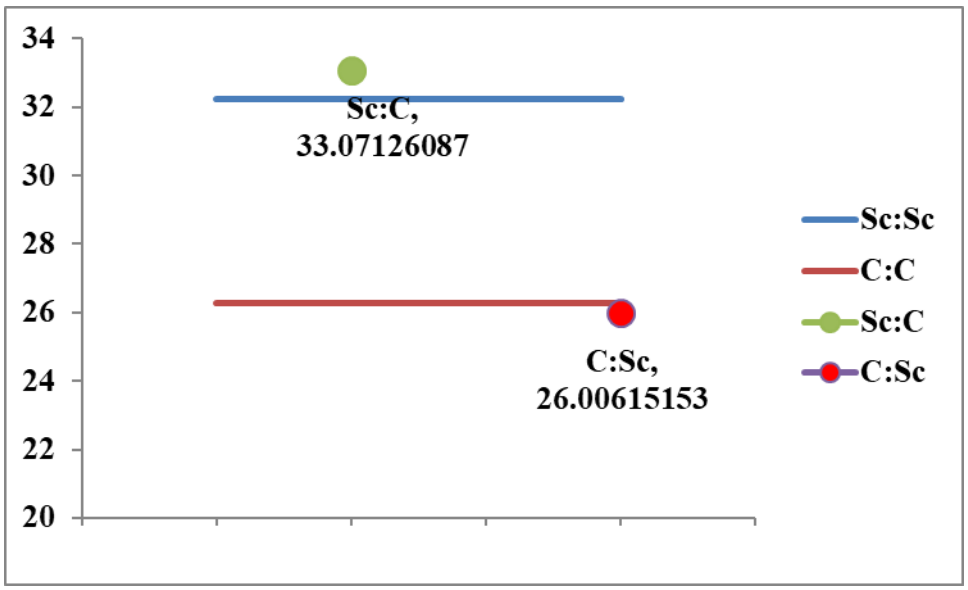

Figure 3. Graphical representation of the quantum well. The red dot shows the Sc as an oxidizing agent. The green dot shows the Sc as a reducing agent (antioxidant) vs. C

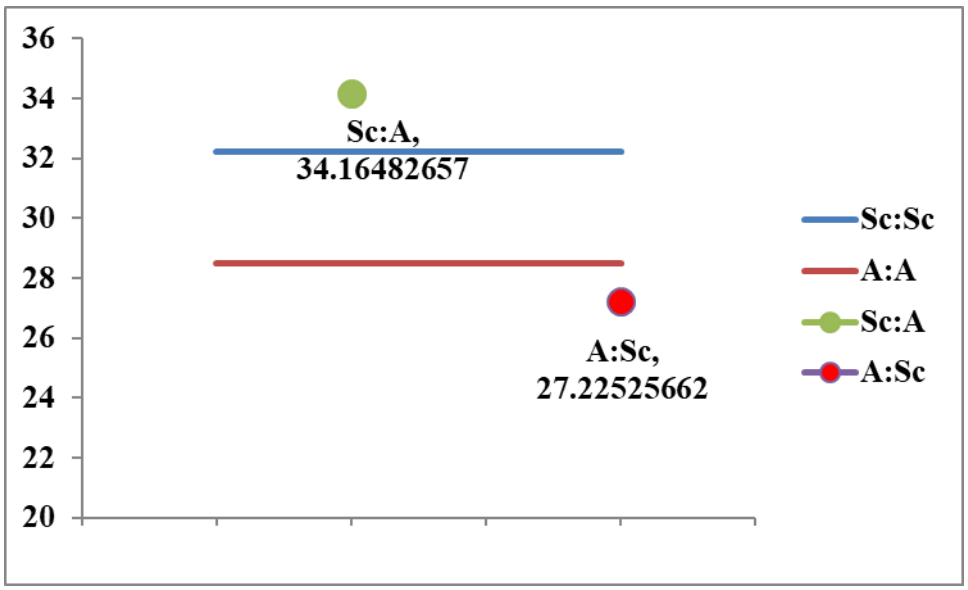

Figure 4. Graphical representation of the quantum well. The red dot shows the Sc as an oxidizing agent; the green dot shows the Sc as a reducing agent (antioxidant) vs. A

CONCLUSIONS

We analyze the chemical-quantum interactions of the Sc vs. NBs that make up DNA and RNA. These interactions are studied in two groups.
A) As pure substances.
We found that Sc has a very high ETC and for that reason, it is very unstable.
Due to this instability of the Sc, it can attack any NB.
B) As substances in crossed bands. HOMO of substance 1 vs. LUMO of substance 2.

We found interactions of high probability and high stability and chemical affinity between the Sc as an oxidizing agent and the NBs C, G, and A.

These interactions are hazardous.

The remaining interactions of the Sc and the NBs are of medium probability and low chemical affinity.

In general, we conclude that the probability that the Sc causes problems such as mutations in both DNA and RNA are very high and have a high chemical affinity.

For laboratory studies, we must consider Chatelier's principles.

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