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Potential Effects of Cake Incorporated with Stevia Leaves and Metformin in Diabetic Rats: A Comparative Study

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Abstract:
The present study was designed to study the effect of cake incorporated with different levels of Stevia leaves (*stevia rebaudiana*) and metformin as ant hyperglycemic medication on diabetic rats. Thirty-six adult male albino rats were used in this study, weighting (150±10g) were divided into six groups, six rats each. Stevia leaves and metformin as powder were added at percent 2.5 % & 5% of the main diet and 250 and 500 mg/kg BW., respectively for 28 days. Diabetic rats were induced Alloxan subcutaneously injection (150 mg/kg body weight). Serum glucose, lipid profiles of triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL-c), very low-density lipoprotein (VLDL-c), and high-density lipoprotein (HDL-c), the activities of the liver enzymes ALT & AST, and the kidney functions of creatinine, uric acid, and urea levels were determined at the end of experimental. From the obtained results it could be concluded that consuming cake incorporated with stevia leaves and metformin caused significant (P≤ 0.05) decrease of serum glucose, liver enzymes activities, kidney functions and enhance of HDL-c, as compared with control (-ve) group. The best result was recorded for 2.5% cake incorporated with stevia leaves and metformin. As conclusion, consuming cake incorporated with stevia leaves and metformin as powder attenuated diabetic effects in rats, which reflects the powerful nutraceutical therapeutic effects.

Keywords*: Natural Sweeteners*, *Diabetic*, *Bakery products*, *Rats*

Introduction

Diabetes is defined as a state of hyperglycemia in either fasting or postprandial states. The chronic hyperglycemia of diabetes mellitus (DM) is associated with end organ damage, dysfunction, and failure in organs and tissues including the retina, kidney, nerves, heart, and blood vessels. The International Diabetes Federation estimates an overall prevalence in 2019

is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045. The prevalence is higher in urban (10.8%) than rural (1). Diabetes mellitus is a rapidly spreading disease that is predicted to affect 6.6 percent of the global population and is expected to increase by 7.8 percent by 2030 [2]. Diabetes is a serious, chronic condition that arises when the pancreas does not create enough insulin or when the body cannot efficiently use the insulin it produces, according to the World Health Organization. As a result, it is a significant public health issue [3]. Organ damage, atherosclerosis, neuropathy, poor immunity, wound healing, and infection susceptibility are all known to occur in diabetic patients as a result of the many negative impacts of insulin resistance and hyperglycemia, often leading to poor postoperative outcomes [4]. Type 2 diabetes mellitus (DM) is probably one of the oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago. Type 2 DM was described as a component of metabolic syndrome (5).

Metformin is considered one of the safest oral hypoglycemic agents. It reduces insulin resistance but does not promote insulin secretion from β-cells, and thus it is not associated with increased risk of hypoglycemia (6). This reduction was sustained in the 20-year follow-up analysis, which again showed that metformin reduced any diabetes-related endpoint by 21% ($p = 0.01$), myocardial infarction by 33% ($p = 0.005$) and all-cause mortality by 27% ($p = 0.002$) (7).

Stevia rebaudiana is a plant that has been used both medicinally and commercially throughout the world which comes from the Asteraceae family and is native to Paraguay. In Stevia leaves, some compounds have 300 times sweetness than cane sugar, namely stevioside (8). Stevioside compounds have also been used as sweetening agents, flavor modifiers, and sugar substitutes in several countries' food industries. The stevioside compound from Stevia leaf extract has been accepted as the third glycogen worldwide. There have been no reports regarding side effects caused by the use of stevioside in humans (9). The metabolic and elimination processes of steviol glycosides (SGs) in humans and animals have the same pathway (10). Glucose compounds will be utilized by intestinal microbes and do not undergo absorption into the bloodstream. Steviol compounds that intestinal microbes have metabolized will leave the body and not accumulate. That has been proven in studies that, through human feces' observation, found that high and low concentrations of steviol do not undergo metabolism in the digestive tract. Thus, result indicating that steviol is the final metabolic product of stevioside (11). Non-nutritive sweeteners have been utilized in the diet of diabetic patients as an agent to replace glucose and sucrose. Since saccharin might be removed from the marketplace. In fact, dry leaves of Stevia rebaudiana is a small herbaceous, it is grown across the world. It's a natural sweetener plant known as "Sweet Weed", "Sweet Leaf", "Sweet Herbs" and "Honey Leaf". Stevia is calorie-free and 300 times sweeter than sugarcane. Stevia for last few years has been seen as healthy replacement of sugar; it contains phytol-chemical compound that helps to cure blood sugar, cholesterol and blood pressure especially for those people who are suffering from metabolic disorders or want to maintain healthy (12). Various studies have been conducted regarding the Stevia feasibility and safety of both humans and animals. Studies

show that oral administration of stevioside in type II diabetes mellitus patients has lower blood glucose levels when compared to controls using cornstarch (13). The study of tolerance test of 5 grams of Stevia rebaudiana leaf extracts given every 6 hours for three days to 16 volunteers significantly improved glucose tolerance, reduced plasma sugar levels during testing and after overnight fasting in all volunteers (14). Leaves of Stevia produce diterpene glycosides (stevioside and rebaudioside), non-nutritive, nontoxic, high-potency sweeteners and may replace sucrose as well as other artificial sweeteners, being 300 times sweeter than sucrose (15).

Materials and methods

Materials

1.Source of stevia leaves

Stevia leaves were obtained from herbal shop in November 2021, Cairo Government, Egypt. Stevia rebaudiana Bertoni is a sweet plant that belongs to the Asteraceae family and is a natural non-calorie bio-sweetener that can help people with diabetes and obesity [16].

2.Source of metformin hydrochloride:

Metformin hydrochloride was obtained from pharmacy in November 2021, Cairo Government, Egypt.

3. Experimental animals

A total of (36) mail albino rats weight ranges between (150 g, ±10g) were obtained from Vaccine and Immunity Organization, Ministry of Health, Helwan Farm, Cairo, Egypt.

4. Alloxan

Alloxan which is chemically known as 5,5-dihydroxy pyrimidine-2,4,6-trione is an organic compound, a urea derivative, a carcinogen and cytotoxic glucose analog (17). The compound has the molecular formula, C4H2N2O2 and a relative molecular mass of 142.06. Alloxan was obtained from El-Gomhoria Company for Trading Chemical, Drugs and Medical Instruments, Cairo, Egypt.

5. Casein, cellulose, choline chloride and DL-Methionine

Casein, cellulose, choline chloride powder and DL methionine powder, were obtained from Morgan co. Cairo, Egypt.

6. The chemicals and kits

Chemical kits used in this study (TC, TG, HDL-c, ALT, AST, ALP, urea, creatinine) were obtained from El-Gomhoria company for chemical, Drugs and Medical Instruments, Cairo, Egypt.

2.Material of products

Wheat flour (72 percent extraction) was provided from The South Cairo mills company, Cairo government, Egypt. Sucrose, butter, fresh whole eggs, skim milk powder, baking powder, vanilla powder, and water are all ingredients in the dough for cake. These items were purchased in Cairo, Egypt, at a local market.

Preparation of stevia leaves

Stevia leaves were ground to obtain the powder according to (18).

Preparation of cake samples

According to approved methods by Raeker and Johnson (19) for cake preparation were slightly altered to make cake ingredients except sugar were blended. The butter and

additional components were creamed at medium speed for 3 minutes, then sugar was added and beaten for 3 minutes, and the beaten eggs and vanilla were added and whipped for 2 minutes before being fastened to the creamed fat-sugar mix and easily beaten at low speed for 5 transactions. The prior mixture was progressively added to and beaten for 5 minutes with wheat flour (WF) and other ingredients. The mixture was poured into size into oven trays and baked at 180°C for 25 minutes in a preheated oven, then allowed to cool at room temperature before being packaged in plastic bags. At varying quantities of 2.5 and 5%, stevia leaves and metformin powder were applied.

Induction of diabetes

The rats with blood glucose level>200 mg/dl were considered to be diabetic according to the procedure reported by Desai and Bhide (20).

Experimental design

The use of (36) male albino rats weight ranges between (150 g ± 10g) during the experiment period.

Rats will feed on basal diet prepared according to American Institute of Nutrition (21) for seven consecutive days to make adjustment and rats are divided into 6 groups each group that consist of six rats as follows: Group (1): Rats were fed on basal diet as a control negative. Group (2): Rats were injected with Alloxan 150 mg and used as positive control group. Group (3): A group infected with diabetes and was fed on cake incorporated with Stevia leaves powder at dose 2.5% of the weight of the diet. Group (4): A group infected with diabetes and was feed on cake incorporated with Stevia leaves powder at dose 5% of the weight of the diet. Group (5): A group infected with diabetes and was fed on cake incorporated with metformin powder at does 250 mg/kg b.w. Group (6): A group infected with diabetes and was feed on cake incorporated with metformin powder at dose 500 mg/kg b.w.

The experiment continued for 28 days, at the end of the experimental period each rat weight separately, then slaughtered and blood samples were collected.

Blood sampling

After fasting for 12 hours, blood samples in initial times were obtained from retro orbital vein, while it obtained from hepatic portal vein at the end of each experiment. blood samples were taken. the first parts of Blood samples were collected into a dry clean centrifuge glass tubes and left to clot in water bath (37º C) for 28 minutes, then centrifuged for 10 minutes at 4000 rpm to separate the serum, which were carefully separated and transferred into clean cuvette tube and stored frozen at -20C till analysis according to the method described by Schermer (22).

Methods

Biochemical analysis:

Enzymatic determination of serum glucose was carried out calorimetrically according to the method of Wang et al(23).Serum total cholesterol was determined according to the colorimetric method described by Thomas(24) Serum triglycerides was determined by enzymatic method using kits according to Young(25) and Fossati and Principle (26).HDL-c was determined according to the method described by Warnick et al(27).VLDL-c was calculated in mg/dl according to Crook (28)using the following formula: VLDL-c (mg/dl) = Triglycerides

/ 5.LDL-c was calculated in mg/dl according to Lee and Nieman (29)as follows: LDL-c(mg/dl) = Total cholesterol –HDL-c -VLDL-c. The serum alanine aminotransferase (ALT), serum aspartate amino transferase (AST), and serum alkaline phosphatase (ALP) were measured using the methods described by Chawla (30), Srivastava et al (31) Huang et al (32), respectively. Urea was determined by enzymatic method according to Tietz (33). Serum creatinine was determined according to method described by Chromy (34). Serum uric acid was determined calorimetrically according to the method of described by Jelikic et al (35) Enzymatic determination of plasma glucose was carried out calorimetrically according to Wang (36).

Statistical analysis

The data were analyzed using a completely randomized factorial design (37) when a significant main effect was detected; the means were separated with the Student –New man-Keuls test Difference between treatments of ($P \leq 0.05$) were considered significant using Costat Program. Biological results were analyzed by one-way ANOVA.

Conflict of interest

The authors state that the publishing of this work does not create a conflict of interest for them. This article is based on a Master thesis that was submitted to Menoufia University's Department of Nutrition and Food Science, Faculty of Home Economics, Shebin El-Kom, Egypt. The number of Ethic committee was #17-SREC-12-2021.

Results and Discussion

The data listed in table (1) illustrates how cake incorporated with different levels of Stevia leaves and metformin powder affect the glucose levels of diabetic rats. The negative and the positive control group differed significantly. The corresponding mean values were 114.35 and 242.22 mg/dl. The diabetic group fed on 500 mg/kg BW metformin powder had the lowest glucose level of any treated groups (diabetic) ever observed. The mean values were 119.10 and 165.00mg/dl, respectively, with the highest value being observed for diabetic group rats fed on 2.5% cake Stevia powder with significant differences. These findings support Carrera-Lanestosa et al (38) who demonstrated that the chemical components of Stevia can lower plasma glucose levels. Stevioside, the primary ingredient in Stevia, lowers blood sugar levels by increasing insulin secretion and sensitivity and lowering glucagon secretion.

Data are shown in table (2). demonstrate the impact of cake containing various concentrations of Stevia leaves and metformin powder on diabetic rats' liver functions (ALT, AST, and ALP). It is obvious to see that the liver enzyme ALT significantly differed between the positive and negative control groups (62.34 and 159.75U/L respective). The diabetic group of rats fed on 5% cake Stevia powder had the lowest levels of the treated group's ALT enzyme. The mean values were 82.34 and 145.90 U/L, respectively, with the highest value being observed for diabetes group rats fed on 250 mg/kg BW cake metformin powder with significant differences ($P \leq 0.05$).

Table (1): Effect of cake incorporated with different levels of Stevia leaves and metformin on glucose levels of diabetic rats

Groups	Parameters
	Glucose level (mg/dl)
Control group (-)	114.35±3.20
Control group (+)	242.22±6.73
Cake + 2.5% Stevia leaves	165.00±4.50
Cake + 5% Stevia leaves	131.45±442
Cake + 250 mg/kg BW Metformin	123.75±335
Cake +500 mg/kg BW Metformin	119.10±3.23
LSD (P≤0.05)	4.342

Each value represents the mean ± SD of three replicates. Mean under the same column superscribed with different letters showed significant differences (p≤0.05)

According to the findings, there is a substantial difference between the negative control group and the positive control group in the case of AST. The relative mean values were 152.20 and 294.75 U/L. The diabetic group of rats fed on 5% cake Stevia powder had the lowest levels of the treated group's AST enzyme. The mean values were 192.25 and 239.57U/L, respectively, with the highest value being observed for diabetes group rats fed on 250 mg/kg BW cake metformin powder with a significant difference (P≤0.05).

The liver enzyme ALP significantly differed between the positive and negative control groups. They were 164.55 and 310 U/L on average, respectively. The diabetic group of rats fed 5% Stevia powder had the lowest ALP enzyme level among any treated groups. The mean values were 183.75 and 283.50 U/L, respectively, with the highest value being observed in the diabetic group of rats administered 250 mg/kg BW cake metformin powder with a significant difference (P≤0.05). These results are in line with Ramos et al (39), who discovered that Stevia could stop liver cirrhosis in rats (CCl4-induced) by maintaining normal liver parenchyma structure, serum necrosis (ALT), and cholestasis (AP, -GTP, and bilirubin). The process is related to stevia's antioxidant action, which inhibits inhibition of hepatic glutathione peroxidase, enhanced lipid peroxidation, and 4-HNE (a membrane marker for oxidative stress) (GSH, oxidative stress marker in the cytosol).

Table (2): Effect of cake incorporated with different levels of Stevia leaves and metformin on liver functions of diabetic rats

Groups	Parameters		
	ALT (U/L)	AST (U/L)	ALP (U/L)
Control group (-)	62.34±0.10	152.20±4.20	164.55±3.30
Control group (+)	159.75±0.60	294.75±6.30	310.00±6.80
Cake + 2.5% Stevia leaves	115.00±0.30	201.00±4.40	217.80±5.40
Cake + 5% Stevia leaves	82.34±0.20	192.25±3.70	183.75±4.50
Cake + 250 mg/kg BW Metformin	145.90±0.50	239.57±5.60	283.50±5.70
Cake +500 mg/kg BW Metformin	130.87±0.40	209.40±4.50	243.65±4.60
LSD (P≤0.05)	2.314	2.635	2.706

Each value represents the mean ± SD of three replicates. Mean under the same column superscribed with different letters showed significant differences (p≤0.05)

Data presented in table (3) revealed how Stevia leaves and metformin powder affected diabetic rats' blood total cholesterol and triglycerides. It goes without saying that the total cholesterol levels between the negative control group and the positive control group were significantly different. 94.00 and 226.15 mg/dl were the respective means. Rats in the diabetic group fed 5% cake Stevia powder had the lowest total cholesterol of among treated groups, according to records. The mean values were 127.25 and 207.40mg/dl, respectively, with the highest value being observed for diabetes group rats fed on 250 mg/kg BW cake metformin powder with a significant difference (P≤0.05).

Data showed that there are substantial differences between the negative control group and the positive control group in the case of triglycerides. There were two different mean values: 83.33 and 178.75. The diabetic group of rats fed 5% Stevia powder had the lowest triglyceride levels of among treated groups. The mean values were 105.74 and 159.75, respectively, with the highest value being observed for diabetes group rats fed on 250 mg/kg BW cake metformin powder with a significant difference. These findings are consistent with Ahmad et al (40), who found that Stevia reduced triglyceride levels by stimulating the liver's lipase enzyme activity, resulting in lipid catabolism and enhanced triglyceride excretion through faces.

Table (3): Effect of cake incorporated with different levels of stevia leaves and metformin on total cholesterol and triglycerides of diabetic rats

Groups	Parameters	
	Total cholesterol(mg/dl)	Triglyceride (mg/dl)
Control group (-)	94.00±0.31	83.33±0.25
Control group (+)	226.15±0.82	178.75±0.71
Cake + 2.5% stevia leaves	157.25±0.52	119.65±0.41
Cake + 5% stevia leaves	127.65±0.40	105.74±0.37
Cake +250 mg/kg BW Metformin	207.40±0.64	159.75±0.50
Cake +500 mg/kg BW Metformin	175.35±0.60	133.59±0.31
LSD (P≤0.05)	3.480	3.358

Each value represents the mean ± SD of three replicates. Mean under the same column superscribed with different letters showed significant differences (p≤0.05)

Data are shown in a table (4) demonstrate the impact of cake Stevia leaves and metformin in powder form on diabetic rats' levels of (HDL-c), (LDL-c), and (VLDL-c). (HDL-c) levels clearly differ significantly between the negative control group and the positive control group. (50.33 and 24.09 mg/dl on average, respectively). The diabetic group of rats fed 5% cake Stevia powder had the highest HDL-c levels of among treated groups. The mean values were 42.65 and 31.80, respectively.

Data showed that there are substantial differences between the negative control group and the positive control group in the case of (LDL-c) levels. There were two mean values 27.01 and 166.3 mg/dl. The diabetic group of rats fed 5% cake Stevia powder had the lowest LDL-c among the treated groups. The mean values were 63.85, with the highest value (139.71 mg/dl) being observed for the diabetic group of rats fed on 250 mg/kg BW cake metformin powder with a significant difference (p<0.05).

Nonetheless, there are notable variations in very high-density lipoprotein cholesterol between the negative control group and the positive control group (VLDL-c). (16.66 and 35.75 mg/dl on average, respectively.) The diabetic group of rats fed on 5% cake Stevia powder had the lowest VLDL-c among the treatment groups. The mean values were 21.15, while the highest value (31.95 mg/dl) was measured in diabetes group rats administered 250 mg/kg BW metformin powder with a significant difference ((P<0.05). Moreover, Brijesh and Kamath (41) discovered that stevia can raise HDL cholesterol levels while decreasing total cholesterol, triglyceride, LDL cholesterol, and VLDL cholesterol. The decrease in total cholesterol levels is caused by an increase in bile acid excretion that is caused by preventing small intestine reabsorption by disrupting micelle formation. The 7-hydroxylase for cholesterol is activated by increased bile acid excretion, it lowers cholesterol by accelerating the conversion of liver cholesterol to bile acid.

Table (4): Effect of cake incorporated with different levels of stevia leaves and metformin on lipid profile of diabetic rats

Groups	Parameters		
	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
Control group (-)	50.33±0.60	27.01±0.12	16.66±0.20
Control group (+)	24.09±0.11	166.31±0.63	35.75±0.51
Cake + 2.5% Stevia leaves	38.14±0.43	95.18±0.32	23.39±0.40
Cake + 5% Stevia leaves	42.65±0.52	63.85±0.27	21.15±0.30
Cake + 250 mg/kg BW Metformin	35.99±0.35	139.71±0.50	31.95±0.40
Cake +500 mg/kg BW Metformin	31.80±0.21	116.85±0.41	26.70±0.33
LSD (P≤0.05)	2.360	2.615	1.115

Each value represents the mean ± SD of three replicates. Mean under the same column superscribed with different letters showed significant differences (p≤0.05)

The effects of cake incorporating Stevia leaves and metformin powder on the renal functions of diabetic rats (serum urea, serum creatinine, and serum uric acid) are shown in the table (5). It is obvious to see that there was a substantial difference between serum uric acid values of the positive and negative control groups. The relative mean values were 3.97and 6.84 mg/dl, respectively.

On the other hand, diabetic group rats fed with 250 mg/kg BW cake combined with metformin powder had the highest uric serum (6.04 mg/dl), while the lowest value for diabetes group rats fed on 5% cake integrated with Stevia powder with significant difference was recorded 4.64 mg/dl. Data for serum urea showed significant differences between the positive control group and negative control group, with mean values of 50.20 and 22.80 mg/dl, respectively.

On the other hand, diabetic group rats fed with 250 mg/kg BW cake combined with metformin powder had the highest serum urea level of the treated group, while the lowest value for diabetes group rats fed on 5% cake corporate with Stevia powder was significantly different by 34.68 mg/dl.

The serum creatinine of the positive control group, on the other hand, was significantly higher than that of the negative control group. The relative mean values were 1.21 and 0.60

mg/dl. The diabetic group of rats fed on 250 mg/kg BW cake corporate with metformin powder had the highest serum creatinine level of any treated group, however. With significant differences, the lowest value was found in diabetic group rats fed on 5% Stevia powder, the mean values which were 0.99 and 0.69 mg/dl, respectively. These results are consistent with Rizwan et al (42), who discovered that giving Stevia to rats had a significant protective effect against kidney failure, which is lethal when combined with gentamicin.

Table (5): Effect of cake incorporated with different levels of Stevia leaves and metformin on kidney functions of diabetic rats

Groups	Parameters		
	Urea (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)
Control group (-)	22.80±0.15	3.97±0.26	0.60±0.13
Control group (+)	50.20±0.61	6.84±0.50	1.21±0.40
Cake + 2.5% Stevia leaves	41.19±0.42	5.34±0.31	0.80±0.38
Cake + 5% Stevia leaves	34.68±0.29	4.64±0.14	0.69±0.22
Cake +250 mg/kg BW Metformin	46.64±0.50	6.04±0.41	0.99±0.41
Cake + 500 mg/kg BW Metformin	39.19±0.33	5.71±0.32	0.89±0.35
LSD (P≤0.05)	1.104	1.335	0.360

Each value represents the mean ± SD of three replicates. Mean under the same column bearing different superscript letters are different significantly (p≤0.05)

Conclusion

Cakes incorporated with Stevia leaf powder can enhance the activities of the liver, kidney, lipid profile and blood sugar. All these effects can be attributed to Stevia plant components' high biologically active content. These findings suggest the use of stevia leaf powder to lower type 2 diabetes-related complications.

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التأثيرات المحتملة للكيك المدعم بأوراق الأستيفيا والميتفورمين فى الفئران المصابة بمرض السكر: دراسة مقارنة

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الملخص العربي:

اجريت هذه الدراسة لمقارنة تأثير مسحوق أوراق الاستيفيا(استيفيا ريبوديانا) والميتفورمين علي الفئران المصابة بمرض السكر. تم استخدام ستة وثلاثين من ذكور فئران الألبينو البالغين في هذه الدراسة ، وزن الفئران (150 ± 10 جم) وتم تقسيمهم إلى ستة مجموعات كل مجموعه بها ستة فئران منهم مجموعة ضابطة سالبة ومجموعة ضابطة موجبة ، وتم اصابة الفئران بمرض السكر عن طريق الحقن بمادة الألوكسان (بتركيز 150مجم/ كجم). تمت إضافة مسحوق أوراق الاستيفيا بنسبة 2,5 ٪ , 5 ٪ من النظام الغذائي الأساسي و الميتفورمين بجرعة 250 ملج/كجم و 500 ملجم/كجم من وزن الجسم. تم تقدير (الكوليستيرول الكلى، الجلسريدات الثلاثية، الكولستيرول مرتفع الكثافة، الكولستيرول منخفض الكثافة، الكولستيرول منخفض الكثافة جدا، الجلوكوز في الدم ، أنزيمات الكبد في مصل الدم (ALT, AST and ALP) ، وظائف الكلى (الكرياتينين وحمض اليوريك واليوريا). من النتائج التي تم الحصول عليها تبين أن التغذية على مسحوق أوراق الاستيفيا والميتافورمين أدى إلى حدوث زيادة كبيرةمعنوية(P≤0.05)في مستوى HDL-c، بينما انخفضت مستويات LDL-c,VLDL-cبنسبة عالية مع وجود فرق معنوى. كذلك حدث انخفاض معنوى فى كلا من وظائف الكلى ووظائف الكبد وانخفاض معنوى فى مستوى الجلوكوز في الدم ، الذي يعكس تأثير علاجي مصاحب للتغذية على مسحوق أوراق الاستيفيا لعلاج مرض السكرى في الفئران. وكانت أفضل نتيجة لتركيز مسحوق مخلوط أوراق الاستيفيا بتركيز 2.5% .

الكلمات المفتاحية:المحليات الطبيعية، السكري، منتجات المخابز، الفئران