Efficacy of The Aqueous Extracts of Guava and Mango Leaves on Diabetic Rats

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Abstract

Diabetes mellitus is a widespread metabolic disorder affecting populations worldwide. Both guava and mango possess significant nutritional value, and their leaves are known for their medicinal properties. The purpose of this study was to evaluate the hypoglycemic potential of aqueous extracts of Guava and Mango leaves either used separately or in a mixture on streptozotocin -induced diabetic rats, also to assess their effects on several biochemical markers associated with diabetes. Thirty male adult rats were divided into five groups, each with six rats as follows: group 1 normal non diabetic rats (negative control); group 2 diabetic untreated rats (positive control); group 3 diabetic treated with guava leaves aqueous extract GLAE) (500 mg/kg b.wt/day); group 4 :diabetic treated with mango MLAE leaves aqueous extract(500 mg/kg b.wt/day); group 5: diabetic treated with mixture of both extracts (500 mg/kg b.wt GLAE+ MLAE). After four weeks of extracts administration, blood samples were taken to assess several biochemical markers. The results of the present study demonstrated a significant increase in blood glucose level, accompanied by a significant decrease in serum insulin level in diabetic untreated rats (positive control group) relative to normal rats. Additionally, there was a marked elevation in the serum levels of urea, creatinine, and uric acid, as well as in the activities of the liver enzymes AST, ALT, and ALP, compared to the normal rats. In contrast, the daily oral administration of GLAE and MLAE, either individually or in combination, for four weeks to diabetic rats resulted in significant reduction in blood glucose levels and significant improvement in serum insulin levels. These changes were associated with improvements in kidney and liver function, as evidenced by the significant reduction in urea, creatinine, and uric acid levels, along with a significant decrease in the serum activities of AST, ALT, and ALP. Therefore, usage of Guava and Mango Leaves may help to enhancement the status in diabetes mellitus

Keywords: Guava leaves, Mango leaves, Diabetes mellitus, Insulin, liver and kidney functions, Rats.

INTRODUCTION

Diabetes is one of the fastest growing global health emergencies of the 21st century. The number of people living with diabetes increases annually, according to the International Diabetes Federation ,589 million people worldwide had diabetes in 2024, and this number is expected to rise to 853 million by 2050 **(IDF, 2025)**. Egypt is ranked among the top ten countries worldwide in terms of diabetes prevalence. The number of individuals affected by the disease in Egypt was 13.2 million in 2024, and it is projected to rise to 24.7 million by the year 2050 **(IDF, 2025)**. Globally, diabetes was responsible for 3.4 million deaths in 2024- 1 every 6 seconds **(IDF, 2025).** By 2030, diabetes will rank as the seventh greatest cause of death worldwide **(WHO, 2016).**

Synthetic hypoglycemic medication currently available on the market are often associated with a range of adverse effects, including gastrointestinal disturbances, weight gain, and hepatic dysfunction. Consequently, there is an urgent need to identify and develop novel therapeutic agents for the prevention and management of diabetes mellitus. Medicinal plants, known for their diverse pharmacological properties and extensive therapeutic potential, have emerged as promising candidates in this regard **(Luo *et al*., 2019).**

Currently, there is increasing interest from the pharmaceutical and nutraceutical industries in plant-based preparations and pure phytochemicals. Notably, the use of plant-derived materials in beverages, food, and medicinal applications primarily based on plant leaves. Among all plant parts, leaves are the largest accumulators of bioactive compounds, particularly secondary metabolites. Several studies have highlighted the phytochemical composition and diverse biological activities of leaf extracts from a wide range of cultivated plant species (**Mannino *et al*., 2020; Mateos-Maces *et al*., 2020)**.

Therefore, our study aimed to evaluate the hypoglycemic potential of aqueous extracts of guava and mango leaves either used separately or in a mixture on streptozotocin -induced diabetic rats, also to assess their effects on several biochemical markers associated with diabetes.

MATERIALS AND METHODS

1. Plant Material: The leaves of Mango (*Mangifera indica*) and guava (*Psidium guajava*) were purchased freshly from Agriculture Research Center, Cairo, Egypt.

2. **Chemicals:** Streptozotocin (STZ) (Batch No.126k1174) was purchased from El-Gomhoriya Pharmaceutical Company, Cairo, Egypt.

3. Experimental animals: Thirty adult male albino rats with body weight ranging from 150 to 200 g were purchased from Farm of experimental animals in Helwan, Egypt. Rats were kept in plastic cages under strict hygienic conditions (22 ± 3ºC, 55 ± 5% humidity and 12-h light: 12-h dark cycle) and fed on the basal diet for one week before start of the experiment for acclimatization. Water was provided *ad libitum* during experimental period (4 weeks).

4. Preparation of plant extracts: Fresh leaves of mango and guava were sorted to remove any dead matter and foreign particles, then thoroughly washed with tap water. After washing, the leaves were cut into small pieces, air-dried at room temperature, and subsequently ground into a fine powder using an electric grinder. The aqueous infusion was prepared according to the method described by **Swanston-Flatt et al. (1990).** Briefly, the powdered plant material (100g) was added to boiling water (1 Liter) and allowed to infuse for 15 minutes. The infusion was then filtered, and the filtrate was freshly used for experimental purposes.

5. Induction of Diabetes: Diabetes was induced by an intraperitoneal injection of freshly prepared STZ at a dose of 45 mg/kg b. dissolved in a citrate buffer (0.1M, pH 4.5) to the overnight fasted rats **(Burcelin et al.,**

1995). After 72 hrs of STZ administration the rats with fasting blood-glucose levels more than 250 mg/dL were considered as diabetic and used for the study according to method of **El-Sawi et al. (2017)**.

6. Experimental design: Thirty rats were divided into five groups (6 rats each).

Group 1: Normal non-diabetic rats (negative control).
Group 2: Diabetic untreated rats (positive control).
Group 3: Diabetic rats orally given guava leaves aqueous extract (GLAE) (500 mg/kg b.wt, once /day) for 4 weeks.
Group 4: Diabetic rats were orally given mango leaves aqueous extract (MLAE) (500 mg/kg b.wt once/day) for 4 weeks.
Group 5: Diabetic rats were orally given a mixture of both GLAE and MLAE (500 mg/kg b.wt. once/day) for 4 weeks.

6- Serum biochemical analysis: Glucose was determined according to the method described by **Asatoor and King (1954).** Serum insulin was determined according to the method described by (**Temple et al., 1992**). Creatinine was determined according to the method described by **Henry (1974).** Serum uric acid concentration was determined according to the method described by **Fossati et al. (1980).** Serum alanine aminotransferase (ALP), Aspartate aminotransferase (AST) and Alkaline Phosphatase (ALP) levels were analyzed enzymatically according to the method described by **Tietz (2006).**

7-Statistical analysis: All data obtained were analyzed using Statistical Package for the Social Sciences (SPSS) for Windows, version 20 **(SPSS Inc., Chicago, IL, USA).** Collected data were presented as mean± standard deviation (SD). Analysis of Variance (ANOVA) test was used for determining the significances among different groups according to **(Armitage and Berry, 1987).** The values were considered to be significantly different when the P value was less than 0.05.

Results

Effect of oral administration of GLAE and MLAE either used separately or in a mixture on serum glucose levels in diabetic rats:

Table (1) illustrates the changes in serum glucose levels in all experimental groups. In diabetic untreated rats (positive control group) there was significant elevation in glucose levels as compared with normal rats (negative control group). However, diabetic rats treated with GLAE and MLAE either individually or in a combination showed significant reduction in blood glucose levels (p<0.05) as compared with diabetic untreated rats (positive control group). The highest reduction in serum glucose levels in diabetic rats was achieved by using mixture of both plant extracts.

Table (1): Effect of oral administration of GLAE and MLAE on serum glucose (mg/dl) in STZ induced diabetic rats.

Groups	Glucose (mg/dl) Mean±SD	Glucose Reduction (%)
Normal rats	88.510±3.12^{d}	
Diabetic untreated rats	250.35±1.75^{a}	
Diabetic rats treated with GLAE	128.50±3.77^{b}	48.67
Diabetic rats treated with MLAE	132.11±3.19^{b}	47.22
Diabetic rats treated with a Mixture of GLAE & MLAE	108.24±1.65^{c}	56.78

Values with different superscript letters within a same column are significantly different at p<0.05, while those with similar or partially similar are not significant.

Effect of oral administration of GLAE and MLAE either used separately or in a mixture on serum insulin levels in diabetic rats:

Results in **Table (2)** showed that the serum insulin level of the diabetic non-treated rats (positive control group) was significantly (p<0.05) lower as compared to normal rats (negative control group).The oral administration of GLAE and MLAE either separately or in

combination to diabetic rats resulted in a significant ($p<0.05$) increase in the serum insulin level compared with positive control group. However, the increase in insulin among treated diabetic rats was significantly lower ($p < 0.05$) than among normal rats (negative control group).

Table (2): Effect of oral administration of GLAE and MLAE on serum insulin (IU/L) in STZ induced diabetic rats.

Groups	Insulin (IU/L) Mean±SD
Normal rats	134.50±2.21[a]
Diabetic untreated rats	77.76±3.17[e]
Diabetic rats treated with GLAE	90.62±2.62[d]
Diabetic rats treated with MLAE	101.28±1.49[c]
Diabetic rats treated with a Mixture of GLAE &MLAE (n=6)	120.26±1.49[b]

Values with different superscript letters within a same column are significantly different at $p<0.05$, while those with similar or partially similar are not significant.

Results of the effect of daily treatment with GLAE and MLAE either separately or in a combination for 4 weeks on serum creatinine, urea and uric acid levels in diabetic rats are presented in **Table (3)**. The results showed a significant decrease ($p<0.05$) in serum creatinine, urea, and uric acid levels in diabetic rats orally given GLAE and MLAE either separately or in combination when compared to the positive control group. Oral administration of mixture of both GLAE and MLAE showed a greater decrease in the serum levels of creatinine, urea & uric than GLAE or MLAE alone.

Table (3): Effect of oral administration of GLAE and MLAE on serum levels of kidney functions (Urea, Creatinine, & Uric acid) in STZ induced diabetic rats.

Groups	Urea (mg/dl) Mean±SD	Creatinine (mg/dl) Mean±SD	Uric acid (mg/dl) Mean±SD
Normal rats	44.36±1.54^{e}	0.45±0.011^{d}	1.01±0.16^{d}
Diabetic untreated rats	94.00±2.16^{a}	1.57±0.017^{a}	2.37±0.15^{a}
Diabetic rats treated with GLAE	67.10±1.12^{c}	0.83±0.013^{b}	1.61±0.15^{bc}
Diabetic rats treated with MLAE	78.21±1.01^{b}	0.85±0.014^{b}	1.82±0.14^{b}
Diabetic rats treated with Mixture of GLAE &MLAE	53.07±1.04^{d}	0.57±0.018^{c}	1.50±0.13^{c}

Values with different superscript letters within a same column are significantly different at $p<0.05$, while those with similar or partially similar are not significant.

Effect of oral administration of GLAE and MLAE either separately or in a mixture on serum levels of liver enzymes (AST, ALT and ALP) in STZ induced diabetic rats.

Table (4) illustrated the effect of GLAE and MLAE on serum levels of liver enzymes, AST, ALT and ALP in STZ-induced diabetic rats. The serum levels of AST, ALT & ALP enzymes were significantly elevated in diabetic non-treated rats (positive control group) compared to the normal rats (negative control group). On the other hand, the oral administration of GLAE and MLAE to diabetic rats significantly decreased ($p<0.05$) the elevated serum levels of AST, ALT & ALP enzymes compared to the positive control group. The results also revealed that the mixture of both GLAE and MLAE showed a greater decrease in the serum levels of AST, ALT, & ALP enzymes than GLAE or MLAE alone in diabetic rats.

Table (4): Effect of oral administration of GLAE and MLAE on serum levels of liver functions (AST, ALT & ALP) in STZ induced diabetic rats

Groups	AST(U/l) Mean ± SD	ALT(U/l) Mean ± SD	ALP(U/l) Mean ± SD
Diabetic untreated rats	148.13±0.64[a]	65.27±1.108[a]	120.19±2.101[a]
Normal rats	89.52±1.47[d]	32.04±0.645[d]	64.93±1.31[d]
Diabetic rats treated with GLAE	117.03±1.08[b]	42.22±0.645[c]	98.22±1.081[b]
Diabetic rats treated with MLAE	120.89±1.47[b]	53.23±0.835[b]	101.42±0.645[b]
Diabetic rats treated with Mixture of GLAE &MLAE	108.61±1.11[c]	34.09±0.958[d]	84.43±1.554[c]

Values with different superscript letters within a same column are significantly different at $p<0.05$, while those with similar or partially similar are not significant

Discussion

In the present study, diabetic untreated rats (positive control group) exhibited a significant increase in serum glucose levels accompanied by a marked decrease in serum insulin levels compared with normal rats (negative control) these findings are in accordance with several previous studies. **Szkudelski (2001)** reported that, hyperglycemia and the reduction in serum insulin levels observed in diabetic rats may result from the destruction of pancreatic β-cells induced by STZ, which impairs insulin production and secretion. Similarly, **Lenzen (2008)** reported that, STZ induces diabetes primarily through the selective destruction of insulin-producing β-cells, rendering them less functional and thereby impairing glucose utilization by peripheral tissues. Moreover, STZ disrupts β-cell function by impairing glucose oxidation and diminishing insulin biosynthesis and secretion **(Nukatsuka et al., 1990).**

The results of the hypoglycemic action of GLAE are in agreement with several previous studies. **Momtaz *et al.,* (2025)** who observed that the aqueous extract of *Psidium guajava* leaves exerts a glucose-lowering effect in alloxan-induced diabetic rats. Guava leaves are rich in flavonoids, especially quercetin, which is considered the principal compound responsible for their antihyperglycemic activity. Flavonoids exert antidiabetic effects either by inhibiting intestinal glucose absorption or by enhancing glucose tolerance. Also, flavonoid compounds present in guava leaves have also been shown to function as insulin secretagogues or insulin mimetics, Furthermore, these bioactive compounds have been found to stimulate glucose uptake in peripheral tissues and regulate enzymatic activity and/or signaling pathways involved in glucose metabolism **(Momtaz *et al.,* 2025)**.

In addition, Luo *et al.* (2019); Gurung *et al.* (2020) reported that guava leaf extract enhances hepatic insulin sensitivity by promoting glycogen synthesis and inhibiting gluconeogenesis. This effect is mediated through modulation of insulin-related signaling pathways that facilitate glucose uptake and metabolism in liver cells.

The antihyperglycemic activity of guava leaf extracts have been attributed to the presence of bioactive flavonoids and phenolic compounds, particularly sinapic acid, which has demonstrated potent antioxidant properties contributing to its ability to reduce blood glucose levels **(Yusuf *et al*., 2022; Jayachandran *et al.,* 2018**). Also, quercetin, a major flavonoid present in the aqueous extract of guava leaves, has been shown to stimulate glucose uptake by hepatocytes and mitigate hyperglycemia in diabetic models. Furthermore, guava leaf extract exerts long-lasting antihyperglycemic effects by modulating the composition of gut microbiota, increasing the abundance of probiotic populations, and thereby improving overall glucose metabolism (**Gurung *et al*., 2020**; **Luambia *et al.,* 2024**).

The antidiabetic effects of *Psidium guajava* leaf extract, could be attributed to the presence of bioactive constituents. Phytochemical screening of the extract revealed the presence of various secondary metabolites, including alkaloids, flavones, tannins, steroidal glycosides, phenols, and coumarins. These compounds, either individually or synergistically, could be responsible for the extract's antidiabetic activity. The extract demonstrated a dose-dependent inhibitory effect on the digestive enzymes α-glucosidase (up to 89.4%) and α-amylase (up to 96.3%). These enzymes play a critical role in carbohydrate digestion, and their inhibition is a well-established therapeutic strategy for managing postprandial hyperglycemia in diabetic patients. Therefore, the ability of the *Psidium guajava* methanolic leaf extract to inhibit α-glucosidase and α-amylase may represent a promising antidiabetic mechanism, likely mediated by its diverse phytochemical profile (**Anand et al., 2013).**

The results of the hypoglycemic action of MLAE in accordance with several previous studies carried out on different mango extracts, **Boas *et al.* (2020)** reported that the observed reduction in plasma glucose levels, enhancement of insulin sensitivity, and elevation in plasma insulin concentrations can largely be attributed to the phenolic compounds present in the ethanolic extract of *Mangifera indica* (EAMI), particularly flavonoids. EAMI had found to contain high levels of phenolic compounds and tannins, and five flavonoids were isolated: kaempferol, fisetin, galangin, chrysin, and luteolin. These phytoconstituents are believed to enhance glucose uptake by insulin-sensitive tissues and suppress hepatic glucose production. **(Boas *et al.*, 2020)**. Also, **Khan *et al.* (2024)** reported that ethanolic extract from *Mangifera indica* leaves demonstrated a significant improvement in fasting blood glucose levels and plasma insulin levels. and suggested that anti-diabetic effects of EEMI are likely the result of synergistic interactions among the bioactive compounds present in the extract. Phytochemical screening of EEMI revealed the presence of alkaloids, tannins, saponins, steroids, and flavonoids.

The antihyperglycemic effects *Mangifera indica* leaf extract may be attributed to various bioactive phytochemicals especially, mangiferin, iriflophenone 3-C-β-D-glucoside, quercetin, gallic acid, and other polyphenolic constituent. Mangiferin has demonstrated antidiabetic activity through enhancement of insulin sensitivity and inhibition of α-glucosidase. Iriflophenone 3-C-β-D-glucoside has also been reported to possess hypoglycemic effects. Furthermore, gallic acid was shown to upregulate GLUT4 expression, thereby promoting glucose uptake. Quercetin, another prominent flavonoid, contributes to glycemic control by protecting pancreatic tissue and enhancing endogenous antioxidant enzyme activity. Phenolic compounds, in general, have been implicated in reducing blood glucose levels by inhibiting α-glucosidase and pancreatic lipase enzymes **(Saleem *et al*., 2019**).

The suppression of carbohydrate-hydrolyzing enzymes is recognized as one of the primary mechanisms through which phenolic compounds exert their anti-diabetic properties **(Ojo *et al.*, 2018)**. In the same cell line **Bhuvaneshwari *et al*. (2014)** demonstrated that the tender mango leaf extract (500 mg/kg) demonstrated potent α-amylase inhibition while the mature leaf extract (500 mg/kg) showed effective α-glucosidase. suggested that bioactive compounds present in *M. indica* leaves may contribute to reducing the risk and progression of diabetes mellitus.

The combination between GLAE and MLAE in the present study caused significant hypoglycemic effect this in accordance with **Rawi *et al*., (2011)** who demonstrated that the combination between *M. indica* and *P. guajava* water extract caused a highly significant decrease in the blood glucose level, and attributed the hypoglycemic effect of tested mixture extracts due to the presence of glycosides, alkaloids, saponins, tannins, resins and triterpenes.

In the present study, the serumlevels of creatinine, urea and uric acid were significantly increased in diabetic rats compared to normal

rats (negative control group) which strongly indicated the impairment of kidney function in diabetic rats.

Diabetic hyperglycemia leads to elevated plasma levels of urea, uric acid, and creatinine, which are recognized as significant biomarkers of renal dysfunction and indicative of a reduced glomerular filtration rate **(Rajaram, 2013).** Also, **Al-Musa and Al-Hashem (201**4) found morphological alterations and elevated levels of urea and creatinine in the kidneys of diabetic animals. They attributed these changes to extensive oxidative damage in renal tissues. oxidative stress is widely recognized as a key pathogenic factor in the development of diabetic nephropathy **(Kumawat et al., 2013)**. Chronic hyperglycemia is believed to trigger oxidative stress, which contributes to the onset of proteinuria, thickening of the glomerular basement membrane, mesangial expansion, reduced filtration efficiency, and nephromegaly, ultimately leading to glomerular sclerosis **(Schena and Gesualdo 2005; Hans et al., 2002).**

In the present study treatment with GLAE resulted in improved kidney functions, by reducing levels of creatinine, urea and uric acid compared with diabetic untreated rats (positive control group). This aligns with **Chu *et al.* (2022)** who reported that guava leaf aqueous extract treated mice demonstrated a significant reduction in blood creatinine levels ($p < 0.05$), with a non-significant downward trend observed in blood urea levels. Similarly, **Radwan *et al.* (2018)** reported that administration of guava leaf extract in diabetic rats resulted in improved renal function, evidenced by reduced creatinine, urea and uric acid levels. These improvements may be attributed to the ability of guava leaf extract to effectively regulate serum glucose levels. Additionally, the antioxidant properties of guava leaf extract may play a complementary role in enhancing renal functions. **Belemtougri *et al.*, (2006)** demonstrated that a hydroalcoholic extract of *Psidium guajava* leaves significantly reduced serum creatinine levels and prevented renal damage. Furthermore, *Psidium guajava* leaves and their flavonoid

constituent rutin have been shown to protect renal tissues from nephrotoxicity induced by guajanoic acid and hexachlorobutadiene **(Ryu et al., 2012).**

The present findings demonstrate that oral administration of MLAE to diabetic rats led to a significant decrease in serum creatinine, urea, and uric acid levels compared to diabetic untreated rats. These reduction strongly indicate improvement in kidney function of diabetic rats. Similar observations by **Maghfuri *et al.,* (2022)** who reported that treatment with *Mangifera indica* leaf (MIL) extract in diabetic rats effectively reduced serum creatinine and urea concentrations, restoring them to near-normal levels. This improvement in renal function may be attributed to the antioxidant properties of the extract. Also, **Mudawi *et al*., (2013)** demonstrated that *Mangifera indica* leaf extract effectively mitigated diabetic complications in the treated groups compared to the untreated diabetic controls. Notably, a reduction in urinary albumin levels was observed, indicating improved kidney function. Mangiferin, a major bioactive compound in *Mangifera indica*, exhibits aldose reductase inhibitory activity and holds significant therapeutic promise for managing diabetic complications, particularly diabetic nephropathy. Consistently, **Sahu *et al.,* (2019)** reported that mangiferin, a major bioactive compound in mango leaves, exerts renoprotective effects through its anti-apoptotic, anti-inflammatory, and antioxidant mechanisms. Supporting this**, Li *et al.,* (2020)** demonstrated that mangiferin significantly attenuated the progression of diabetic nephropathy and improved renal functions.

In diabetes, liver damage may occur during the later stages of the disease due to disruptions in lipid metabolism, as well as increased gluconeogenesis and ketogenesis **(Virdi et al., 2003).** The liver is among the primary organs affected by oxidative stress induced by hyperglycemia, which can lead to hepatic tissue damage. hyperglycemia enhances the production of mitochondrial reactive oxygen species (ROS), which is considered a critical factor in the progression of diabetes-related

complications (**Palsamy *et al.,* 2010)**. The elevated activities of serum aminotransferases, specifically AST and ALT are common indicators of liver dysfunction and more frequently observed in individuals with diabetes compared to the general population **(Arkkila et al., 2001; Bennett and Pegg, 1981).** The increase in aminotransferase levels may be attributed to hepatic cellular damage caused by STZ-induced diabetes **(Najla et al., 2012; Zafar et al., 2009; Salih et al., 2014).**

In the present study aqueous extract of guava leaves (GLAE) (500 mg/kg b.wt.) resulted in significant decrease in the elevated levels of AST, ALT and ALP enzymes in diabetic rats. These findings similar to previous results recorded by **Radwan *et al* (2018**) who reported that, daily administration of guava leaf aqueous extract to diabetic rats effectively improve the levels of AST, ALT, and ALP. Also, **Taju *et al.,* (2011)** revealed that administration of 500 mg/kg of aqueous leaf extract significantly reduced the elevated levels of AST, ALP, ALT, and restored total protein levels. In addition, **Chen *et al.* (2011)** revealed that the administration of guava leaf extracts demonstrated hepatoprotective potential against ethanol-induced hepatotoxicity. Among the different extracts tested, the hot water extract provided the greatest protection against ethanol-induced hepatic damage.

Oral administration of *Psidium guajava* aqueous extract at a dose of 250 mg/kg resulted in a significant reduction in the elevated activities of AST and ALT (**Rawi et al., 2011).** These could be evidence for the extract's potent hepatoprotective and antioxidant properties. These effects are likely due to the presence of bioactive constituents, primarily flavonoids, caryophyllene oxide, caryophyllene, and various tannins. Given that antioxidants are known to mitigate chemically induced hepatic injury, these compounds may play a critical role in protecting liver function (**Chen and Yen, 2007**). Furthermore, Guava leaf polysaccharides (GLP) possessed strong free radical scavenging activity *in vitro*. In experiments using STZ-induced diabetic mice showed that GLP not only exerted notable anti-diabetic effects but also alleviated

pathological damage in key organs such as the liver (**Luo et al., 2019**). Similar observations reported by **Uboh *et al.*, (2010)** revealed that the potential hepatoprotective effects of the *P. guajava* leaves extract may be due to its bioactive constituents, particularly flavonoids, known for their potent antioxidant effects. which effectively inhibits the peroxidation of polyunsaturated fatty acids in cellular membranes. Furthermore, the presence of saponins, which are also found in the extract, may contribute to its beneficial effects by exerting hypocholesterolemic activity, potentially reducing the metabolic load on the liver.

In the present study the oral administration of MLAE (500 mg/kg) resulted in significant decrease in the elevated levels of AST, ALT and ALP in diabetic rats. Similar findings were reported by Maghfuri et al. (2022), who observed a significant reduction in the activities of ALT, AST, and ALP in diabetic rats following treatment with mango leaf aqueous extract (MIL). This reduction indicates the potential hepatoprotective effect of MIL, which attributed to the antioxidant and anti-inflammatory properties of the bioactive compounds present in the extract.

Phytochemical screening of *Mangifera indica* have confirmed the presence of key phytoconstituents such as mangiferin, quercetin, and isoquercetin. These compounds are believed to contribute significantly to the plant's diverse biological effects **(Thomas *et al*., 2025).** Mangiferin, a naturally occurring C-glycosylated xanthone, is a pharmacologically active flavonoid predominantly derived from the leaves of the mango tree (*Mangifera indica* L.). This compound exhibits a broad spectrum of therapeutic and preventive properties, including antimicrobial, anti-inflammatory and antioxidant activities **(Aswal *et al.,* 2020).**

Several studies have demonstrated the hepatoprotective effect of **mango leaf extracts, Gazwi and Mahmoud (2019)** indicated that treatment with *Mangifera indica* (*M. indica*) leaf aqueous extract effectively mitigated the hepatic dysfunction and normalized the elevated

serum biomarkers associated with chronic CCl_4-induced hepatotoxicity. These biochemical findings were corroborated by histopathological analysis, which revealed improved liver architecture in treated groups. Collectively, the study demonstrates that M. indica leaf aqueous extract possesses hepatoprotective potential against CCl_4-induced liver injury. Also, **Ramírez *et al.* (2018)** investigated that mango leaf tea exhibited a hepatoprotective effect by decreasing oxidative stress and steatosis, and improving the lipid metabolism which may attributed the presence of mangiferin and other bioactive compounds in mango leaves.

Mangifera indica leaf extract at a dose of 50 mg/kg demonstrated superior hepatoprotective activity, due to its potent free radical scavenging capacity **Karuppanan *et al.* (2014**). Another study by **Kumar *et al*., (2021)** found that administration of *Mangifera indica* leaves (MILs) tea to rats fed a high-fat diet exerts hepatoprotective effects by promoting anti-inflammatory and lipid-regulatory pathways, particularly through PPAR-α activation and NF-κB inhibition. These molecular effects were accompanied by a notable reduction in hepatic fat droplet accumulation and an overall improvement in hepatic steatosis.

The combination between GLAE and MLAE in the present study caused significant reduction in the elevated levels of liver enzymes (AST, ALT and ALP) in diabetic rats. This in accordance with **Rawi *et al.* (2011)** who found that, the activities of ALT, AST, and ALP in streptozotocin-induced diabetic rats, were significantly elevated. However, these enzyme activities were notably improved following treatment of tested plant extracts.

In conclusion, the present study demonstrated that oral administration of aqueous extract of Guava and mango leaves either separately or in a combination exhibited significant hypoglycemic effects associated with improvement in kidney and liver functions in diabetic rats as hyperglycemia-related complications.

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فعالية المستخلص المائي لأوراق الجوافة والمانجو على الفئران المصابة بالسكري

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الملخص العربي

داء السكري هو اضطراب أيضي واسع الانتشار يؤثر على السكان في جميع أنحاء العالم، يتمتع كل من الجوافة والمانجو بقيمة غذائية كبيرة، وأوراقهما معروفة بخصائصها الطبية. الغرض من هذه الدراسة هو تقييم إمكانية خفض نسبة السكر في الدم للمستخلصات المائية لأوراق الجوافة والمانجو إما المستخدمة بشكل منفصل أو في خليط على الفئران المصابة بمرض السكري الناجم عن الاستربتوزوتوسين وتقييم آثارها على العديد من العلامات الكيميائية الحيوية المرتبطة بمرض السكري. تم تقسيم ثلاثين فأرًا بالغًا من الذكور إلى خمس مجموعات، كل منها بستة فئران، وتم تقييمها على النحو التالي: المجموعة ١ فئران طبيعية غير مصابة بالسكري (مجموعة ضابطة سلبية)؛ المجموعة ٢ فئران مصابة بالسكري غير معالجة (مجموعة ضابطة إيجابية)؛ المجموعة ٣ مصابة بالسكري عولجت بمستخلص مائي لأوراق الجوافة 500) (GLAX مجم / كجم من وزن الجسم / يوم)؛ المجموعة ٤: مصابة بالسكري عولجت بمستخلص مائي لأوراق المانجو (٥٠٠ مجم / كجم من وزن الجسم / يوم)؛ المجموعة الخامسة: مرضى السكري وعولجت بمزيج من مستخلصات كلا النباتين (٥٠٠ ملجم/كجم من وزن الجسم 500 + GLAE ملغم/كغم من وزن الجسم/يوم (MLAE بعد أربعة أسابيع من إعطاء المستخلصات، تم أخذ عينات دم لتقييم العديد من العلامات الكيميائية الحيوية. أظهرت نتائج الدراسة الحالية زيادة كبيرة في مستويات الجلوكوز في الدم، مصحوبة بانخفاض كبير في مستويات الأنسولين في المصل في الفئران المصابة بالسكري غير المعالجة (مجموعة الضابطة الإيجابية). بالإضافة إلى ذلك، كان هناك ارتفاع ملحوظ في مستويات اليوريا والكرياتينين وحمض اليوريك في المصل، وكذلك في أنشطة إنزيمات الكبد AST و ALTوALP، مقارنة بالفئران العادية (مجموعة الضابطة السلبية). في المقابل، أدى الإعطاء الفموي اليومي للمستخلصات المائية لأوراق الجوافة والمانجو – إما بشكل

فردي أو مجتمعة – لمدة أربعة أسابيع في الفئران المصابة بالسكري إلى انخفاض كبير في مستويات الجلوكوز في الدم وتحسن كبير في مستويات الأنسولين في المصل. ارتبطت هذه التغيرات بتحسن في وظائف الكلى والكبد، كما يتضح من الانخفاضات الكبيرة في مستويات اليوريا والكرياتينين وحمض اليوريك، إلى جانب انخفاض كبير في نشاط إنزيمات AST و ALT و ALPفي مصل الدم.

الكلمات المفتاحية: أوراق الجوافة، أوراق المانجو، داء السكري، ستربتوزوتوسين، مستويات الجلوكوز، مستويات الأنسولين، إنزيمات الكبد، وظائف الكلى، الفئران.