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Potential Hypoglycemic Effects of Mango (*Mangifera indica L.*) Peel Powder in Streptozotocin-Induced Diabetic Rats

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ABSTRACT:

Mango-based food industries generate numerous by-products, particularly peels abundant in active compounds and flavonoids. This study examines the potential effects of mango peel powder (MPP) on diabetic rats. Forty male rats were randomly assigned to two primary groups. The first group (n=10 rats) was provided with a basal diet (BD) and served as the normal control group. The second group, comprising 30 rats, received a single intraperitoneal injection of streptozotocin (STZ; dose 45 mg/kg) to induce diabetes. This group was further subdivided into three equal subgroups (n=10): the second subgroup, the positive control, was fed the BD, while the third and fourth subgroups were fed BD supplemented with 5% and 10% (w/w) MPP, respectively. Results showed that STZ injection showed an evident increase in fasting blood glucose (FBG) levels and insulin resistance (HOMA-IR) indexes, demonstrating increases of 193.15% and 33.08%, respectively, compared to the normal control group. Results showed that the introduction of MPP at the specified concentrations led to significant reductions ($p \leq 0.05$) in these values, showing decreases of 51.25% and -17.40% for FBG, and 8.45% and -5.14% for HOMA-IR, correspondingly. Furthermore, MPP at a concentration of 10% significantly enhanced liver and kidney functions and malondialdehyde (MDA) levels. Moreover, MPP exhibited notable antioxidant properties, as evidenced by an increase in the activities of superoxide dismutase (SOD) and glutathione (GSH) enzymes. In conclusion, mango peels represent a promising by-product that may contribute to the sustainable development of functional products while simultaneously improving blood glucose and insulin levels in diabetes management.

Keywords: Diabetes, Mangiferin, Homa-IR, Oxidative Stress, GSH, Byproducts.

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1. INTRODUCTION

Food waste and by-products of fruit and vegetable industries have become one of the most important issues threatening the entire world due to their negative impact on the environment, climate and public health. Fruit peels are commonly discarded and constitute 15 to 60 percent of the waste in fruit

processing [1,2]. According to the Egyptian Ministry of Environment's report on the state of the environment in Egypt for 2024, the total waste in Egypt has increased to 50 million tons annually of agricultural waste and 12 million tons annually of food processing waste due to the increase in food production as a result of the huge population increase. Therefore, Egypt seeks to green transition to preserve the environment from this waste and reduce its risks to achieve Egypt's Vision 2030 for sustainable development. On the other hand, these wastes contain large amounts of biologically active substances that are believed to improve health [3]. As a result, these wastes can be managed and used to produce exceptional value-added products, which are mostly used in the food, cosmetic, and pharmaceutical industries[4,5]. Furthermore, dietary fiber (DF), polyphenols (PP), flavonoids, carotenoids, isoflavones, phenolic acid, tannins, isothiocyanates, lignins, and saponins-all of which can be utilized to treat or prevent a number of illnesses are abundant in the by-products of the fruit and vegetable industries[6]. Additionally, a number of in vitro and in vivo studies have shown that a number of phytochemicals isolated from fruit wastes can prevent or manage a number of illnesses, such as excessive blood pressure, diabetes, cancer, and heart disease [7].

One of the most widely grown and consumed tropical fruits in the world, the mango (Mangifera indica L.) is renowned for its high vitamin and antioxidant content [8]. Mangos (Mangifera indica L.), a drupe fruit class, belong to the Anacardiaceae family. [9,10]. Over 50 million tons of mangos are produced worldwide each year [11]. However, depending on the type and techniques employed, processing mangoes results in significant waste, mostly in the form of peels and kernels, which account for 35–60% of the fruit's weight. [12]. Mango can produce up to 60% of polluting by-products, including its peel [13]. The high biological oxygen demand (BOD) of these mango by-products makes disposal a major concern [14]. However, it has been widely noted that mango peel contains a high concentration of beneficial compounds, such as flavonoids, phenolic acids, fiber, vitamins, and carotenoids [9,15]. Antioxidant substances like these could lower chronic disease risk by eliminating free radicals [16]. Additionally, numerous studies have demonstrated the numerous advantages of mango peels, since they contain dietary fiber and polyphenols that support blood sugar regulation, cholesterol reduction, and digestive health [17]. Moreover, nutritious fiber makes up 45–50% of the dry weight of mango peels. Fiber, especially its soluble and insoluble forms, lowers blood sugar, lowers cholesterol, and promotes digestive health [18]. Beta-carotene and lutein in mango peel protect against macular degeneration due to age and enhance eye health [19] . Mango peels also contain bioactive compounds that improve health, such as antioxidants, which help lower oxidative stress, which can lead to diabetes, cancer, and cardiovascular disease [20]. Polyphenols found in mango peels have been shown to lower oxidative stress in vitro, suggesting that regular consumption may enhance health [17]. Additionally, Byproducts from mangoes have antioxidant and anti-inflammatory qualities. Numerous cancers, heart disease, and arthritis are all made more likely by chronic inflammation [21]. Furthermore, By inhibiting pro-inflammatory cytokines, the compound mangiferin, which is present in mango peel, lowers inflammation [22]. Also, mango peel fiber controls blood pressure and blood sugar, while unsaturated fatty acids in mango kernels lower LDL cholesterol [22]. As a result, mango peel may one day be utilized as a treatment for a number of clinical conditions, including diabetes [23].

Diabetes mellitus (DM) is ranked among the top five reasons of death worldwide [25]. Aside from deaths, diabetes is also associated with serious health consequences [26,27].

However, the prevalence of diabetes is rising worldwide; in 2021, 537 million persons (one in every ten people) were diabetic. By 2030, this figure is expected to increase to 643 million, and by 2045, it will reach 783 million [24].

Due to a lack of sufficient research to clarify the biological and biochemical role of mango peel powder (MPP), the aim of this research is to evaluate the mango peel powder's potential to prevent diabetes among diabetic rats. To assist explain the above likely roles, this investigation will also examine the proximate composition, bioactive component content of powdered mango peel..

2. MATERIAL AND METHODS

2.1 Materials

2.1.1 Plant Material

Al-Obour market in Cairo, Egypt, provided the mangos (Mangifera indica L.), which were processed to obtain peels and guarantee their quality.

2.1.2 Diet, Chemicals and kits

Dietary ingredients: DL-Methionine, cellulose, casein, and powdered choline chloride were acquired from Morgan Co. in Cairo, Egypt. Sterozotocin (STZ) was purchased from El-Gomhoriya Company in Cairo, Egypt. The analysis kits were obtained from the Bio Diagnostics Company Cairo, Egypt.

2.2. Methods

2.2.1. Preparation of Mango Peel Powder (MPP)

Following a thorough washing of the mangoes under running water, they were allowed to air dry at ambient temperature. A peeler was subsequently employed to remove the skin from the mangoes. After weighing the peels using a scale, they were evenly distributed across drying trays and placed in a tray dryer adjusted to a temperature of 50°C for a duration of eighteen hours. To achieve a consistent particle size, the dried peels were processed into a powder utilizing a grinder and then sieved through a 250 µm mesh screen. In accordance with the procedure detailed in reference [28], the resulting powder was stored in airtight bags and placed in a desiccator for further analysis.

2.2.2. Phenolic compounds quantification

High-performance liquid chromatography was used to ascertain the phenolic component composition of MPP [29]. A gradient elution was carried out using solvents A (water with 0.1% (v/v) acetic acid) and B (acetonitrile with 0.1% (v/v) acetic acid) in a zorbax eclipse plus C8 column (4.6 mm x 250 mm i.d., 5 µm). The injection volume was 20 µL, and the flow rate was 1 mL/min. At 280 nm, UV detection was set. Each phenolic component was quantified using a standard curve that was created by introducing standards of various concentrations into the HPLC instrument. By adding standards to the sample, peak identification was made easier, and peak areas were computed by contrasting them with the standard peaks.

2.2.3. Biological Experimental

2.2.3.1.Ethical Approval

All the experimental and animal care protocols were ethically approved by the Institutional Animal Care and Use Committee (IACUC) at Menoufia University, Sheibin El-Kom, Egypt (Approval No. MUFHE/S/NFS/44/24). All biological experiments were performed in compliance with the policies of the IACUC for the use and care of laboratory animals.

2.2.3.2.Animals

For this investigation, adult male albino rats weighing 150.64 ± 8.9 g each were acquired from the Ministry of Health and Population's Helwan Station in Helwan, Cairo, Egypt. Every rat was kept in a controlled environment with a 12:12 light/dark cycle, 22 ± 2 ◦C, and 50 ± 15% humidity.

2.2.3.3.Basal Diet (BD).

The basic diet offered by AIN was eventually composed of casein (150 g/1 kg diet), unsaturated fats (100 g/1 kg diet), sucrose

(220 g/1 kg diet), maize starch (440 g/1 kg diet), cellulose (40 g/1 kg diet), a salt (40 g/1 kg diet), and a vitamin mixture (10 g/1 kg diet) [30]. Additionally, the composition of vitamin and salt mixtures is based on [31] and [32], respectively.

2.2.3.4.Experimental design

Induction of diabetes mellitus: A dose of 45 mg/kg body weight of STZ was administered intraperitoneally (IP) within 5 minutes after being dissolved in 0.1 M citrate buffer (pH 4.5) in a volume of 1 mL/kg body weight. After three days, reagent strips (AccuChek®, Roche, Germany) were used to assess fasting blood glucose (FBG) in order to confirm the presence of diabetes. Rats were classified as diabetic if their blood glucose levels were between 300 mg/dL [33]. Compared to another inducer, alloxan, STZ was employed because it was more effective in causing diabetes mellitus and rats were more tolerant of it. Previous comparison trials have shown that STZ is more effective than alloxan at producing diabetic mellitus [34]. Additionally, percentages of mango peel were chosen based on earlier research by [86], which found that comparable levels were useful.

Every biological experiment carried out complies with the National Research Council's Commission on Life Sciences, Institute of Laboratory Animal Resources' decisions [35]. Following a two-week acclimatization period, forty male rats were randomly assigned to two main group. The first main group (10 rats) fed on the basal diet as normal control group. The second main group (30 rats) injected with STZ at a dose of 45 mg/kg BW as a single intra-peritoneal injection to induce diabetes, then classified into three equal sub groups (n=10) as follow: group (2), as a positive control group, fed on BD and groups (3 and 4) fed on BD containing 5 and 10 % (w/w) of mango peel powder (MPP), respectively.

2.2.3.5.Biological Evaluation

Body weight was measured weekly and the diet was documented daily throughout the experiment's duration (28 days). The following formulas were used in accordance with [36] to calculate the body weight gain (BWG), feed intake (FI), and feed efficiency ratio (FER): BWG (g)=(Final weight – Initial weight) and FER= Grams gain in body weight (g/28 day)/ Grams feed intake (g/28 day).

2.2.3.6.Blood Sampling

Rats were sedated with ether, and blood samples were taken from the abdominal aorta at the conclusion of the 4-week trial following a 12-hour fast. In order to separate the serum, blood samples were put in dry, clean centrifuge tubes, let to clot at room temperature, and then centrifuged for 10 minutes at 3000 rpm. [39]. For serum, after being cautiously aspirated, it was transferred into sterile glass tubes and frozen at -20°C.

2.2.3.7. Biochemical analysis

Blood biochemical analysis. Every diabetic rat was fasted for the whole night. Using the glucose oxidase method with a pre-standardized glucometer and reagent strips, fasting blood glucose (FBG) levels were determined [38]. An ELISA kit (Elabscience, Bethesda, MD, USA) was used to measure serum insulin levels in accordance with the manufacturer's instructions. Using the formula HOMA-IR = (fasting blood glucose level × insulin level)/405, the homeostasis model assessment of insulin resistance (HOMA-IR) was computed from fasting blood glucose and insulin levels.

Liver functions enzymes. The approach of [39], [40], and [41] was used to quantify the activities of serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST) in serum. A approach of [42] was used to measure the activity of alkaline phosphatase (ALP).

Oxidant and antioxidant enzymes. Values for glutathione activity (GSH), malondialdehyde (MDA), and superoxide dismutase (SOD) were determined using the methods of [43], [44], and [45], respectively.

Kidney functions. The method of measuring serum creatinine, urea, and uric acid were employed by [46], [47] and [48], respectively.
Lipid profile. Using the techniques of [49], [50], [51], and [52], serum levels of triglycerides (TGs), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were evaluated.

2.2.4. Statistical analysis

A computerized Costat program was used to statistically evaluate all of the data using a one-way ANOVA. Means ± and standard deviation (SD) were used to present the results. Treatment differences were deemed significant at $P \leq 0.05$ [53].

3. Results and Discussion

Figure 1 displays the polyphenols' chromatographic separation in MPP. Table 1 displays the mean of three determinations of the content of each phenolic component, which was computed from the associated calibration curve. According to these findings, the most prevalent polyphenols were quercetins and catechins, which had 94.25 and 89.73 µg/g of dry extract, respectively.
In line with the present results, a recent study showed that mango peel has a higher antioxidant potential than grapes and black limes [54]. Also, using LC-MS/MS in MPP, 68 phenolic compounds were discovered, including epicatechin, procyanidin B2, caseic acid, quercetin, gallic acid, and chlorogenic acid [54]. Furthermore, researchers discovered different levels of TFC, such as 54.67 to 109.76 mg GAE/g, 45.56 to 90.89 mg CE/g DW, 21.6 ± 0.05 mg catechin equivalent/g [56], and 135.04 mg quercetin equivalent/g [55] in MPP. Additionally, the results of this investigation are in line with the various gallic acid compositions that have been reported in mango peel extracts in the reviewed literature, which range from 14.5 to 791.5 µg/g DW and 23 to 23,816 µg/g DW [57,58–59].
However, it was discovered that the caffeic acid concentration varied from 16.6–67.3 µg/g dry weight and 33.03–144.3 µg/g dry weight, while the chlorogenic acid content of various mango peel extracts ranged from 760–2280 µg/g dry weight and 44.05–271.9 µg/g dry weight [60] & [61]. In addition, catechin levels in various mango peels ranged from 45.73 to 115.5 µg/g dry weight, according to other research [62], which is in line with the current study's findings.

Table 1. HPLC profiles of mango peel powder (MPP)

Compounds	Retention time (Rt)	Conc. (µg/g)
Catechins	03:45±0:01	89.73±5.32
Kaempherol	07:25±0:02	16.32±3.61
Gallic acid	09:50±0:02	49.48±3.25
vanillic acid	11:10±0:01	56.5±4.35
Quercetin	15:20±0:05	94.25±6.31
Caffeic acid	17:45±0:03	24.74±2.65
Chlorogenic acid	31:10±0:04	36.65±2.84
Sinapic acid	33:30±0:07	25.25±1.56

Each value is the Mean ± SD of three replicates.

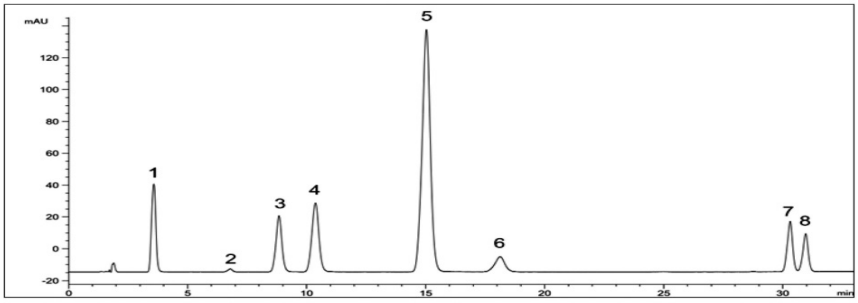


Figure 1. HPLC chromatogram of MPP. Peaks: 1, catechins; 2, quercetins; 3, kaempherol; 4, gallic acid; 5, vanillic acid; 6, caffeic acid; 7, chlorogenic acid; 8, sinapic acid

The effects of a dietary intervention containing mango peel powder (MPP) on the BWG, FI, and FER of diabetic rats were displayed in Table 2. Based on these findings, rats injected with STZ (model control) had lower BWG, FI, and FER rates than the normal group, respectively, by -51.15, -26.9, and -35.29%. However, after four weeks of feeding rats MPP (5 and 10 g/100 g diet), the diabetic rats (model control) had significantly ($p \leq 0.05$) lower BWG, FI, and FER rates than the normal group, which were -43.77, -20.5, and -29.41%, -15.20, -4.53, and -11.76, respectively. The diabetic rats' rates of increase in BWG, FI, and FER showed a largely dose-dependent pattern.

STZ reduced the BWG, FI, and FER in the current investigation. These outcomes aligned with those of [5], who discovered that STZ (55 mg/kg, i.v.) led to a significant decline in body weight and fasting hyperglycemia. The results of the current study showed that MBB led to a significant improvement in BWG, FI, and FER. These findings aligned with those of [5], who discovered that the intervention with mango MPP improved the prior criteria. Mangiferin, present in mango peel, has strong anti-diabetic properties and increased bodyweight reduction at various points during the trial compared to the diabetes vehicle-treated controls. The study by [11], which found that MPP enhanced the body weight gain and the food intake of diabetic rats, corroborated the current findings. Additionally, these findings are consistent with those of [75], who discovered that weight loss was lessened in the group of diabetics (MPD) who had mango peel treatment, which had a gain comparable to that of the control group.

Table 2. Impact of mango peel powder (MPP) on rats treated with STZ in terms of BWG, FI, and FER

Groups	BWG (g/day)		FI(g/day)		FER	
	Mean ±SD	Change %	Mean ±SD	Change %	Mean ±SD	Change %
G1 (-)	4.34±0.13a	---	24.94±1.5a	---	0.17±0.02a	---
G2 (+)	2.12±0.18c	-51.15	18.21±1.13c	-26.9	0.11±0.03c	-35.29
G3 (5%)	2.44±0.17c	-43.77	19.81±1.65c	-20.5	0.12±0.01c	-29.41
G4 (10%)	3.68±0.14b	-15.20	23.81±1.06b	-4.53	0.15±0.05b	-11.76

Each value represents the mean value of three replicates ± SD. Means under the same column with different superscript letters exhibited significant at $P \leq 0.05$. G1, normal group; G2, model group (diabetic); G3 and G4, model group treated with 5 and 10 % of MPP, respectively. BWG, body weight gain; FI, feed intake; FER, feed efficiency ratio.

The impact of mango peel powder (MPP) intervention on changes in FBG, insulin concentrations in serum, and HOMA-IR indexes was displayed in Table 3. From such data, it is noticed that the mean values of the model group's FBG level and HOMA-IR indexes were significantly ($p \leq 0.05$) higher than those of the normal group by 193.15 and 33.08 %, respectively. In comparison, insulin concentration in the model group was significantly($p \leq 0.05$) lower than the normal group by -54.6%, respectively. On the other hand, when rats were fed MPP (5 or 10 g/100 g diet) for four weeks, their serum insulin levels, HOMA-IR indices, and FBG levels all were significantly ($p \leq 0.05$) dropped. There was a dose-dependent increase in the HOMA-IR and insulin indices and a decrease in FBG.

The current data demonstrated that STZ's cytotoxic effects, which destroyed the structure and functionality of the beta cell membrane in the pancreas, could dramatically raise FBG and lower insulin concentrations. These results are consistent with those of other writers who discovered that experimental rats treated with a single intraperitoneal dose of STZ [1,3]. The preferential damage to the pancreatic islets of Langerhans causes a lack of insulin generation and activity, which in turn causes a loss in the tissues' ability to use glucose, which in turn causes diabetes [2].

On the other hand, these results showed that the FBG, insulin, and HOMA-IR indices improved in diabetic rats at varying rates when MPP was added to their diet. These results agreed with [65], who proposed that mangiferin, the primary compound derived from mango peels, has a strong anti-diabetic effect due to its capacity to increase insulin sensitivity and its effects on the activity of digestive enzymes, which can indirectly change glycemia and, consequently, insulin sensitivity. In addition, it has been demonstrated that flavonoids like quercetin, which are included in the powdered mango peel, have anti-diabetic properties through a mode of action linked to improved peripheral sensitivity to the hormone, pancreatic islet regeneration, and the promotion of insulin secretion [16]&[63]. According to other research, quercetin (intraperitoneally) enhanced insulin sensitivity in obese mouse models through a mechanism involving the flavonoid's binding to GLUT4 and encouraging the uptake of glucose by cells via this transporter [68] & [75]. In addition to preventing compensatory hyperplasia and maintaining pancreatic β-cell mass in in vivo models, quercetin, which is included in MPP, can help regulate fasting, postprandial glycemia, and insulinemia [69,70].

Furthermore, polyphenols and flavonoids that target many molecules involved in the management of numerous pathways, such as reducing hyperglycemia via controlling the liver's metabolism of glucose, were reported by [64,[66]. Mango peel also contains gallic acid, an important chemical that may help prevent chronic diseases through its antioxidant properties [71,72]. Additionally, [73] & [74] showed that gallic acid enhances insulin secretion and cell regeneration in a mouse model of diabetes.

Table 3. Impact of mango peel powder (MPP) on rats treated with STZ in terms of FBG, insulin, and HOMA-IR

Groups	FBG (mg/dl)		Insulin (mg/dl)		HOMA-IR (mg/dl)	
	Mean ±SD	Change %	Mean ±SD	Change %	Mean ±SD	Change %
G1 (-)	103.63±1.7d	---	31.90±1.3a	---	8.16±0.42b	---
G2 (+)	303.8±4.7a	193.15	14.48±1.05d	-54.6	10.86±0.79a	33.08
G3 (5%)	156.75±1.38b	51.25	17.43±0.19c	-45.36	6.74±0.11c	-17.40
G4 (10%)	112.39±2.8c	8.45	27.9±0.24b	-12.5	7.74±0.13b	-5.14

Each value represents the mean value of three replicates ± SD. Means under the same column with different superscript letters exhibited significant at P ≤ 0.05. G1, normal group; G2, model group (diabetic); G3 and G4, model group treated with 5 and 10 % of MPP, respectively. FBG, fasting blood glucose; HOMA-IR , homeostatic model assessment for insulin resistance.

The impact of mango peel powder (MPP) on diabetic rats' liver functions (ALT, AST, and ALP) is indicated in table 4. According to these data, the STZ-treated rats showed significantly (p≤0.05) higher levels of ALT (265.3%), AST (243.39%), and ALP (84.12%) than the normal group. But when rats were fed MPP (5 and 10 g/100 g diet) for four weeks, their ALT, AST, and ALP levels significantly (p≤0.05) decreased by 108.6, 74.94, and 29.2%, 19.04, 19.16, and 9.24% compared to the normal group, respectively. The ALT, AST, and ALP levels in the diabetic rats reduced in a dose-dependent manner.

The results of this study showed that STZ caused liver dysfunction, which resulted in an increase in liver enzymes (AST, ALT and ALP). These outcomes aligned with the findings of [76] who demonstrated that STZ's cytotoxic effects, which released these enzymes into the bloodstream after destroying the intracellular organelles and liver cell membrane's structure and functionality.

Also, elevated insulin resistance and blood sugar by STZ raise AST and ALP levels, as well as reactive oxygen species (ROSs) that interact with membrane polyunsaturated fatty acids [16]. Consequently, it is known that antioxidant polyphenols, including

mangiferin, which is present in mango peel, can diminish the rise in ALT, AST, and ALP levels [76], this aligns with the findings of the current study. in addition, [78] and [33] reported that the hypercholesterolemic and hyperglycemic rats' high levels of AST, ALT, and ALP were decreased by MPP mango peel, which is high in magniferin. It was hypothesized that the potent antioxidant qualities of polyphenols found in mango peels were what prevented lipid peroxidation and, as a result, reduced liver enzyme concentrations [63,75,76]. Furthermore, these findings concurred with those of [16], who discovered that MPP ingestion decreased the concentration of alkaline phosphatase (ALP).

Table 4. Impact of mango peel powder (MPP) on rats treated with STZ in terms of ALT, AST, and ALP

Groups	ALT (U/L)		AST (U/L)		ALP (U/L)	
	Mean ±SD	Change %	Mean ±SD	Change %	Mean ±SD	Change %
G1 (-)	52.15±1.3d	---	50.97±1.4d	---	172.79±1.89d	---
G2 (+)	190.51±1.1a	265.3	175.03±1.02a	243.39	318.15±2.26a	84.12
G3 (5%)	108.83±1.3b	108.6	89.17±1.48b	74.94	223.25±2.54b	29.2
G4 (10%)	62.08±2.8c	19.04	60.74±1.67c	19.16	188.77±2.86c	9.24

Each value represents the mean value of three replicates ± SD. Means under the same column with different superscript letters exhibited significant at P ≤ 0.05. G1, normal group; G2, model group (diabetic); G3 and G4, model group treated with 5 and 10 % of MPP, respectively. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase.

Table 5 displays the impact of the mango peel powder (MPP) intervention on the glutathione activity (GSH), malondialdehyde (MDA), and superoxide dismutase (SOD) levels of diabetic rats. According to these results, STZ led to a significant (p≤0.05) drop in SOD and GSH levels, with the ratios being -58.6 and -40.89% of the normal group, respectively. On the other hand, the MDA concentration showed the reverse trend, rising by 69.1% compared to the normal group. MPP caused a considerable (p≤0.05) decrease in MDA and a significant (p≤0.05) rise in SOD and GSH content. The MPP intervention showed a dose-dependent increase in the rate of SOD and GSH growth and MDA decrease.

STZ causes high blood sugar and diabetes, according to [1]. Elevated blood sugar in diabetic rats results in the generation of hydrogen peroxide, which in turn causes the production of oxygen free radicals such O2 and OH [33].

However, these findings demonstrated that MPP decreased oxidative stress and enhanced antioxidant enzymes. In line with the results of this study, [80] demonstrated that MPE showed enormous potential in scavenging free radicals and lowering the absorption capacity of oxygen radicals. Also, these results are consistent with the study conducted by [16] who demonstrated that patients' antioxidant status improved and their TBARS readings reduced after receiving MPP.

Such data was agreed with the results of [1] & [37], which showed that the mechanism of this improvement is due to the availability of a high percentage of carotenoids, such as beta-carotene and quercetin, soluble fiber, and polyphenols in mango peel powder, in addition to the chemical substance mangiferin, which has antioxidant activity and the ability to lower blood sugar. Additionally, [8] & [9] discovered that flavonoids such as kaempferol, quercetin, isorhamnetin, and flavanols which found in MPP have antioxidant qualities that help alleviate oxidative stress. Phenols have the ability to eliminate free radicals by giving them electrons or hydrogen [79]. The reactive potential of the hydroxyl group on the aromatic ring or the phenol moiety of phenolics is what gives them their antioxidant qualities[20].

These findings also concur with those of [11] and [77], who discovered that a diet supplemented with mango peels could reduce or even reverse the lipid peroxidation (MDA)

brought on by diabetes. As a result, eating powdered mango peel reduces cholesterol and effectively prevents lipid peroxidation [16].

Table 5. Impact of mango peel powder (MPP) on rats treated with STZ in terms of SOD, GSH, and MDA

Groups	SOD (U/mg tissue)		GSH (ng/mg/ tissue)		MDA (U/mg/ tissue)	
	Mean ±SD	Change %	Mean ±SD	Change %	Mean ±SD	Change %
G1 (-)	38.9±1.17a	---	12.03±0.57a	---	46.79±0.91c	---
G2 (+)	16.07±1.2d	-58.6	7.11±0.34d	-40.89	79.13±1.28a	69.1
G3 (5%)	19.16±0.7c	-50.74	10.14±0.32c	-15.7	64.90±0.59b	38.7
G4 (10%)	25.92±0.18b	-33.36	11.96±0.45b	-0.58	51.48±1.59c	10.02

Each value represents the mean value of three replicates ± SD. Means under the same column with different superscript letters exhibited significant at P ≤ 0.05. G1, normal group; G2, model group (diabetic); G3 and G4, model group treated with 5 and 10 % of MPP, respectively. SOD, superoxide dismutase ; GSH, glutathione activity; MDA, malondialdehyde

Table 6 displays the kidney function (creatinine, uric acid, and urea) data of rats who received STZ injections and intervention with mango peel powder (MPP). These results found that the STZ-treated group had significantly ($p < 0.05$) higher levels of creatinine, uric acid, and urea than the normal group, by 147.2, 42.77, and 169.6%, respectively. The creatinine, uric acid, and urea levels of the MPP-treated groups at dosages of 5 and 10%, however, were significantly ($p \leq 0.05$) lower than those of the STZ-injected group by 25, 27.7, and 93.76%, 5.6, 14.5, and 52.2% in comparison to the normal group, respectively. So, STZ has detrimental impacts on kidney function measures, according to the current research data.

The findings of this study demonstrated progress in the levels of creatine, uric acid and urea due to the dietary intervention feeding with MPP. The current study's findings are in line with a recent investigation that found that mango peel extract can lower urea and creatinine levels [81]. Additionally, another study discovered that rats with Gentamicin (GM)-induced kidney injury had lower levels of urea and creatinine due to the anti-oxidative and anti-inflammatory qualities of mango polyphenols [75], [76]. Furthermore, in diabetic and hypercholesterolemic rats, the benefits of mangiferin and mango peel extract have been documented against serum urea and creatinine levels [71] and [75]. Also, the current findings are consistent with those of [81], who demonstrated that mango peel extract (MPE) reduced creatinine levels in diabetic rats by 6.19%. They attributed this to the presence of mangiferin in mango peel.

Table 6. Impact of mango peel powder (MPP) on rats treated with STZ in terms of creatinine, uric acid and urea

Groups	Creatinine (mg/dl)		Uric acid (mg/dl)		Urea (mg/dl)	
	Mean ±SD	Change %	Mean ±SD	Change %	Mean ±SD	Change %
G1 (-)	0.72±0.2c	---	3.53±0.34d	---	21.78±0.81d	---
G2 (+)	1.78±0.11a	147.2	5.04±0.50a	42.77	58.71±1.01a	169.6
G3 (5%)	0.90±0.06b	25	4.51±0.09b	27.7	42.20±1.40b	93.76
G4 (10%)	0.76±0.07c	5.6	4.04±0.09c	14.5	33.17±2.11c	52.2

Each value represents the mean value of three replicates ± SD. Means under the same column with different superscript letters exhibited significant at P ≤ 0.05. G1, normal group; G2, model group (diabetic); G3 and G4, model group treated with 5 and 10 % of MPP, respectively.

Table 7 displays the impact of mango peel powder (MPP) on the diabetic rats' serum lipid profile. Such data showed that, the STZ-treated rats had significantly ($p \leq 0.05$) higher levels of TC (115.6%), TGs (89.06%), and LDL-C (288.3%) than the normal group, whereas HDL-C declined (-17.1%). However, when rats were fed MPP (5 and 10 g/100 g diet) for 4

weeks, their serum TC, TGs, and LDL-C levels reduced significantly (p≤0.05) by 53.02, 33, and 93.95%, 9.23, 2.9, and 14.5% in comparison to the normal group, respectively. A dose-dependent pattern was seen in the rate at which HDL increased and TC, TGs, and LDL decreased.

One of the main causes of diabetic mellitus is dysregulation of lipid metabolism, which is typified by changes in the amounts and roles of different fats. The buildup of certain fatty acid metabolites, decreased HDL-c, and elevated triglycerides all lead to insulin resistance and poor glucose utilization [82]. Consistent with a study [84], STZ lowered HDL-c while dramatically raising LDL-c, VLDL-c, TG, and TC levels in the current investigation as compared to control rats. Additionally, [85] discovered that diabetic rats treated with STZ (55 mg/kg, i.p.) showed definite anomalies in lipid metabolism, as demonstrated by the considerable increase in plasma total cholesterol, triglycerides, LDL-C, atherogenic index, and HDL-C levels. This dyslipidemia was in line with [83] who discovered that development of diabetes caused a large rise in blood TG, TC, LDL-c, and a considerable drop in HDL-c. The present study demonstrated that MPP significantly ameliorated STZ-induced dyslipidemia by improving TG, TC and HDL. These results are consistent with [81] who revealed that MPP's mangiferin had strong anti-hyperlipidemia and anti-atherosclerotic properties by significantly lowering plasma total cholesterol, TG, and LDL-C in diabetic rats. This was accompanied by a significant rise in HDL-C levels and a decrease in the atherosclerotic index. Furthermore, the results of this study are consistent with those of [78] who demonstrated that the mango peel decreased lipid levels, improved insulin synthesis, and lowered blood sugar levels. Moreover, soluble fiber, polyphenols, and carotenoids, such as beta-carotene and quercetin, are responsible for these positive effects.

Table 7. Impact of mango peel powder (MPP) on rats treated with STZ in terms of TC, TGs, HDL-c and LDL-c

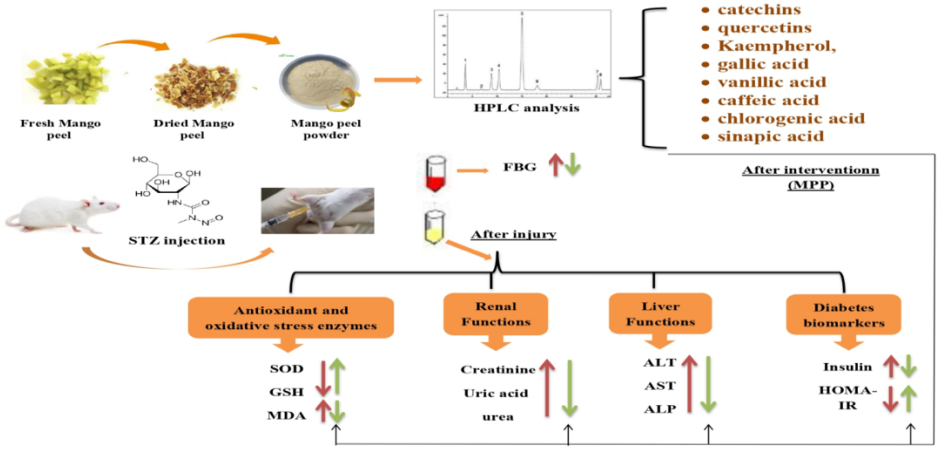
Groups	TC (mg/dl)		TGs (mg/dl)		HDL-c (mg/dl)		LDL-c (mg/dl)	
	Mean ±SD	Change %	Mean ±SD	Change %	Mean ±SD	Change %	Mean ±SD	Change %
G1 (-)	112.81±1.04d	---	94.81±1.19c	---	49.55±0.89a	---	42.87±1.7d	---
G2 (+)	243.24±2.3a	115.6	179.25±1.5a	89.06	41.06±0.14d	-17.1	166.5±2.3a	288.3
G3 (5%)	172.63±1.7b	53.02	126.13±1.6b	33	43.49±0.92c	-12.2	83.15±2.5b	93.95
G4 (10%)	123.23±2.4c	9.23	97.55±2.5c	2.9	47.35±0.57b	-4.4	49.10±1.4c	14.5

Each value represents the mean value of three replicates ± SD. Means under the same column with different superscript letters exhibited significant at P ≤ 0.05. G1, normal group; G2, model group (diabetic); G3 and G4, model group treated with 5 and 10 % of MPP, respectively. TC, total cholesterol; TGs, triglycerides; HDL-c, high density lipoprotein; LDL-c, low density lipoprotein.

4. Conclusion.

The findings of this investigation have proven how effectively mango peel powder can comparatively reduce oxidative stress and hyperglycemia in diabetic rats. The bioactive components from food byproduct (mango peel) offer a comprehensive treatment to combat ROS produced in the body and improve insulin resistance in diabetes patients, according to the current research findings. As a result, they are helpful in limiting the harm that it does by utilizing financial resources that would otherwise be wasted and contribute to pollution. These findings offer a foundation for the production of functional meals and drinks that can help prevent and/or alleviating of type 2 diabetes utilizing mango peel that contains mangiferin.

Figure 2. Graphical summary showing potential hypoglycemic effects of MPP in streptozotocin-induced diabetic rats



CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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التأثيرات المحتملة لخفض سكر الدم لمسحوق قشر المانجو في الفئران المصابة بمرض السكري المستحث بالستربتوزوتوسين

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الملخص العربى:
تخلف الصناعات الغذائية القائمة على المانجو العديد من النواتج الثانوية والمخلفات الغذائية، وخاصة القشور، والتى يصعب التخلص منها، مما يسبب مخاطر صحية بسبب التلوث البيئى، على الرغم من أنها غنية بالعديد من المركبات النشطة والفلافونويدات. لذلك، هدفت هذه الدراسة إلى تقييم التأثير المحتمل لمسحوق قشر المانجو على الفئران المصابة بمرض السكري. تم توزيع أربعون فأرًا ذكرًا بشكل عشوائى على مجموعتين رئيسيتين؛ المجموعة الرئيسية الأولى (10 فئران) تتغذى على النظام الغذائى الأساسى كمجموعة ضابطة طبيعية؛ المجموعة الرئيسية الثانية (30 فأرًا) تم حقنها بالستربتوزوتوسين بجرعة 45 مجم / كجم من وزن الجسم كحقنة واحدة داخل الصفاق للتسبب في مرض السكري، ثم تم تقسيمها إلى ثلاث مجموعات فرعية متساوية (ن=10) على النحو التالى: المجموعة (2)، كمجموعة ضابطة إيجابية، تتغذى على الوجبة الأساسية والمجموعات (3 و 4) تتغذى على الوجبة الأساسية محتوية على 5 و 10 ٪ (وزن/ وزن) من مسحوق قشر المانجو، على التوالى. تسبب حقن الفئران بالستربتوزوتوسين فى زيادة معنوية ($p \leq 0.05$) فى مستويات سكر الدم الصائم ومؤشرات مقاومة الأنسولين بنسبة 193.15 و 33.08٪ على التوالى مقارنة بالمجموعة الضابطة الطبيعية. ومع ذلك، أدى التدخل الغذائي باستخدام مسحوق قشر المانجو بالتركيزات السابقة إلى انخفاض معنوي ($p \leq 0.05$) فى هذه القيم والتى سجلت 51.25 و -17.40 و 8.45٪ و -5.14 و٪ على التوالى. كما أظهر مسحوق قشر المانجو بتركيز 10٪ أيضًا تحسنًا كبيرًا فى وظائف الكبد والمالونديالدهيد ووظائف الكلى. علاوة على ذلك، كان لمسحوق قشر المانجو دور مضاد للأكسدة، حيث تسبب فى زيادة إنزيم سوبر أكسيد ديسميوتيز والجلوتاثيون. وبالتالى، فإن قشور المانجو تعتبر من المنتجات الثانوية الرائعة التى يمكن أن تساهم فى التنمية المستدامة للمنتجات الوظيفية وتحسين مستويات سكر الدم والأنسولين لمرضى السكري.

الكلمات الكاشفة: مرض السكري، المانجيفيرين، مقاومة الأنسولين، الإجهاد التأكسدي، الجلوتاثيون، المنتجات الثانوية.

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