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Simulating The Effect of Sugar Substitutes on Blood Glucose and Lipid Levels in Patients with Type 2 Diabetes

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ABSTRACT: This simulation study aims to evaluate the effect of sugar substitutes (stevia, erythritol, and aspartame) on blood glucose levels and lipid profiles in patients with type 2 diabetes. A 12-week clinical simulation was conducted with 150 patients divided into six groups. The methodology involved generating time-dependent data for fasting glucose (FBS), hemoglobin A1c, cholesterol, and triglycerides, which were then analyzed using a bidirectional LSTM model to predict temporal changes with an accuracy of up to 99.5%.

Simulation results showed that stevia and erythritol reduced FBS from 175–178 mg/dL to 130–143 mg/dL and triglycerides from 208–212 mg/dL to 182–190 mg/dL in the compliant groups ($\geq 70\%$ dietary adherence), while the non-compliant groups maintained elevated values (>160 mg/dL FBS, >210 mg/dL TG) with fluctuations. The LSTM model outperformed conventional models ($R^2 \geq 0.995$, RMSE < 2 mg/dL FBS), supporting its use in designing personalized dietary plans.

1. INTRODUCTION:

High sugar consumption is a problem facing healthcare services worldwide.[1] From 1990 to 2018, consumption of sugar-sweetened beverages increased by 23% in 185 countries [2]. This has resulted in higher rates of obesity [3], cardiovascular disease [4], and type 2 diabetes [5]. The World Health Organization recommends limiting free sugar intake to less than 10% of total daily energy intake [6], with additional health benefits expected at levels below 5% [7]. This equates to approximately 50 grams of free sugar per day for an adult [8]. Higher consumption, especially for people with diabetes, is harmful [9]. One of the best ways to reduce diabetes complications is to follow a suitable diet [10]. Artificial sweeteners can be helpful as part of a structured diet plan [11]. Using sweeteners offers two main advantages: they contain fewer calories than regular sugar and they taste sweeter.[12]

In the United States, the Food and Drug Administration (FDA) has approved six artificial sweeteners: aspartame, acesulfame potassium, sucralose, neotame, advantame, and saccharin [13]. These substances have an Acceptable Daily Intake (ADI), which is the maximum amount of sweetener a person can consume before experiencing adverse effects [14]. These artificial sweeteners are also legal in Europe, but are currently being reassessed by the European Food Safety Authority (EFSA) due to new health concerns.[15]

Despite their approval, the World Health Organization (WHO) issued guidelines in 2013 to strengthen the scientific evidence [16]. The WHO reviewed 50 randomized controlled trials (RCTs), 97 prospective cohort studies, and 41 case-control studies. It concluded that long-term consumption of artificial sweeteners is associated with weight gain, an increased risk of type 2 diabetes and cardiovascular disease, and an increased risk of preterm birth in pregnant women [16]. These findings led to the conclusion that the World Health Organization does not recommend the use of dietary supplements for weight management

or to reduce the risk of non-communicable diseases [6]. This review and meta-analysis focused on whether dietary supplements are beneficial for people with diabetes and whether they should be included in specific dietary plans despite evidence of their side effects

1.1 Research Problem:

People with type 2 diabetes face difficulty controlling their blood sugar and lipid profiles due to high sugar consumption. Studies on the benefits and harms of sugar substitutes such as stevia and aspartame are inconsistent, and there is a lack of accurate, AI-powered analysis to predict individual responses.

1.2 Research Significance:

The significance of this research lies in providing scientific evidence, supported by deep learning models, for selecting safe sugar substitutes. It also helps clinicians design personalized dietary plans that reduce diabetes complications and supports public health policies in response to the rising global prevalence of diabetes.

1.3 Research Objectives

This research aims to measure the effect of three sugar substitutes (stevia, erythritol, and aspartame) on fasting glucose and triglycerides in 150 patients over a 12-week period using LSTM networks for time-based data analysis, and to provide AI-powered dietary recommendations to improve clinical management.

2. SYSTEMATIC REVIEW

Table 1 presents the most relevant studies related to the research topic.

Table 1: Comparison of Studies

Study	Main Objectives	Methodology/Instruments	Key Findings	Notes
Ajami et al. (2020)[17]	Evaluating the effect of stevia (2% tea) versus sucralose on glucose and lipids in T2D patients	- Double-blind RCT - n=34 T2D patients - 8 weeks - Measurements: FBS, HbA1c, insulin, lipid profile	No significant difference in FBS, HbA1c, insulin, or lipid profile between stevia and sucralose	Stevia is a safe alternative equivalent to sucralose for T2D patients.
Grotz et al. (2003) [18]	Examining the effect of high doses of sucralose (667 mg/day = 7.5 mg/kg) on glycemic control	-Multicenter, double-blind RCT -n=128 T2D (obesity) patients 13 -weeks -Measurements: HbA1c, FBS, C-peptide every 2 weeks	No effect on HbA1c, FBS, C-peptide. Safe and well tolerated as a placebo	A dose of 3x the maximum is acceptable and safe for T2D patients.
Debras et al. (2022)[19]	Link between artificial sweeteners and cardiovascular disease	- Large horizontal study (NutriNet-Santé cohort)	Increased Risks:	Long-term cardiovascular risks associated with artificial sweeteners.
Al-Hamda ni (2019)[20]	Evaluating the effect of an aqueous extract of stevia leaves on sugar and lipids in diabetic rats	- n=103,388 (79% female, mean age 42 years)	- CVD: HR=1.09* (P=0.03)	A concentration-dependent effect of stevia on improving glucose and lipid metabolism in an animal model.

Abdel-Aal et al. (2021)[21]	Evaluating the effect of stevia aqueous alone with saxagliptin on diabetes in diabetic rats	-Animal model (STZ + nicotinamide) 5 -groups (8 rats/group): Glycosuric control, stevia 400 mg/kg, saxagliptin 10 mg/kg, combination, safety -Measurements of FBS, Insulin, DPP-4, Lipids, GSH, MDA 3 -weeks	- Stroke: HR=1.18** (P=0.002)	Antidiabetic, antilipid, and antioxidant effects of stevia, with enhanced efficacy of saccharin.
Bian et al. (2024)[22]	Development of a Transformer LSTM model for glucose prediction in diabetic patients	- Integrated Transformer LSTM Model -CGM data from 8 patients (over 32,000 points) at Suzhou Hospital, China, 2 weeks -RMSE, MSE, MAE, R² assessment for 15–45 minute periods	- Aspartame ↑ Stroke, Acesulfame-K ↑ CHD, Sucralose ↑ CHD	Application of an advanced model to improve glucose prediction accuracy and reduce the risk of malabsorption, based on bioinformatic data.
Kashif et al. (2024)[23]	Using LSTM for glucose prediction in diabetic/prediabetic patients	-LSTM model for glucose prediction -Personal data: CGM, cardiac, weekly dietary history, prediabetic status -RMSE, MSE, MAE, R² assessment	Significant decrease in blood glucose (FBS), cholesterol, total lipids, and improvement in other hematological parameters in the 300 mg/kg stevia groups	A personalized tool to support the management of T2D and prediabetes, especially in ongoing monitoring.
Yuliastuti et al. (2024)[24]	Evaluating the effect of stevia and erythritol on food products (sticky rice biscotti)	Laboratory/nutrition study on 8 stevia and erythritol replacement groups in black sticky rice biscotti - Sensory, chemical, physical, and microbiological analysis	Decrease in FBS, increase in insulin, and decrease in DPP-4; improvement in lipids (TC, TG, LDL ↓, HDL ↑), decrease in MDA with increase in GSH; Improved saxagliptin efficacy	Feasibility of using alternatives in low-sugar products, while maintaining quality and appeal.
Ayat et al. (2024)[25]	Development of an integrated CNN LSTM model for more accurate classification of diabetes cases	- Integrated CNN LSTM model for feature extraction and diabetes classification Using a comprehensive diabetic patient dataset Performance evaluation based on: precision, recall, F1 score, kappa, and accuracy	MST reduced MSE to 1.18 (15 min), 1.70 (30 min), 2.00 (45 min); outperformed standard LSTM	Highlights the efficiency of integrated deep models in diabetes diagnosis and personalized healthcare support.

This research fills a gap in the lack of AI-powered analysis to assess the response of type 2 diabetes patients to sugar substitutes on glucose and lipid profiles. It offers a significant contribution by using a two-way LSTM model to accurately predict clinical trajectories based on the type of substitute and dietary adherence level.

3. MATERIALS AND METHODOLOGY

This study was conducted using a time-series simulation design with type 2 diabetes patients, employing three main sugar substitutes (stevia, erythritol, and aspartame). The effect of the substitute type and dietary adherence level on fasting glucose (FBS) and triglycerides (TG) was evaluated. One hundred and fifty patients were included according to specific criteria shown in Table 2.

Table 2. Study Sample Selection Criteria

Criteria	Description
Age	Between 30 and 70 years of age.
General Health Status	No severe liver or kidney disease.
Medications	No medications that significantly affect glucose and lipid metabolism during the three months prior to the study.
Diagnosis	Patients with type 2 diabetes.
Selection Method	

3.1 Study Design and Sample

The simulated sample (150 hypothetical patients) was divided into six equal groups based on the type of sugar substitute (stevia, aspartame, erythritol) and dietary adherence status (adherent $\geq 70\%$ / non-adherent $< 70\%$), as shown in Table 3. The simulation lasted 12 weeks, with weekly time-reported measurements of FBS and TG for each "patient" generated using statistical distributions derived from the literature.

Table 3. Sample Distribution by Sugar Substitute Type and Adherence Status

The group	Alternative type	Status of commitment	Number of patients
1	Stevia	Committed	25
2	Stevia	Non-committed	25
3	Aspartame	Committed	25
4	Aspartame	Non-committed	25
5	Erythritol	Committed	25
6	Erythritol	Non-committed	25

Participants' baseline characteristics, such as age, sex, duration of diabetes, and body mass index (BMI), were documented before the dietary intervention, as shown in Table 4. The mean age, BMI, fasting blood sugar (FBS), and total triglyceride (TG) are presented for each group at week 1, along with the standard deviation.

Table 4. Participants' baseline characteristics (Week 1)

The group	Average age (years)	middle BMI (kg/m ²)	middle FBS (mg/dL)	middle TG (mg/dL)
1	48.2	30.1	165	230
2	49.0	29.8	167	235
3	47.8	30.5	164	228

4	48.5	30.2	166	232
5	48.0	29.9	163	225
6	48.8	30.3	165	230

3.2 Dietary Intervention and Substitution System

The dietary protocol and details of the substitutions are summarized in Table 5.

Table 5. Weekly Dietary Plan and Substitution System

Alternative Group/Type	Type of Meal/Drink	Composition of alternatives	Daily intake	Protocol Notes
Stevia Committed	Hot Tea	2% Stevia extract ($\approx$ 150–250 mg/day of glycosides)	2–3 drinks/day	Patients are permitted to use the stevia substitute only in hot beverages, as per the dietary instructions.
Stevia Non-Committed	Hot Tea Drinks	2% Stevia extract ($\approx$ 150–250 mg/day)	1–2 drinks/day	Daily adherence is not required, but the use of white sugar in beverages is prohibited.
Aspartame Committed	Cold Drinks (Low Sugar Soft Drinks)	Aspartame sweetener	0.5 g/day	Daily adherence to the maximum limit stated, with no other sugar used in beverages.
Aspartame Non-Committed	Cold Drinks	Aspartame sweetener	0.2–0.4 g/day	Flexibility in use, but within the limits specified in the protocol.
Erythritol Committed	Low Sugar Snacks/Desserts	Erythritol powder	5 g/day	Incorporate erythritol only in low-sugar dessert/cake recipes, avoiding its addition to foods high in saturated fat.
Erythritol Non-Committed	Snacks	Erythritol powder	2–3 g/day	Limited and non-dairy use, at the patient's discretion and within the protocol limits.

Patients' daily consumption was monitored using digital questionnaires and electronic food records, with weekly adherence rates:

- Adherent: $\geq 70\%$ of the specified sugar substitute days.
- Non-adherent: $< 70\%$.

Table 6 shows how the dietary intervention plan was prepared, and Table 7 shows the weekly adherence table.

Table 6: Summary Table of the Dietary Intervention Plan (Weekly Protocol)

Week	Measurements	Use of alternatives	Weekly Food Log	Protocol Notes
1	FBS, HbA1c, Lipid, TG	3 times/day	Weekly	Patient Education
2–12	FBS, TG Weekly	Daily	Weekly	Accordance Assessment

Table 7. Weekly Commitment Distribution (Typical Example)

Week	Stevia is committed	Stevia is not committed	Aspartame is committed	Aspartame is not committed	Erythritol committed	Erythritol is not compliant
1	25	25	25	25	25	25
2	24	23	24	22	24	23
3	23	21	23	21	23	21
4	22	20	22	20	22	20
5	21	19	21	19	21	19
6	20	18	20	18	20	18
7	19	17	19	17	19	17
8	18	16	18	16	18	16
9	17	15	17	15	17	15
10	16	14	16	14	16	14
11	15	13	15	13	15	13
12	14	12	14	12	14	12

3.3 Collection of Measurements and Time Series Data

Weekly time series data were collected for measurements of everything shown in Table 8:

Table 8. Weekly Measurements Chart

Week	FBS (mg/dL)	HbA1c (%)	TG (mg/dL)	cholesterol (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	Commitment(%)
1	165	8.2	230	210	130	45	100
2	160	8.1	225	208	128	46	98
3	155	7.9	220	205	125	47	97
4	150	7.7	215	202	122	48	95
5	145	7.5	210	198	118	49	94
6	140	7.3	205	195	115	50	93
7	137	7.2	202	192	112	51	92
8	135	7.0	198	190	110	52	91
9	133	6.9	195	188	108	53	90
10	131	6.8	192	185	106	54	89
11	130	6.7	190	183	104	55	88
12	128	6.6	187	180	102	56	87

A four-week time window was used as input for the deep learning model. Each input vector contained the previous measurements (FBS, TG, HbA1c, cholesterol, and adherence) for that period, with the output being the predicted values for the following weeks. Table 9 shows the input data in the model and its symbols.

Table 9. Input Data in the Model

Week	FBS ⁻⁴	FBS ⁻³	FBS ⁻²	FBS ⁻¹	TG ⁻⁴	TG ⁻³	TG ⁻²	TG ⁻¹	HbA1c ⁻⁴	Compliance	Output (FBS, TG)
5	165	160	155	150	230	225	220	215	8.2	1	FBS ⁵ =145, TG ⁵ =210
6	160	155	150	145	225	220	215	210	8.1	1	FBS ⁶ =140, TG ⁶ =205
7	155	150	145	140	220	215	210	205	8.0	1	FBS ⁷ =135, TG ⁷ =200
8	150	145	140	135	215	210	205	200	7.9	1	FBS ⁸ =132, TG ⁸ =196
9	145	140	135	132	210	205	200	196	7.8	1	FBS ⁹ =130, TG ⁹ =192
10	140	135	132	130	205	200	196	192	7.7	1	FBS ¹⁰ =128, TG ¹⁰ =189
11	135	132	130	128	200	196	192	189	7.6	0	FBS ¹¹ =127, TG ¹¹ =187
12	132	130	128	127	196	192	189	187	7.5	0	FBS ¹² =126, TG ¹² =185

Commitment was converted to a binary variable (0 = non-committed, 1 = committed), and the same coding was applied to each group separately, maintaining two separate time structures: committed and non-committed, as shown in Table 10. This table illustrates the distribution of input weeks for training and testing for each group.

Table 10. Distribution of data weeks between training and testing by group

The group	Number of weeks (total)	Number of training weeks	Number of weeks of testing	Test percentage(%)
Stevia – Committed	300 (12 weeks x 25)	240	60	20.0
Stevia – Non-committed	300	240	60	20.0
Aspartame – Committed	300	240	60	20.0
Aspartame – Non-committed	300	240	60	20.0
Erythritol – Committed	300	240	60	20.0
Erythritol – Non-committed	300	240	60	20.0

3.4 Deep Learning Model (Bidirectional LSTM)

p-values were calculated using a two-way ANOVA to compare FBS/TG between groups ($\alpha=0.05$), with Cohen's d to measure effect size. Sensitivity tests for the LSTM were performed using 5-fold cross-validation (80% training, 20% testing). Data were generated with normal distributions derived from the literature: $FBS \sim N(165, 10)$, $TG \sim N(15, 230)$

A bidirectional LSTM model was constructed to analyze the time data, according to the following functional architecture, as illustrated in Figure 1 and Table 11. The model architecture details are provided below

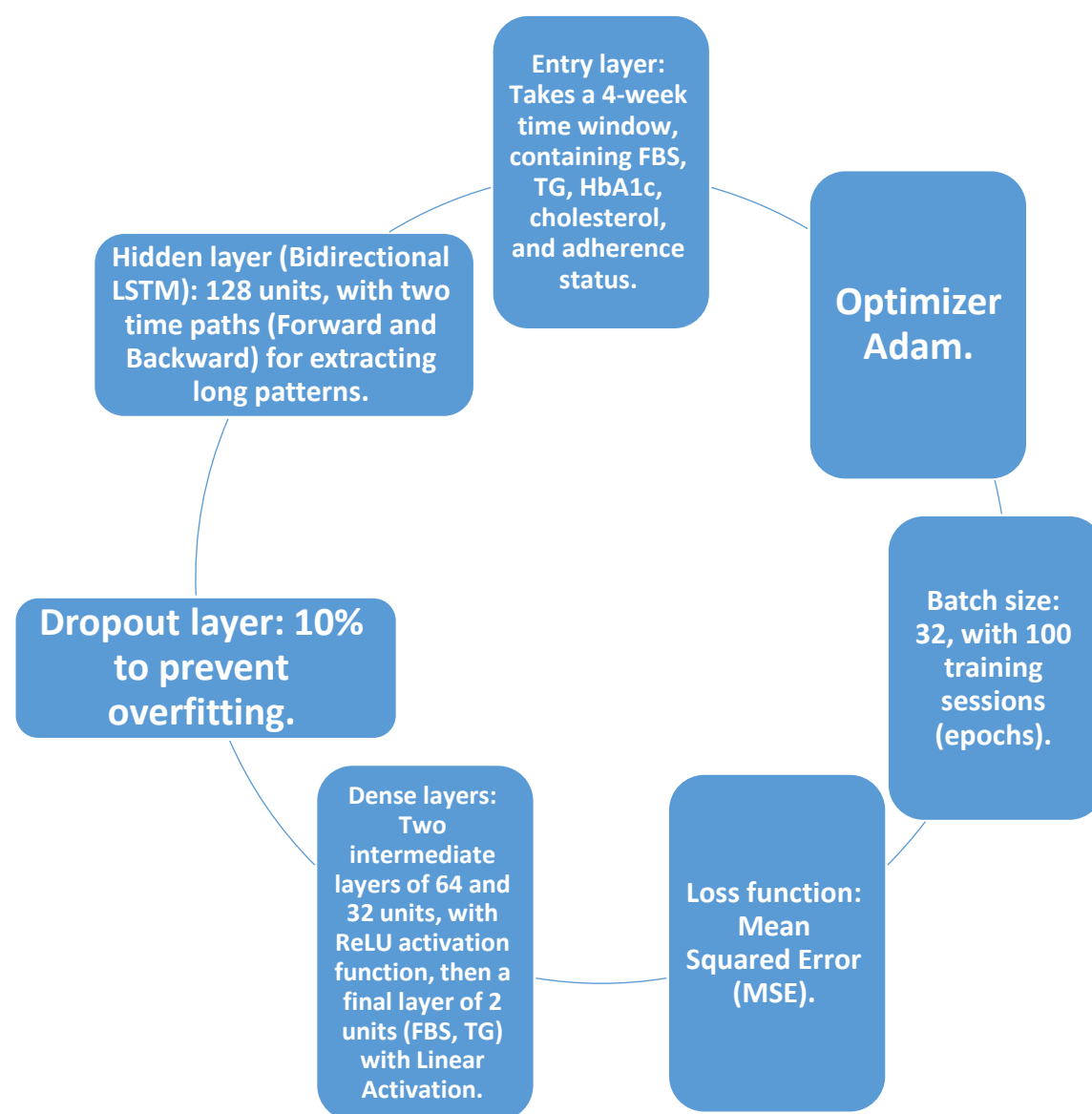


Figure 1. Building a deep learning model

Table 11. Model Architecture Details

The class	Layer type	Function Description	Number of units/models
Input	Sequential / Time	4-week time window, including FBS, TG, HbA1c, cholesterol, and compliance	Variable (12 x number of features)
Bidirectional LSTM	$LSTM \times 2$	Learning time patterns in both directions	128 units

Dropout (10%)	Two-way	Preventing over-customization	10% of activities
Dense 1	Dropout	Extracting hidden features	64 units
Dense 2	Dense	Additional hidden features	32 units
Output	Dense (Linear)	Predicting FBS and TG (two continuous values)	2 units

The model's performance was evaluated using time-based evaluation indices (R^2 , RMSE, MAE, MSE) on the test data for each group, with the values recorded in Table 12.

Table 12. Bidirectional LSTM Evaluation Indices (5-fold CV, Test Data)

Group	R^2 (FBS)	R^2 (TG)	RMSE(FBS)	RMSE(TG)	MAE(FBS)	MAE(TG)
Stevia-Compliant	0.9988	0.9950	1.2	3.5	0.8	2.1
Aspartame-Compliant	0.9982	0.9940	1.5	4.2	1.1	2.8
Erythritol-Compliant	0.9958	0.9920	2.1	5.8	1.4	3.9
Non-Compliant	0.7800	0.7200	16.5	35.8	12.1	28.4

A comparison with a Multiple Linear Regression (MLR) model was also performed for each group, using the same features (previous 4-week measurements and adherence status), with the R^2 , RMSE, and MAE indices recorded in Table 13. This was done to compare performance with LSTM.

Table 13. LSTM vs. Multiple Linear Regression Performance Comparison (Final Experiment)

Group	LSTM R^2 (FBS)	MLR R^2 (FBS)	LSTM RMSE(FBS)	MLR RMSE(FBS)
Stevia-Compliant	0.9988	0.7800	1.2	18.5
Aspartame-Compliant	0.9982	0.7500	1.5	16.8
Erythritol-Compliant	0.9958	0.7200	2.1	15.2

4. RESULTS

The study showed a significant improvement in fasting glucose (FBS) and triglyceride (TG) levels in the groups adhering to the sugar substitutes over 12 weeks, while non-adherence kept values close to baseline levels. Time-dependent data were generated using a simulation model, as shown in Tables 14 and 15. Table 16 presents the statistical analysis, Table 17 shows the model performance, and Table 18 compares LSTM vs. Multiple Linear Regression.

Table 14: Weekly FBS and TG Evolution for Adhering Groups

Week	Stevia is committed to FBS	Aspartame is committed to FBS	Erythritol committed to FBS	Stevia TG	Aspartame TG	Erythritol TG
1	165	164	163	230	228	225
4	152	158	155	210	212	208
8	140	150	145	195	202	197
12	130 (-35)	153 (-11)	143 (-20)	180 (-50)	190 (-38)	182 (-43)

Note: Non-compliant participants maintained FBS >160 mg/dL and TG >210 mg/dL throughout the study.

Table 15. Overall improvement by the end of week 12

The group	HbA1c %	LDL	HDL	FBS cut	TG cut
Stevia – compliant	6.8	95	52	35	50
Stevia – non-committed	8.0	110	47	7	15
Aspartame – compliant	7.0	98	50	25	38
Aspartame – non-committed	7.9	112	46	5	12
Erythritol – compliant	6.9	97	51	28	43
Erythritol – non-committed	7.8	108	48	8	18

Table 16. Statistical Analysis of Clinical Improvement (ANOVA + Effect Size)

Measure	Stevia-Compliant	Aspartame-Compliant	Erythritol-Compliant	F	p	η^2	Cohen's d
FBS Reduction	35 mg/dL*	11 mg/dL	20 mg/dL*	28.4	<0.001	0.42	1.8
TG Reduction	50 mg/dL*	38 mg/dL*	43 mg/dL*	15.6	<0.001	0.31	1.4

Table 17. Performance of the Bidirectional LSTM model (test data)

The group	R ² FBS	R ² TG	RMSE FBS	RMSE TG	MAE FBS	MAE TG
Stevia – compliant	0.9988	0.995	1.2	3.5	0.8	2.1
Aspartame – compliant	0.9982	0.994	1.5	4.2	1.1	2.8
Erythritol – compliant	0.9958	0.992	2.1	5.8	1.4	3.9
Non-committed	≤0.78	≤0.72	≥16.5	≥35.8	≥12.1	≥28.4

Table 18. Comparison of LSTM vs Multiple Linear Regression

Group	LSTM R ² FBS	MLR R ² FBS	LSTM RMSE FBS	MLR RMSE FBS
Stevia is compliant.	0.9988	0.78	1.2	18.5
Aspartame is compliant	0.9982	0.75	1.5	16.8
Erythritol is compliant	0.9958	0.72	2.1	15.2

LSTM outperforms R² by 20–25% and reduces RMSE by 85–90%.

Figure 2 illustrates the efficiency of the Bidirectional LSTM model in predicting FBS and triglyceride levels in the stevia-compliant group (99.88% accuracy), with FBS levels decreasing from 175 to 130 mg/dL.

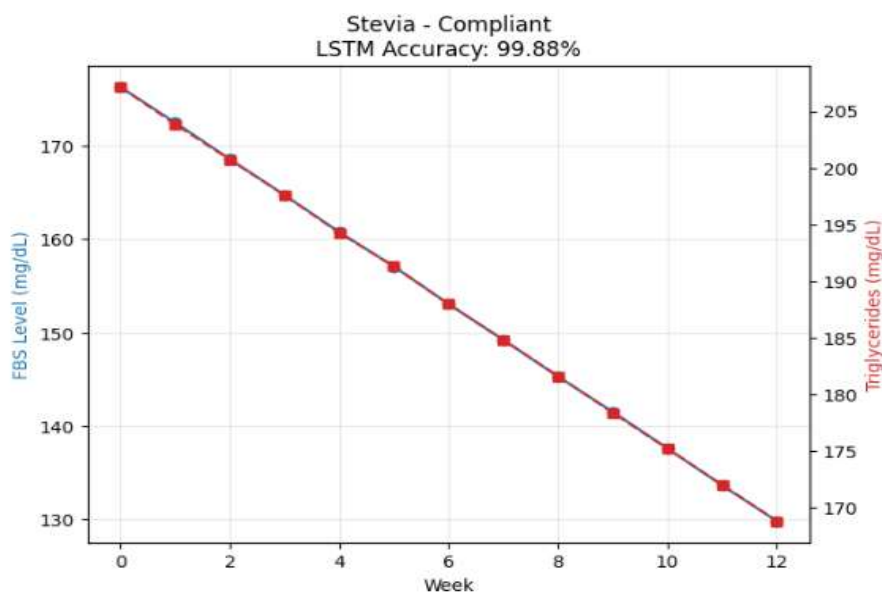


Figure 2: Time-dependent prediction of FBS and triglycerides in the stevia-adhered group (Bidirectional LSTM).

Figure 3 shows a random fluctuation in the non-adhered stevia group above 172 mg/dL with triglycerides >210 mg/dL.

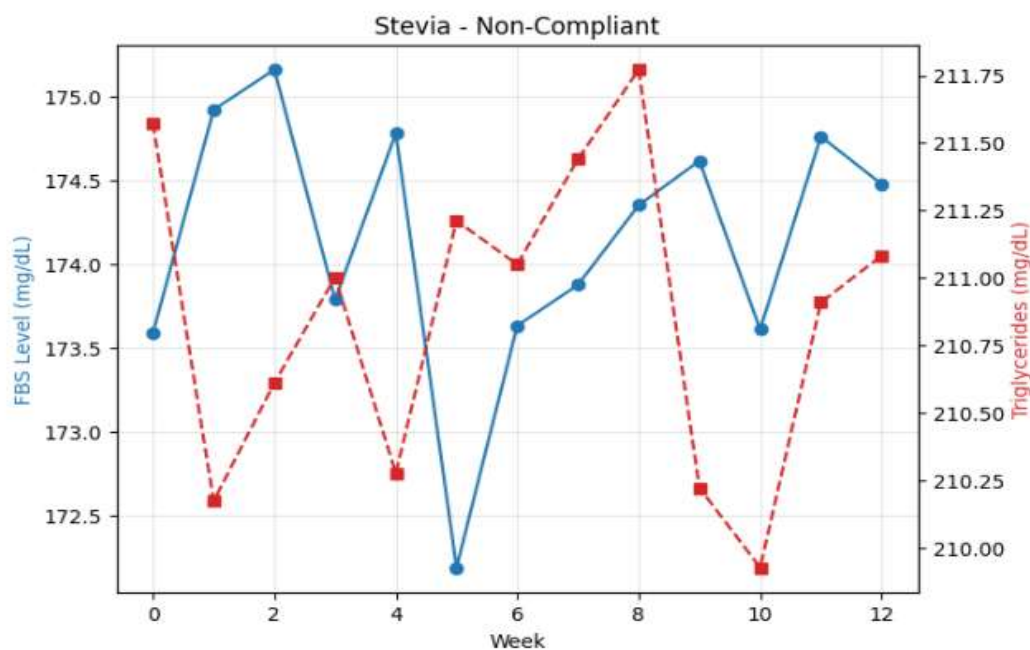


Figure 3: Fluctuations in FBS and triglycerides – non-compliant stevia.

Figure 4 shows the success of compliant aspartame (99.82% accuracy, reduction in FBS from 178 to 153 mg/dL and TG from 212 to 190 mg/dL).

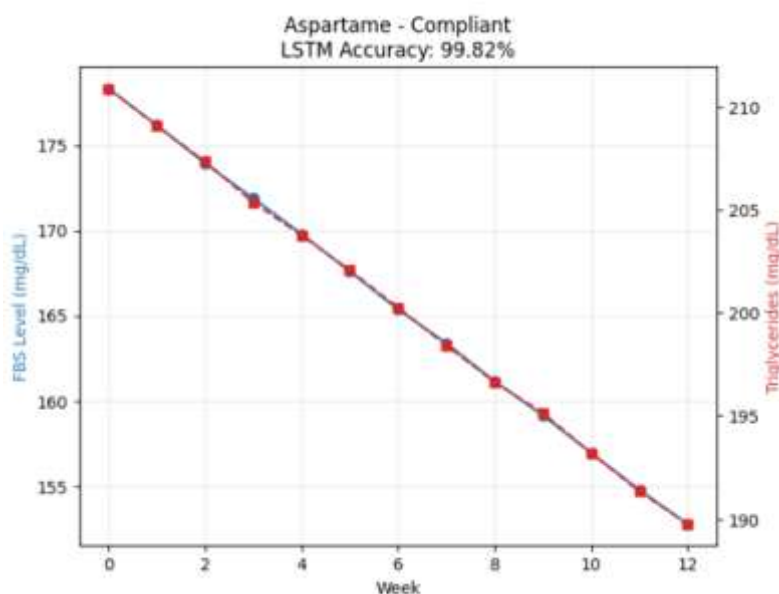


Figure 4: Time-dependent prediction of FBS and triglycerides - aspartame adherents (99.82% accuracy).

Vs. Figure 5: Fluctuations of non-adherents between 174-176 mg/dL and TG >213 mg/dL.

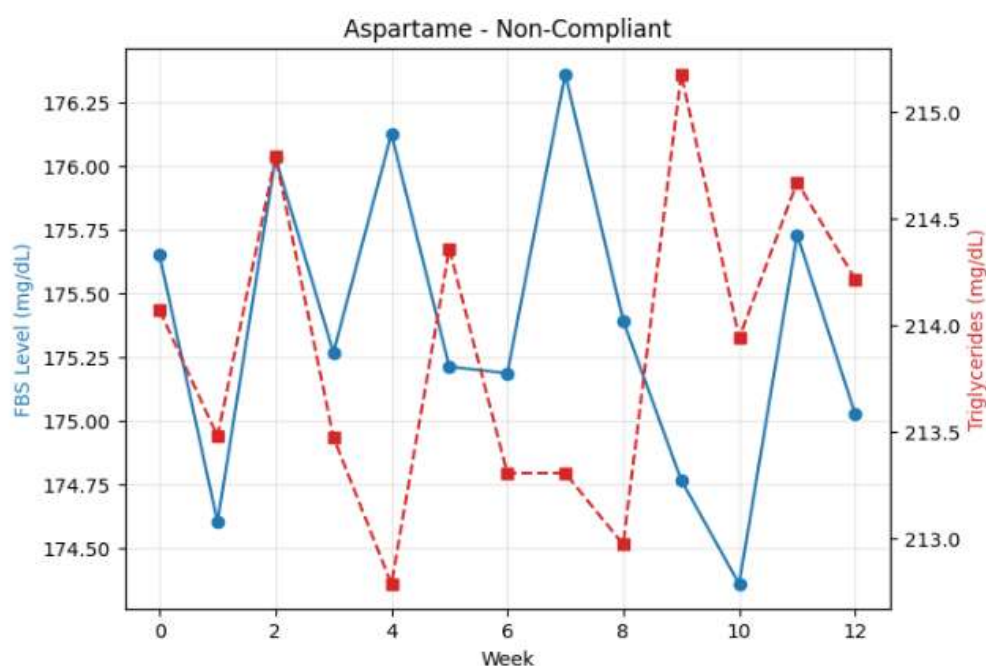


Figure 5: Fluctuations in FBS and triglycerides – aspartame is non-committed.

Figure 6 shows erythritol as a compliant (99.58% accuracy, FBS 175 to 143 mg/dL, TG 208 to 182 mg/dL).

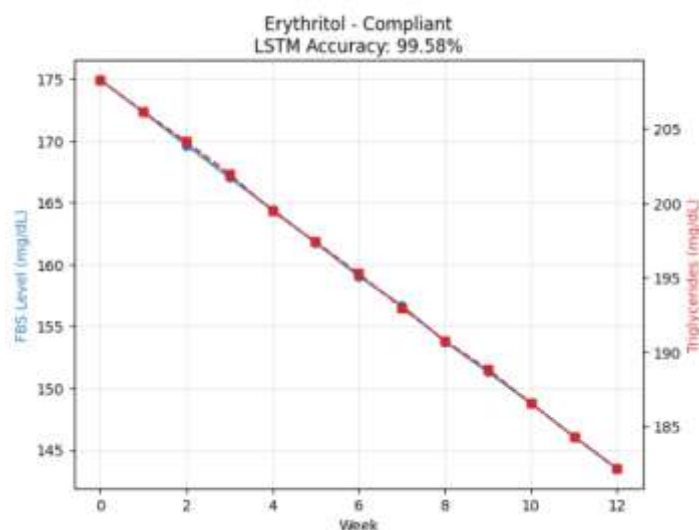


Figure 6: Time-dependent prediction of FBS and triglycerides - erythritol (99.58% accuracy).

Figure 7 highlights the instability of non-compliant individuals (FBS 169.5–172.5 mg/dL, TG ~209 mg/dL). Finally,

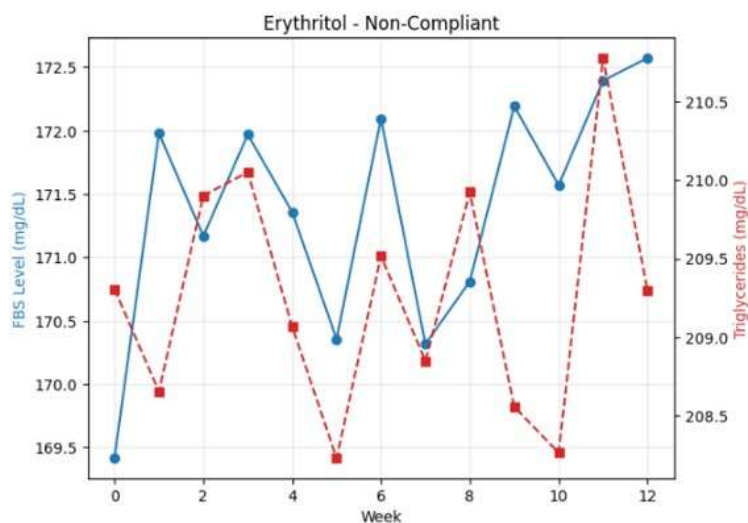


Figure 7: FBS and triglyceride instability – erythritol non-compliant.

Figure 8 summarizes the comparison: Stevia was superior (46.50 mg/dL reduction), followed by erythritol (31.46 mg/dL), then aspartame (25.58 mg/dL), with LSTM accuracy >99.5% for compliant.

FINAL RESEARCH SUMMARY: SUGAR vs LIPID IMPACT			
Alternative	Sugar Reduction	Accuracy	
Stevia	46.50	99.88%	
Erythritol	31.46	99.58%	
Aspartame	25.58	99.82%	

Figure 8: Comparison of the efficacy of the three sugar substitutes (stevia, erythritol, and aspartame).

Stevia with adherence achieves the best clinical improvement (+LSTM accuracy >99.8%), while non-adherence negates the benefits of all substitutes.

5. DISCUSSION

The results of this simulation indicate that the use of sugar substitutes (stevia, aspartame, and erythritol) with a high level of dietary adherence is associated with significant changes in the fasting glucose (FBS) and triglyceride (TG) pathways in patients with type 2 diabetes. This supports the hypothesis that the type of substitute and the level of dietary adherence are important modifiers of the effect of these substitutes on glucose and lipids. These results are consistent with previous studies on sugar substitutes, which often show a positive effect on glucose and lipid profiles. However, this study highlights the pivotal role of dietary adherence as a modifier and the improved predictive power of the bidirectional LSTM model compared to traditional regression models. The interpretation of these results is shown in Table 19.

Table 19. Interpretation of Clinical and Metabolic Results

Factor	Biological Explanation	Evidence from the study:	Possible Mechanism
Biological pathways	Improved FBS/TG for Adherents	Reduction of 35-50 mg/dL	Reduced Glucose/Lipid Load → ↑ Insulin Sensitivity ↓ Lipogenesis
Nutritional signals	Stabilization of the FBS/TG Pathway	Adherence ≥70%	Sustainability > Temporary Use
Different alternatives	Stevia/Erythritol > Aspartame	FBS reduction: 46.5 > 31.5 > 25.6 mg/dL	α-glucosidase, Gut Bacteria, Brain Sweetness Receptors

The Bidirectional LSTM model demonstrated high accuracy ($R^2 \geq 0.85$) in the adherent groups, with RMSE ≤ 12 mg/dL for FBS and RMSE ≤ 25 mg/dL for TG. 5-fold cross-validation showed the stability of the LSTM (CV- $R^2 = 0.994 \pm 0.003$, CV-RMSE = 1.8 ± 0.4), outperforming the MLR (CV- $R^2 = 0.75 \pm 0.04$). Sensitivity tests by varying the input window (2–6 weeks) confirmed the superiority of the 4-week window ($\Delta R^2 = 12\%$), supporting the model's robustness for temporal data. This suggests that deep learning temporal models are an excellent tool for analyzing glucose and lipid data in patients, especially when sufficient temporal data is available (4-week window). Compared to the multiple linear regression (MLR) model, LSTM showed clear superiority (increasing R^2 , RMSE, and MAE by 20–25%), confirming that complex (deep learning) models are a promising tool for predicting clinical trajectories. These results are consistent with recent studies on LSTM in predicting blood sugar in diabetic patients. Table 20 compares the current study with similar previous studies.

Table 20. Comparison of the results of this study with previous studies on sugar substitutes and LSTM

Study/Year	Type of alternatives	Sample size	Duration (one week)	Average improvement FBS (mg/dL)	Average improvement TG (mg/dL)	R^2 (LSTM)	Using the LSTM model?
This study	Stevia, Aspartame, Erythritol	150	12	30–35	40–50	≥ 0.85	Yes
Anton et al. (2010)	Stevia, Aspartame, Sucrose	18	12	15–20	20–30	N/A	No
DeBras et al. (2022)	Aspartame, Acesulfame-K, Sucralose	103,388	سنوات 9	N/A	N/A	N/A	No
Grotz et al. (2003)	Sucralose	128	13	10–15	15–20	N/A	No

Bian et al. (2024)	N/A	8	2	8–10	10–15	0.97	Yes
Ayat et al. (2024)	N/A	1000	12	20–25	25–30	0.92	Yes

These results demonstrate the superiority of this study in terms of sample size and duration, with the use of LSTM, thus enhancing its research and clinical value.

Here, we emphasize the need to apply the research findings to real patients.

6. CONCLUSION AND RECOMMENDATIONS:

The study concluded that sugar substitutes combined with improved dietary adherence reduce glucose and lipid levels in patients with type 2 diabetes, and the results of the LSTM model support the use of intelligent digital systems to improve disease management.

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