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Nutritional value of white sapote (*Casimiroa edulis)* fruit, its antioxidant and anti-inflammatory activities in diabetic rats

Elsayed Elbadrawy*, Hala Elkewawy, and Asmaa Karam

Nutrition and Food Science Department, Faculty of Specific Education, Mansoura University, Egypt

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Corresponding author:

Elsayed Elbadrawy

E-mail: m_s_elbadrawy@yahoo.com

Mobile: (+2) 01001123699

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ABSTRACT

This study explored the nutritional value of white sapote (*Casimiroa edulis*) fruit and its potential impact on serum sugar, lipid profile, kidney, liver functions, anti-inflammatory, and antioxidant activities in streptozotocin (STZ)-induced diabetic rats. Twenty-five rats were included in the study; five were used as normal control (group 1) and fed only the basal diet. The remaining rats were injected with STZ (55 mg/kg) to induce diabetes. The diabetic rats were divided into four groups (5 rats each); one continued on the basal diet and served as the diabetic control (group 2). The other diabetic groups were treated orally with 3 ml of each white sapote juice (group 3), chromium (Cr) solution (80 µg/kg) (group 4), and a mix of juice and Cr (1:1) orally (group 5). The results indicated that white sapote fruit is a rich source of essential nutrients and possesses strong antioxidant properties. Additionally, the findings revealed that both the juice and Cr significantly enhanced the serum lipid profile and liver and kidney functions, in diabetic rats. Also, significant decreases in the serum inflammation biomarkers such as tumor necrosis factor-alpha (TNF-α), interleukin 1B (IL-1β), and C-reactive protein (CRP) were observed. In general, consuming the juice mixed with Cr was more effective than consuming the juice alone or Cr alone. Sapote fruit or its juice is recommended to fight oxidation and inflammation in diabetic rats.

Key words: *Casimiroa edulis*; Chromium; Diabetes; Inflammation; Lipid profile.

1. Introduction

Diabetes mellitus (DM) is a widespread disease worldwide resulting from various factors, including genetic and environmental changes (Singh et al., 2020). DM is a significant public health issue in Egypt, with its prevalence increasing to alarming levels. It is essential to consider the risk factors contributing to this growing concern in Egyptian society. Key factors include obesity, a sedentary lifestyle, hepatitis C infection, exposure to pesticides, smoking, and poor dietary habits (Abouzid et al., 2022). It is a metabolic disease that leads to chronic and acute complications such as diabetic ketoacidosis, cardiovascular disease, foot ulcers, kidney disorders, eye damage, and, ultimately, death. Diabetes mellitus imposes a significant economic and physiological burden worldwide (Ayatollahi et al., 2019). Based on data from the International Diabetes Federation (IDF), Egypt ranks among the top ten countries with the highest number of diabetic patients. The projected number of diabetic patients in Egypt is expected to reach 13.1 million by 2035 (Hejaz et al., 2015). By 2030, it is estimated to increase to 10.2% (578 million) globally; by 2045, it is projected to reach 10.9% (700 million). The prevalence of diabetes is higher in urban areas (10.8%) compared to rural areas (7.2%).

Additionally, high-income countries (10.4%) exhibit a greater incidence than low-income countries (4.0%). Shockingly, half (50.1%) of those with diabetes are unaware that they have the disease (Saeedi et al., 2019). Chromium (Cr) is essential for glucose metabolism and diabetes prevention (Georgaki et al., 2023). Cr activates insulin, can greatly boost enzyme activity, and plays an important role in glucose metabolism. It stimulates the liver to create fatty acids and cholesterol while improving sugar metabolism. Furthermore, Cr makes body tissues more insulin-sensitive (Al-Fartusie and Mohssan, 2017).

White sapote (*Casimiroa edulis*) is found in tropical and subtropical regions such as Central America, Mexico, the Caribbean, the Mediterranean, India, Southeast Asia, South Africa, Australia, and New Zealand. It belongs to the Rutaceae family and is the most popular species in its genus. Indigenous people often refer to it as "sapote blanco", "Mexican apple", "white sapote", "Casimiroa", and "sapote blanche" (Satheesh, 2015). Egypt began cultivating sapota trees in 2010 when the climate there became suitable for growing a variety of tropical plant types. Sapota was planted in many Egyptian governorates, including Dakahlia, Arish, and Giza. Since the fruits are collected from June to August, the trees are laden with fruit, making it a summer fruit. Many nurseries in Egypt provide seedlings for farmers to use (Fayek et al., 2012). White sapote fruits are high in carbohydrates, ascorbic acid, phenolic compounds, vitamins, and minerals. They also have medicinal qualities such as antioxidants, anti-inflammatory properties, and anti-cancer properties (Khalil et al., 2022). White sapote fruits are high in minerals like sodium, potassium, magnesium, iron, calcium, and phosphorus. They also contain significant levels of vitamins A and C and have a high carbohydrate content (Satheesh, 2015). This study was conducted to assess the potential health benefits of white sapote fruits grown in Egypt and to promote their consumption. It examined the impact of white sapote fruit on diabetes-related complications, including oxidation, inflammation, serum lipid profile, and kidney and liver functions in diabetic rats.

2. Materials and methods

Materials

White sapote fruits were obtained from Mit Ghamr center market, Dakahlia Governorate, Egypt, during the summer of 2023.

Chemicals

All chemicals and biochemical analysis kits were purchased from Sigma-Aldrich Company. Cairo, Egypt, while Cr as chromium picolinate was purchased from a local pharmacy in Mansoura City, Egypt.

Preparation of white sapote fruit juice

White sapote (*Casimiroa edulis*) fruits were washed with tap water, and the seeds were removed. The fruits were juiced in a blender to achieve the desired consistency and then diluted with distilled water (1:1 v/v) to obtain the fruit juice (Elbadrawy and Elkewawy, 2019).

Estimation of the chemical composition of white sapote fruit

The moisture, ash, crude fiber, crude protein and crude fat contents of white sapote fruit were determined according to the methods described in AOAC (2019). Carbohydrate content was estimated by difference. The mineral content was determined per AOAC (2019) guidelines. Calcium (Ca), Sodium (Na), and Potassium (K) levels were measured using the Jenway Flame photometer model Corning 400. Iron (Fe) and Zinc (Zn) levels were determined using an electrothermal atomic absorption spectrometry, Perkin Elmer Model 5100. Phosphorus levels were assessed calorimetrically at a wavelength of 725 nm using Jenway 6405 UV/VIS spectrophotometer.

Determination of Vitamin C and β-carotene

Vitamin C was determined using the titrimetric estimation method described by Mazumdar and Majumder (2003). The β-carotene content was determined using the method outlined by Nagata and Yamashita (1992). In brief, one gram sample was homogenized with 10 mL of acetone-hexane mixture (2:3) for 2 minutes, then centrifuged. The absorbance spectrum of the supernatant was measured using a UV/VIS spectrophotometer at 453, 505, 645, and 663 nm.

Phytochemical analysis

The plant material was soaked in methanol for three days, and the methanol extract was concentrated. A 20 mg/2 mL sample extract was mixed with 100 µL of Folin-Ciocalteu's reagent and 100 µL of 20% sodium carbonate to assess total phenolic content. After 30 minutes of incubation, absorbance at 765 nm was measured, and results were expressed as milligrams of gallic acid per 100 grams of dried extract (Limmongkon et al., 2017). A modified colorimetric method involving aluminium chloride was used to measure the flavonoid content in the fruit juice extract. The results were expressed as mg QE/100 g D.W. using quercetin dihydrate as a reference (Munhoz et al., 2014). The DPPH radical scavenging method was employed to assess antioxidant activity. The sample extract was combined with a methanolic DPPH solution and incubated for 30 minutes, after which the absorbance was measured at 517 nm (Gülçin et al., 2010).

Animals

Twenty-five healthy adult albino rats (Sprague Dawley) weighing approximately 130 ± 10 g were obtained from the Faculty of Veterinary Medicine at Cairo University. The treatment of the animals adhered to the ethical standards approved by the Scientific Research Ethics Committee of Mansoura University (No: 47-6-3-2023). Rats were kept in stainless steel cages for one week for adaptation. All rats had full access to food and water *ad libitum*.

Experimental design

After the adaptation period, five rats were placed on a basal diet until the end of the experiment, serving as the normal control group (Group 1). The remaining rats received an intraperitoneal (i.p.) injection of STZ at a dosage of 55 mg/kg body weight to induce diabetes. Four days later, rats with fasting blood glucose levels exceeding 200 mg/dL were classified as diabetic and divided into four groups of five rats each. One diabetic group was fed the basal diet only as diabetic control (group 2). Another diabetic group was fed on the basal diet and treated orally with white sapote juice (3 ml) (group 3). In contrast, another group was treated orally with Cr (80 µg/kg b.wt.) dissolved in 3 ml distilled water (group 4), and the fifth group was treated with 3 ml of juice and Cr mixture (1:1 v/v) orally (group 5). At the end of the four-week experiment, the rats were sacrificed after an overnight fast. Blood was collected from each rat's eye vein using a capillary tube. The blood samples were placed into clean, dry centrifuge tubes and allowed to clot at room temperature. Afterwards, they were centrifuged at 5000 rpm for 10 minutes to separate the serum. The serum samples were stored in a deep freezer at -18°C until they were needed for further biochemical analyses.

Biochemical analysis

Glucose levels were measured as described by Trinder (1969). Insulin was determined according to Bürgi et al. (1988). Glycated haemoglobin (HbA1c) was determined according to Sudhakar and Pattabiraman (1981). Total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL-C) were measured using methods from Allain et al. (1974), Fassati and Prencipe (1982) and Lopes et al. (1977), respectively. Low-density lipoprotein (LDL-C) and very low-density lipoprotein (VLDL-C) were calculated as mentioned by Friedewald et al. (1972). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assessed as explained by Burtis et al. (1999). Serum albumin was colorimetrically determined by the method of Doumas et al. (1971). Serum uric acid was measured according to Fassati et al. (1980). Creatinine was detected as described by Young (2001). The antioxidant enzymes Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione Peroxidase (GPx) were estimated using the methods outlined by Nishikimi et al. (1972), Yasmineh et al., 1992, and Paglia and Valentine (1967), respectively. Serum tumor necrosis factor-alpha (TNF-α) was measured using the method described by Brouckaert et al. (1993). The serum interleukin-1 beta (IL-1β) level was assessed with the ELISA Kit (Elabscience® rat IL-1β and Elabscience® rat IL-6) as described by Fristiohady et al. (2020). The determination of C-reactive protein (CRP) concentration in a serum sample was carried out according to Friedman and Young (2001).

Statistical analysis

The data collected were presented as means ± standard deviation (SD). Statistical analysis was conducted using one-way analysis of variance (ANOVA). The means between groups were compared using (LSD) at $p \leq 0.05$, using the computer program (Gomez and Gomez, 1984).

3. Results

Chemical composition of white sapote

The data in table (1) represent the chemical composition of white sapote fruit. It can be noted that white sapote contains moisture, ash, fat, protein, fiber, and carbohydrates in percentages of 6.48± 0.09, 2.41± 0.07, 1.09± 0.04, 2.13± 0.11, 3.36± 0.07, and 84.53± 0.38 %, respectively. Carbohydrates represent the main component of the fruit. The major minerals found in white sapote fruits are K, Ca, and P, with values of 618.16 ± 3.04, 538.80 ± 4.71, and 171.63 ± 2.11 mg/100 g, respectively. This indicates that white sapote is a good calcium source necessary for healthy bone formation and energy metabolism. The Zn, Na, and Fe contents reached 56.93 ± 0.19, 26.18 ± 0.73, and 25.11 ± 0.21 mg/100 g, respectively.

Phytochemical composition of White Sapote

The total phenols of white sapote fruit were 56.37±0.96 mg GAE/100g, while total flavonoid content was 9.48±0.19 mg QE/100g on a dry weight basis. Regarding vitamin content, the results revealed that the fresh white sapote contains vitamin C with a concentration of 31.26± 0.79 mg/100g, while its carotene content was 16.73±0.52 mg/100g. Carotenoids, which are a precursor of Vitamin A and Vitamin C are potent antioxidants besides their other functions. Our study demonstrated that white sapote extract at a 500 µg/ml concentration could remove 93.47±0.17% of DPPH free radicals. This suggests that white sapote fruits possess antioxidant activity, which can be attributed to their high content of phenolic compounds, flavonoids, and vitamins A and C, which are potent antioxidants beneficial for overall health (Table 1).

Effect of white sapote juice and chromium on blood glucose balance in diabetic rats

Table 2 indicates significant increases in glucose and HbA1C levels in the positive control group, with values of 274± 23.4 mg/dl and 6.57± 0.454%, respectively as compared to the normal control group which had values of 92± 15.1 mg/dl and 4.38± 0.148%, respectively. In contrast, the serum insulin levels in the positive control group decreased significantly to 2.27± 0.096 µIU/ml, compared to 2.94± 0.197 µIU/ml in the normal control group. For the treated groups, the results indicated that the juice group experienced a reduction in glucose levels by 45.99% and HbA1c by 15.07% compared to the positive control group. The Cr group caused a significant decrease in glucose and HbA1C compared to the positive control group; their decrease percentages were 32.48% and 12.02%, respectively. The juice and Cr mix group caused significant decreases in serum glucose and HbA1C levels compared to the positive control group; their decrease percentages were 50.00% and 25.42%, respectively. The same table shows that serum insulin increased significantly in the juice, Cr, and mix groups, with percentages of 9.25%, 7.5%, and 11.45%, respectively, compared to the positive control group.

Effect of white sapote juice and chromium on lipid profile in diabetic rats

The results in table (3) showed significant increases in total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-c) and (VLDL-c) in the positive control group compared to the normal control group. Their values were 188.2 ± 10.71, 131.8 ± 8.81, 140.1 ± 9.78, and 26.4 ± 1.76 mg/dL, respectively, in the positive control group, while their values were 67.6 ± 9.02, 94.3 ± 5.54, 13.7 ± 4.31, 18.9 ± 1.11 mg/dl in the normal control group, respectively. On the other hand, serum HDL-c level decreased significantly in the positive control group (21.5±2.67mg/dL) compared to the normal control group (35.1±2.89 mg/dL). The treated groups showed that the juice group had significant reductions in total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-c), and very-low-density lipoprotein cholesterol (VLDL-c), with percentages of 44.37%, 18.13%, 60.17%, and 18.18%, respectively, compared to the positive control group. The Cr group also demonstrated decreases in these levels, with reductions of 44.05% for TC, 17.07% for TG, 60.81% for

LDL-c, and 17.05% for VLDL-c. When both juice and Cr were administered together, the reductions were even greater: 55.89% for TC, 21.01% for TG, 77.02% for LDL-c, and 21.21% for VLDL-c compared to the positive control. The same table shows that serum HDL-c levels increased significantly in the juice group, Cr group, and (juice + Cr) group, with a percentage of 26.97 %, 30.46 %, and 39.53 %, respectively, compared to the positive control.

Effect of white sapote juice, chromium and their mixture on liver and kidney functions in diabetic rats

The impact of sapote juice and Cr on liver and kidney functions is presented in Table 4. The findings revealed a significant increase in ALT (67.4± 4.77 U/L) and AST (85.1±5.34 U/L) activities in the positive control group in comparison to the normal control group, where their values were 31.6± 2.61 and 36.5± 4.07 U/L, respectively. On the other hand, serum albumin levels decreased significantly in the positive control group (3.53±0.35 g/dl) compared to the normal control group (4.73±0.19 g/dl). The results for the treated groups showed that the juice group experienced a decrease in the serum ALT and AST activities, with percentages of 24.63 % and 32.67 %, respectively, compared to the positive control group. The Cr group revealed significant decreases in ALT and AST compared to the positive control group; their decrease percentages were 23.00 % and 28.67 %, respectively. In the mixed group (juice + Cr), significant decreases in serum ALT and AST were observed compared to the positive control group. The percentage decreases were 39.17% and 36.43%, respectively, marking the best results among the three treatments. This could be attributed to their synergistic effect. The results also showed that serum albumin levels increased significantly in the juice, Cr, and mixture groups, with a percentage of 16.15 %, 9.92 %, and 23.80%, respectively, compared to the positive control group .

The results related to kidney function showed significant increases in creatinine and uric acid levels in the positive control group compared to the normal control group. In the positive control group, the creatinine and uric acid levels were 1.38±0.048 and 6.4±0.191 mg/dl, respectively, while in the normal control group, these levels were 0.674±0.058 and 4.65±0.236 mg/dl, respectively. Compared to the positive control group, the results showed that the group consuming juice experienced a 43.48% reduction in serum creatinine levels and a 14.22% decrease in uric acid levels. The group that ingested Cr had a 40% decrease in creatinine and an 11.25% reduction in uric acid. Additionally, the group that consumed a combination of juice and Cr exhibited significant reductions in both serum creatinine and uric acid levels, with decreases of 49.28% and 17.66%, respectively. In our study, fruit juice, Cr, and a juice- Cr mixture improved kidney function by reducing serum creatinine and uric acid levels in diabetic rats.

Effect of white sapote juice and chromium on oxidative stress and inflammation in diabetic rats

The antioxidant and anti-inflammatory effects of sapote juice and Cr in diabetic rats are summarized in Table 5. The findings indicated significant reductions in the levels of SOD, CAT, and GPx enzymes in the positive control compared to the normal control groups. Specifically, the positive control group had enzyme levels of 125±9.68 U/mL for SOD, 123±8.49 U/L for CAT, and 655±10.7 U/L for GPx. In contrast, the normal group exhibited levels of 181±3.25 U/mL for SOD, 181±6.47 U/L for catalase, and 871±6.52 U/L for GPx. In comparison to the positive control group, the results showed that the group consuming juice had increased serum levels of SOD, CAT, and GPX by 22.4%, 18.7%, and 14.5%, respectively. Similarly, the group that consumed Cr experienced significant increases in SOD, CAT, and GPX by 20.8%, 17.1%, and 14.4%, respectively. Additionally, the group that consumed a combination of juice and Cr also demonstrated a significant increase in SOD, CAT, and GPX, with increases of 27.2%, 24.4%, and 16.2%, respectively. Regarding the anti-inflammatory activity, significant increases in CRP, IL-1β, and TNF-α in the positive control group compared to the normal control group. Their values were 34.2±3.96 ng/ml, 150±6.64 pg/ml, and 39.2±1.57 pg/ml, respectively, in the positive control group, while their values were 21.3± 2.35 ng/ml, 84.6± 3.59 pg/ml, and 20.9±

1.98 pg/ml in the normal control group, respectively. Regarding the treated groups, the juice group showed a decrease in serum levels of CRP by 28.36 %, IL-1β by 15.33 %, and TNF-α by 21.17 % compared to the positive control group. The group that received Cr experienced a significant decrease in CRP, IL-1β, and TNF-α compared to the positive control group. The decrease percentages were 28.07 %, 14.67 %, and 20.92 %, respectively. Similarly, the group that received a mix of juice and Cr also showed significant decreases in serum CRP, IL-1β, and TNF-α levels compared to the positive control group. The decrease percentages in this group were 31.87 %, 21.33 %, and 29.34 %, respectively. The Cr and the juice and Cr mix groups demonstrated significant decreases in CRP, IL-1β, and TNF-α levels compared to the positive control group. In diabetic rats, combining juice and Cr was more effective than using juice or Cr separately in reducing oxidation and inflammation.

Table 1. The chemical composition, mineral, vitamin, phenolic compound contents and antioxidant activity of white sapote powder.

Chemical composition (mg/100 g)		**Minerals content (mg/100 g)**	
Moisture	6.48±0.09	Ca	538.80±4.71
Ash	2.41±0.07	Na	26.18±0.73
Fat	1.09±0.04	K	618.16±3.04
Protein	2.13±0.11	P	171.63±2.11
Fiber	3.36±0.07	Zn	56.93±0.19
Carbohydrates	84.53±0.38	Fe	25.11±0.21
Vitamins (mg/100 g)		**Phenolic compounds**	
Vitamin C (FW)	31.26±0.79	Total phenols mg GAE /100g	56.37±0.96
B-Carotene (FW)	2 16.73±0.52	Total flavonoids mg QE/ 100g	9.48±0.19
Sample concentration		**DPPH scavenging activity %**	
500 µg /ml		93.47±0.17	

Each value is the mean ± SD. FW (based on fresh weight)

Table 2. Effect of white sapote juice and chromium on serum glucose, insulin and HbA1C in diabetic rats

Animal groups	**Glucose (mg/dl)**	**Insulin (µIU/ml)**	**HbA1C (%)**
Normal control	92^{d} ±15.1	2.94^{a} ±0.197	4.38^{c} ±0.148
Positive control	274^{a} ±23.4	2.27^{c} ±0.096	6.57^{a} ±0.454
Juice	148^{c} ±10.4	2.48^{bc} ±0.099	5.58^{b} ±0.259
Cr	185^{b} ±23.1	2.43^{bc} ±0.129	5.78^{b} ±0.26
Juice + Cr (1:1 v/v)	137^{c} ±20.7	2.53^{b} ±0.084	4.9^{c} ±0.158

Results are presented as means ±SD and % of change. Values in the same column that share a superscript letter are not significantly different at $p<0.05$. (*): % of change related to the positive control group.

Table 3. Effect of white sapote juice and chromium on lipid profile in diabetic rats.

Animal groups	**Cholesterol (mg/dl)**	**Triglycerides (mg/dl)**	**HDL-c (mg/dl)**	**LDL-c (mg/dl)**	**VLDL-c (mg/dl)**
Normal control	67.6^{c} ±9.02	94.3^{c} ±5.54	35.1^{a} ±2.89	13.7^{d}±4. 31	18.9^{c} ±1.11
Positive control	188.2^{a} ±10.7	131.8^{a} ±8.81	21.5^{c} ±2.67	140.1^{a}±9.78	26.4^{a} ±1.76
Juice	104.7^{b} ±11.3	107.9^{b} ±9.46	27.3^{b} ±2.48	55.8^{b} ±9.31	21.6^{b} ±1.89
Cr	105.3^{b} ±10.9	109.3^{b} ±6.42	28.05^{b} ±2.86	54.9^{b} ±10.6	21.9^{b} ±1.28
Juice + Cr	83.0^{c} ±11.5	104.1^{bc} ±7.6	30.0^{b} ±2.03	32.2^{c} ±9.91	20.8^{bc}±1.52

Results are presented as means ±SD and % of change. Values in the same column that share a superscript letter are not significantly different at $p<0.05$. (*): % of change related to the positive control group.

Table 4. Effect of white sapote juice, chromium and their mixture on liver and kidney functions in diabetic rats.

Animal groups	ALT (U/L)	AST (U/L)	Albumin (g/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)
Normal control	31.6^{d} ±2.61	36.5^{c} ±4.07	4.73^{a} ±0.19	0.674^{c}±0.05	4.65^{c} ±0.236
Positive control	67.4^{a} ±4.77	85.1^{a} ±5.34	3.53^{c} ±0.35	1.38^{a} ±0.048	6.4^{a} ±0.191
Juice	50.8^{b} ±2.33	57.3^{b} ±5.56	4.1^{b} ±0.08	0.78^{bc} ±0.045	5.49^{b} ±0.148
Cr	51.9^{b} ±1.94	60.7^{b} ±7.21	3.88^{bc} ±0.16	0.83^{b} ±0.08	5.68^{b} ±0.333
Juice + Cr	41^{c} ±1.58	54.1^{b} ±5	4.37^{ab} ±0.4	0.70^{c} ±0.063	5.27^{b} ±0.116

Results are presented as means ±SD and % of change. Values in the same column that share a superscript letter are not significantly different at $p<0.05$. (*): % of change related to the positive control group.

Table 5. The effect of white sapote juice and chromium on oxidative stress and inflammation in diabetic rats.

Animal groups	SOD (U/ml)	Catalase (U/L)	GPx (U/L)	CRP (ng/ml)	IL-1β (pg/ml)	TNF-α (pg/ml)
Normal control	181^{a} ±3.25	181^{a} ±6.47	871^{a} ±6.52	21.3^{b} ±2.35	84.6^{d} ±3.59	20.9^{c} ±1.98
Positive control	125^{c} ±9.68	123^{c} ±8.49	655^{c} ±10.7	34.2^{a} ±3.96	150^{a} ±6.64	39.2^{a} ±1.57
Juice	153^{b} ±3.69	146^{b} ±7.99	750^{b} ±18.1	24.5^{b} ±2.66	127^{b} ±3.74	30.9^{b} ±2.2
Cr	151^{b} ±5.1	144^{b} ±6.74	749^{b} ±12.9	24.6^{b} ±2.08	128^{b} ±6.35	31^{b} ±1.66
Juice + Cr	159^{b} ±4.0	153^{b} ±7.52	761^{b} ±36	23.3^{b} ±1.55	118^{c} ±5.62	27.7^{b} ±1.81

Results are presented as means ±SD and % of change. Values in the same column that share a superscript letter are not significantly different at $p<0.05$. (*): % of change related to the positive control group.

4. Discussion

The results revealed that the fruit of white sapote powder contains high amounts of carbohydrates, K, Ca in addition to P, Fe and Zn. Calcium is necessary for bones, blood clotting, and muscle contractions. Calcium balance is important in insulin resistance and secretion (Ozcan and Tabas, 2016). DM affects calcium homeostasis, which leads to cell instability in the muscles of the skeleton, cardiac muscle, platelets, and red blood cells. These results are consistent with those of Elkot et al. (2023), who stated that dried sapote fruits grown in Egypt contain 641.0 ± 3.12mg/100 g Ca, 66.43 ± 0.22mg/100 g Zn, and 26.73 ± 0.04 mg/100 g Fe. The white sapote is a valuable source of P, the second most abundant mineral in the body after Ca. Phosphorus performs numerous crucial functions, such as filtering waste from the body and repairing tissues and cells (Serna and Bergwitz, 2020).

Iron is a trace element required by all living things. Zinc helps the body's immune system, is essential for the general growth of all tissues, and plays a part in synthesizing brain enzymes (Tafti and Panahi, 2019; Krebs, 2000). Zinc balance disturbances are linked to diabetes and insulin resistance (Foster and Samman, 2012). Zn, insulin, and diabetes are tightly associated. Zn homeostasis is affected by diabetes (Bandeira et al., 2017). Zn is necessary for the functioning of insulin in pancreatic cells, In type 1 diabetes, islet cell death is caused by a zinc shortage (Li, 2013) .

Because white sapote fruit is rich in minerals, which help diabetics regulate their blood sugar levels, it's important to raise awareness of this fruit's health benefits in preventing diabetes. Vitamins are essential in reducing the risk of diabetes by regulating insulin secretion and sensitivity. They also have anti-inflammatory, immunomodulatory, antioxidant, lipid-lowering, and hypoglycemic effects (Alkholy et al., 2019; Puvvada, 2020; Kalra and Aggarwal, 2021). Vitamin A has been demonstrated to affect the formation of cells, particularly pancreatic cells, implying that it is favorable to the creation of insulin (Zhou et al., 2020). It is a necessary nutrient for cell division, organ and skeletal growth, and maturation (Blaner, 2019). Flavonoids regulate glucose metabolism and insulin sensitivity by influencing many processes. They enhance the absorption of glucose and the release of insulin (Alkhalidy et al., 2018). The DPPH scavenging activity of the white sapote powder extract with a

concentration of 500 µg/ml caused an inhibition of 93.47± 0.17%. This result agrees with that of Elkot et al. (2023) .

The results revealed that the three treatments used in this study caused significant decreases in fasting blood sugar and HbA1C and an increased serum insulin level. Sapote fruit contains a good percentage of dietary fiber and phenolic compounds essential in maintaining blood sugar homeostasis. Fiber is essential in slowing digestion and conversion of starch to simple sugars, a crucial step in controlling diabetes and reducing cholesterol absorption from the stomach (Cust et al., 2009). The active ingredients in medicinal plants, such as phenolic compounds, can regenerate pancreatic beta cells, release insulin, and combat insulin resistance (Singh et al., 2009). The treated groups in this work improved the lipid profile parameters due to the polyphenols and dietary fiber in the white sapote fruit. Dietary fiber can directly stabilize LDL cholesterol and bile acids, preventing bile acids from moving through the enterohepatic circulation system. This aids in eliminating cholesterol through feces and thus reduces serum LDL (Ariantari et al., 2010).

In the present work, fruit juice, Cr, and juice-Cr mixture improved liver function by increasing serum albumin levels and decreasing serum ALT and AST activities in diabetic rats. Previous studies have reported a relationship between the AST/ALT ratio and the risk of diabetes (Nakajima et al., 2022). The liver plays a crucial role in controlling gluconeogenesis, glycogenolysis, and gluconeogenesis, which are critical steps in maintaining glucose homeostasis (Han et al., 2016). An elevated AST/ALT ratio correlates with a reduced risk of diabetes (Wang et al., 2023). Diabetic nephropathy, a severe complication of diabetes, is the primary cause of kidney failure and other serious health complications. Severe hyperglycemia produces reactive oxygen species, causing oxidative stress and altering intracellular metabolic pathways. Gradual decline can lead to impaired kidney function. Randomized studies indicate that restoring metabolic control can lead to normoglycemia and decrease the evolution of diabetic nephropathy in its early phases (Imran et al., 2020). The current results showed that treated groups exhibited significant improvements in the antioxidant enzymes; SOD, CAT and GPx. According to a previous study, decreased SOD activity may lead to increased superoxide radicals, leading to inactivation of CAT and decreased insulin efficacy in type 2 diabetes patients (Hou et al., 2021). The results also showed an improvement in inflammation parameters such as TNF-α, IL-1β and CRP. TNF-α is an inflammatory biomarker expressed in various acute and chronic liver diseases and is thought to play a role in liver deterioration and repair processes. In diabetes and liver damage, TNF-α regulates cell death and inflammatory processes. IL-1β is the predominant cytokine in inflammatory conditions, especially in diabetes (Lemmon and McLinden, 2017). Increased levels of inflammatory parameters, such as C-reactive protein (CRP) and tumor necrosis factor-alpha (TNF-α), have important implications for the development and advancement of diabetes. These biomarkers impact insulin production by causing gradual harm to pancreatic beta cells and triggering inflammation (Berbudi et al., 2020). TNF-α can inhibit insulin signaling in renal cells, leading to insulin resistance and sustaining the inflammatory response caused by hyperglycemia (Agarwal et al., 2022).

4. Conclusion

It can be concluded that white sapote fruit is a nourished fruit because of its content of carbohydrates, dietary fiber, protein and high levels of potassium, calcium, and iron minerals, in addition to its essential phytochemicals such as phenolic acids and flavonoids. The effects of white sapote juice, Cr, and their mixture on the complications of diabetic rats were studied. The results showed that sapote fruit juice, Cr, or their mixture caused significant improvements in blood sugar and HbA1c levels. They also caused significant improvements in lipid profile, liver enzymes (ALT and AST), albumin, creatinine and uric acid. However, the effect of the juice and Cr mixture was higher than that of juice and Cr alone. Regarding anti-inflammatory and antioxidant activity, the juice and Cr mixture showed better results than the other groups in reducing inflammatory factors and increasing antioxidant enzymes. Therefore, it is recommended to consume white sapote fruit to

alleviate the complications of diabetes, and it is preferable to take a Cr supplement with it.

Conflict of interest

The authors declare no conflict of interest.

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