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Effect of Aqueous Extract Mangifera Indica Leaves, as Functional Foods.

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Abstract: Traditional Medicines derived from medicinal plants are used by about 60% of the world's population. This search focuses on Mangifera Indica as Herbal drugs and plant using in the treatment of diabetes, especially in Egypt. Diabetes is an important human ailment afflicting many from various walks of life in different countries. In Egypt it is proving to be a major health problem, especially in the urban areas. Though there are various approaches to reduce the ill effects of diabetes and its secondary complications, herbal formulations as functional foods are preferred due to lesser side effects and low cost. One of the etiologic factors implicated in the development of diabetes and its complications is the damage induced by free radicals and hence an antidiabetic compound with antioxidant properties would be more beneficial. Therefore information on antioxidant effects of these medicinal plants is also included and investigated. Diabetes is a chronic metabolic disorder characterized by altered carbohydrate, fat and protein metabolism, and an increased risk of multiple complications. Effect of aqueous mango leaves extract at doses of 30, 50 and 70 mg on Alloxan-induced diabetic rats were studied, Sprauge-Dawley albino rats (35 male) , weighing 150 to 160 g were divided into 5 groups and administered aqueous mango leaves extract daily for 42 days. Blood samples were taken from each rat and tested for blood glucose, total cholesterol, (LDL), (VLDL), (HDL), triglycerides, urea, uric acid and creatinine levels, serum total protein, albumin, globulin and liver enzymes activities, Also, phytochemical. Screening of (MANGIFERA INDICA) Mango leaves including total phenols, flavonoides, tannins and saponins contents were determined. In Streptozotocin - induced diabetic rats, blood glucose, triglycerides, total cholesterol, LDL, VLDL, urea, uric acid, creatinine and liver enzymes activities (AST and ALT) were significantly increased, while HDL, serum total protein, albumin and globulin were significantly decreased compared with the negative control rats. Treating diabetic rats with 30, 50 and 70 mg aqueous mango leaves extract caused a significant improvement in these biochemical measures and the best results were achieved by using 70 mg mango leaves extract followed by 50 and 30 mg aqueous extract, respectively. It could be concluded from these results that, aqueous mango leaves extract which was found to be rich in total phenols and total flavonoides which considered powerful antioxidants should be used in manufacture processes of the natural products as functional foods or as a dietary supplement with anti-diabetic activity as hypoglycemic effect. It is hoped that this study would lead to the establishment of some compounds that could be used to formulate new and more potent natural drugs of natural origin. Studies are in progress to further evaluate the mechanisms of action of *M. indica* extracts on some parameters and variables associated with human diseases.

Key words: Streptozotocin-induced diabetic rats, Mangifera leaves extract; Blood glucose; Total flavonoides; hypoglycemic effect.

INTRODUCTION

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter[1]. A number of medicinal plants, traditionally used for over 1000 years named rasayana are present in herbal preparations of Indian traditional health care systems[2,3]. In Indian systems of medicine most practitioners formulate and dispense their own recipes [4]. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in

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India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world[4].

Diabetes mellitus is a metabolic disease characterized by hyperglycemia caused by defective insulin secretion and / or action, resulting in long term multi-organ complications[5]. Chronic hyperglycemia causes damage to the eyes, heart, kidneys, nerves, and blood vessels[6]. The current review focuses on herbal drug preparations and plants used in the treatment of diabetes mellitus, a major crippling disease in the world leading to huge economic losses.

On the other hand, high glucose level was found to increase the production of free radicals, as determined by cell damage markers. Increased oxidative stress has been implicates in the pathogenesis of diabetic complications and reduced levels of antioxidants are found in blood and tissue in both human and experiments diabetes[7-9].

The leaves of Mangifera Indica plant are used as an antidiabetic agent in Nigerian folk medicine, although when aqueous extract given orally did not alter blood glucose level in either normoglycemic or Streptozotocin induced diabetic rats. However, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The results indicate that aqueous extract of *Mangifera indica* possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose[10].

Though different types of oral hypoglycemic agents are available along with insulin for the treatment of diabetes there is an increased demand by patients to use the natural products with anti-diabetic activity[11]. One such plant expected to have anti-diabetic activity is Mangifera Indica (mango plant).

Several studies in animal models with diabetes have shown that both short and long term hypoglycemic effects of mango leaves and other sources were proven, its mechanism for lowering glucose levels is unknown, and however, some studies suggest facilitation of glucose uptake peripherally[12,13]. and Perez *et al.,* [14], definitely, Potential hypolipidemic effects in diabetic rats have also been shown with mango leaves extract and other natural sources[15,16].

Mangiferin has antihepertic activity with inhibitory effect on the early stages of reproduction of Herpes virus. Mangiferin has an immunostimulating effect on both cellular and hormonal immunity link. Mangiferin is a normal metabolite also to be found in mango leaves. In the Republic of Vietnam a technology has been elaborated, and subsequently improved, for obtaining Mangiferin from mango leaves Pharmacokinetics of Mangiferin in the blood after oral administration: A small amount of free Mangiferin is observed in the blood plasma after single use of Mangiferin at dose range between 50 mg/kg and 1000 mg/kg. Plasma level of Mangiferin is not over 0.05 µg/ml over 24-hour follow-up. Mangiferin metabolite is not detected in the blood within 24 hours after oral administration. Excretion of free Mangiferin in the urine is not over 0.1% within 24 hours[17].

The administration of aqueous extract obtained from a decoction of mango leaves to Streptozotocin induced diabetic rate led to a decline in the levels of total cholesterol and a decrease in the total cholesterol/HDL-cholesterol ratio with respect to the control group, together with a reduction of the hyperglycemia[18].

The safety of many natural sources has been investigated in several studies, with no sign of toxicity [19], and Malomo, S.O.[20].A number of data showed that the presence of phenolics in foods and natural sources are particularly important for their oxidative stability and anti-microbial protection. Phenolics possess a wide spectrum of biochemical activities such as antioxidant, ant-mutagenic, ant-carcinogenic, as well as ability to modify gene expression[21]. Phenols, especially those with multiple phenolics groups, are better antioxidants than the well-known antioxidant vitamins[22].

The antioxidant capacities of the extracts prepared from mango leaves or fig leaves , as natural sources are consistent with total flavonoides and phenolic contents[23,24]. The aqueous extract of mango stem bark and natural sources (fig leaves) showed in presence of galic, tannins, saponins, reducing sugars and flavones aglycones. It was concluded that the extract contains important constituents for pharmacological activities [25,26]. Recoveries above 85% were obtained for chlorogenic acid, rutin and psoralen from leaves extract or natural sources by using the sea sand extraction method[27].

The aim of this study is to examine and understand, the effect of aqueous extract from mango leaves in various doses (30 mg. 50 mg and 70 mg) on serum glucose, lipid profiles, and liver and kidney functions in induced diabetic rats. Also, the photo chemicals screening including, total phenols, flavonoides. Tannins and saponins were determined in the aqueous mango leaves extract, and what the formula, and model which by we can use of mango leaves as neutracetical or therapeutic form.

MATERIALS AND METHODS

Materials: mango leaves (Mangifera Indica.) were collected from the fields surrounding the Cairo-Alexandria desert road ,special farms in El-Behaira

governorate and carefully washed with tap water and left to dry in the dark at room temperature. The air-dried leaves were converted to powder form using an electric machine. The air-dried powdered leaves (100g) were macerated for 24 hr. with distilled water (1 L), and then filtered to obtain the water extract. The extract was allowed to dry under vacuum using rotary evaporator and the residue was stored at-20°C until used. The residue was dissolved in adequate water to obtain 30, 50 and 70 mg/ml as concentration.

Streptozotocin (STZ): was obtained from Sigma chemical company and used as a diabetogenic agent.

Animals and Experimental Diets: Thirty five male Sprague-Dawley albino rats weighing 150 to 160 g were purchased from the Egyptian Organization for Biological Products and Vaccines, Ministry of health, Giza, Egypt. All rats were fed on basal diet for one week (adaptation period). The basal diet consisted of casein (10%), cellulose (5%) salt mixture (4%), vitamin mixture (1%), corn oil (10%) and corn starch (70%) according to[28]. After the adaptation period, diabetes was induced by intraperitoneally injection of 150 mg/kg body weight of Streptozotocin dissolved in 0.9% w/v of NaCl according to the method described by[29]. Blood samples were collected after 48 hr. of injection and glucose levels were determined. Rats with blood glucose level higher than 250 mg/dl were considered to be diabetic. Five groups of rats (7 rats each) were studied according to the following scheme for 42 days: (1) negative control (non diabetic rats), (2) positive control (untreated diabetic rats), (3) diabetic rats orally dosed with 30 mg mango leaves extract, (4) diabetic rats orally dosed with 50 mg mango leaves extract and (5) diabetic rats orally dosed with 70 mg mango leaves extract. The aqueous extract of mango leaves was administered for each rate once daily using a stomach tube. Blood samples were collected from orbital plexus venous into centrifuge tubes and the serum was separated and stored at 20° C for analysis.

Biochemical Analysis: Serum glucose levels were determined according to the method described by Trinder[30]. Serum total cholesterol, (high- density lipoprotein cholesterol and low-density lipoprotein were determined according to the methods of Roeschlua *et al*.,[31]; Assmann[32], Hatch and Less[33], and Uwajima *et al*.,[34], respectively. Asparate amino transferase (AST) and alanine amino transferase (ALT) activities were calorimetrically determined according to the method of Bergmeyer and Harder[35]. Serum urea was measured by the method of Wybenca *et al*., [36]. Serum creatinine was estimated by the method of Tomas[37]. Uric acid was determined according to the method described by Fossa *et al*.,[38] using spectrophotometer. Serum total protein content was estimated by the method of Lowery *et al*.,[39] using bovine serum albumin as standard. Albumin was determined by an enzyme-linked immunosorbent assay as described by Borcea *et al*.,[40]. Globulin was calculated by subtracting albumin from serum total protein content.

Phytochemical Analysis: The total phenolics content was determined by using the Folin-Ciocalteu assay as described by Vinson *et al*.,[41]. Total phenolics content was expressed as Gallic acid equivalents. Total flavonoides content was determined by using the aluminum chloride method mentioned by Harbourne JB [42]. Tannins were determined by Folin Denis Spectrometric method as described by Pearson[43]. Saponins were measured according to Evans[44].

Statistical Analysis: The standard analysis of variance procedure in a completely randomized design was applied for the present data according to Gomez and Gomes[45] and Fisher, R.A.,[46]. Least significant difference (LSD) and Duncan's test were done to compare a pair of group means. The level of statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

Effect of aqueous mango leaves extract on body weight and blood glucose levels in diabetic rats are shown in Table (1). Streptozotocin -induced diabetic rats gained on average less body weight than the negative control rats over the whole period of the study. Final body weight of the negative control rats was significantly higher than initial body weight and all the diabetic groups. The reduction in body weight for the three doses of mango leaves extract was significantly lower than the control rats. Reduction in body weight due to administration of 50 and 70 mg mango leaves extract was no significantly different. These results are in agreement with the results mentioned by Ichiki H, *et al*.,[47]. This found a significant decrease in body weights of the rats administered aqueous ethanol extracts of mango stem bark compared with control group.

From Table (1), blood glucose levels increasing by 1.8 folds in diabetic rats compared with the negative control rats. The significant increase in the levels of blood glucose in Streptozotocin –induced diabetic rats could be due to it is a beta cytotoxic induces chemical diabetes through damaging insulin-secreting cell[48]. At the end of the experiment, blood glucose levels in diabetic rats dosed with 30, 50 and 70 mg aqueous mango leaves extract decreased significantly than those of the diabetic control rats. The decrease in blood

glucose levels as a result of treatments was 31.20%. 37.78% and 43.29% for 30, 50 and 70 mg aqueous mango leaves extract, respectively. The dose of 70mg mango leaves extract is the best for controlling blood glucose level which was not significantly different than the negative control rats. In this respect,[49]. found that the bark and roots extracts of mango significantly lowered the blood sugar level of hyperglycemic rats. Also, Miura T *et al*.,[50] and Mangola, E.N.,[51] observed that aqueous extract from mango leaves showed a clear hypoglycemic effect in diabetic rats. Also may be mediated through stimulation of insulin release resembling the oral hypoglycemic drugs or peripheral glucose utilization[52]. This may be due to the presence of some hypoglycemic principles in mango leaves extract which were similar to insulin or oral hypoglycemic drugs.

Table (2 –A, B) represents the effect of aqueous mango leaves extract on serum triglycerides level and lipid profiles in diabetic rats. Diabetes results in a significant increase in triglycerides level compared with the non diabetic rats. Treating diabetic rats with 30, 50 and 70 mg aqueous mango leaves extract showed a significant reduction in serum triglycerides level compared with the control rats[53]. Mango leaves extract (70 mg/ml) was not significantly different when compared with the negative control rats for triglycerides levels. Serum using 70 mg fig leaves extract. From data in Table (2-B), it could be observed that total cholesterol, LDL-cholesterol and VLDL-cholesterol levels increased significantly in diabetic rats compared with the negative control rats as a results of diabetes[54]. When diabetic rats administered with 30, 50 and 70 mg mango leaves extract the levels of lipid profiles were significantly reduced compared with the positive control rats. The highest reduction was achieved by using 70 g aqueous mango leaves extract followed by 50 mg and 30 mg mango leaves extract, respectively, for the three lipid profiles. Diabetes caused a significant decrease in HDL-cholesterol level when compared with the negative control rats. Treating diabetic rats with 30, 50 and 70 mg aqueous mango leaves extract caused a significant increase in the levels of HLD-cholesterol compared with the untreated diabetic rats[55]. The highest increase in HDL-cholesterol level was achieved by using 50 and 70 mg aqueous mango leaves extract which was not significantly different from each other.

H o L[56], and Moharib, S.A.,[57] reported that administration of aqueous extract of mango leaves results in decreased plasma triacylglycerol and butyrate levels in Streptozotocin treated rats. Seth S.D., Sharma B[4] found significant decrease triglycerides levels after the intraperitoneally injection of aqueous extract of mango leaves in hypertriglyceridemic rats. While the plasma totals cholesterol levels showed no significant difference in relation to baseline levels. These results suggest the presence of some compounds in the aqueous mango leaves extract that influence lipid catabolism. In another study reported by Garcia D *et al*.,[25], and Edwin, E.; *et al*.[58]. Treatment with water extract of the bark of mango plant and Ficus bengalensis linn aerial roots and barks decreased the serum cholesterol level by 59% triacylglycerol by 54% an LDL+VLDL- cholesterol by 60% compared with control rats.

Data presented in Table (3) show the effect of aqueous mango leaves extract on kidney functions in diabetic rats. Serum urea, uric acid and creatinine levels (mg/dl) which were the bio-chemical parameters that are related to kidney functions increased significantly in diabetic control rats compared with the negative control rats as results of diabetes. This may be due to the hyperglycemia which caused damage to kidneys[6]. Treating diabetic rats with aqueous mango leaves extract caused a significant reduction in serum urea. Uric acid and creatinine levels compared with diabetic control rats. The highest reduction was achieved by using 70 mg aqueous mango leaves extract followed by 50 mg and 30 mg mango leaves extract respectively.

The significant increase in serum urea, uric acid and creatinine levels suggests renal malfunction. Creatinine levels are indicators of renal functions, with increased levels appearing in the event of significant impairment[59,60]. There is considerable evidence that increased oxidative stress may participate in the pathogenesis of diabetic complications, including nephropathy[61]. This shows that with significant increase in the levels of kidney markers, about 75% of the nephrone might have been damaged[8,62]. From the above mentioned data, it could be concluded that, all tested diabetic groups which were administered aqueous mango leaves extract with different doses (30mg, 50 mg and 70 mg) improved their renal functions.

Table (4) shows the effect of aqueous mango leaves extract on liver functions in diabetic rats. Diabetes resulted in a significant increase in liver enzymes aspartate amino transferase (AST) and alanine amino transferase (ALT) activities compared with the negative control rats as a result of diabetes and oxidative stress which reduced liver functions. Significant increases of AST and ALT as shown in the results suggest possible necrotic injury of the liver or cholestasis with hepatocellular necrosis[63]. Liver enzymes activities were decreased to the normal levels found in the negative control rats after treatment with 30, 50 and 70 mg aqueous mango leaves extract.

Table 1: Effect of aqueous mango leaves extract on body weight and blood glucose levels in diabetic rats:

Time Groups	Body weight (gm)		Blood glucose levels (mg/dl)	
	Initial	Final	point of start	At the end
Negative control	159.33 ^{A}	167.55 ^{B}	138.39 ^{D}	141.33
Positive control	157.55 ^{A}	134.33	254.26	258.60
mango leaves extract (30 mg)	156.67 ^{A}	124.67 ^{D}	256.19 ^{A}	174.58 ^{B}
mango leaves extract (50 mg)	159.00 ^{A}	121.33 ^{E}	256.33 ^{A}	161.11 ^{C}
mango leaves extract (70 mg)	161.33 ^{A}	117.55 ^{E}	255.49 ^{A}	145.33 ^{D}
L.S.D		4.93		15.34

Table 2-A: Effect of aqueous mango leaves extract on serum triglycerides level and lipid profiles in diabetic rats (mg/dl):

Group Time	Triglycerides levels		Total cholesterol		HLD-cholesterol	
	point of start	End	point of start	End	point of start	End
Negative control	62.34 ^{A}	63.38^{A}	81.53^{A}	83.67	37.01^{A}	37.25^{A}
Positive control	109.06^{B}	125.79^{B}	99.04^{B}	100.56^{B}	51.95^{B}	50.85^{B}
mango leaves extract (30 mg)	113.56^{B}	86.45^{C}	102.88^{B}	93.91^{C}	54.40^{B}	42.98^{C}
mango leaves extract (50mg)	112.74^{B}	83.94A^{C}	101.74^{B}	88.56^{D}	54.32^{B}	35.33^{A}
mango leaves extract (70 mg)	110.48^{B}	68.61^{A}	100.96^{B}	84.59^{A}	52.93^{B}	32.94^{A}
L.S. D.	17.17		3.92		5.64	

Table 2-B: Effect of aqueous mango leaves extract on serum triglycerides level and lipid profiles in diabetic rats (mg/dl):

Group Time	LDL-cholesterol		VLDL-cholesterol	
	point of start	End	point of start	End
Negative control	12.47^{A}	32.05^{A}	33.35^{A}	13.07^{A}
Positive control	21.91^{B}	25.18^{B}	24.55^{B}	25.16^{C}
mango leaves extract (30 mg)	22.71^{B}	25.77^{B}	33.63^{AC}	27.29^{D}
mango leaves extract (50mg)	22.55^{B}	24.87^{B}	36.44^{D}	16.79^{D}
mango leaves extract (70 mg)	22.09^{bB}	25.93^{B}	37.93^{D}	13.72^{A}
L.S. D.	0.93		2.36	

Table 3: Effects of aqueous mango leaves extract on kidney functions in diabetic rats (mg/dl):

Groups	Urea (mg/dl)		Uric acid (mg/dl)		Creatinine (mg/dl)	
	point of start	End	point of start	End	point of start	End
Negative control	81.13A	82.40A	1.03A	1.13A	1.11A	1.13A
Positive control	92.52B	93.59B	2.55B	2.59B	2.31B	2.34B
mango leaves extract (30 mg)	94.53B	89.45C	2.57B	1.99C	2.38B	1.70A
mango leaves extract (50 mg)	91.87B	76.38D	2.55B	1.97C	2.58B	1.63A
mango leaves extract (70 mg)	94.32B	74.56D	2.57B	1.87C	2.32B	1.58A
L.S.D.	3.28		0.39		0.58	

From Table (4), it could be observed that, diabetes caused a significant decrease in total protein, albumin and globulin levels (g/dl) in serum of diabetic rats. Treating diabetic rats with aqueous mango leaves extract caused significant increase in total protein and albumin levels compared with untreated diabetic rats. Measurement of the activities of various enzymes and non-enzymatic indices in tissues and body fluids play a significant and well-known aid in disease investigation and diagnosis. Tissue damage is usually associated with the release of enzymes to the affected organ or tissue into circulation[64]. The significant decrease in total protein and albumin with diabetes are indication of compromised liver excretory function and impairment of the liver function, which improved by treating with aqueous mango leaves extract used in this study Martinez G *et al*.,[65], Rashad, M.M *et al*.,[66] and Hassan, S.W. *et al*.,[67]. found that, serum total protein, AST and ALT levels were improved by feeding lambs on dietary inclusion of mango leaves.

Table (5) represents the phytochemical constituents which found in aqueous extract of mango leaves. Mango leaves extract (70 mg) contained higher contents of total phenols and flavonoides than the other doses which were found to be 9.15 ± 0.08 and 0.68 ± 0.05 mg/g extract for total phenols and total flavonoides, respectively. Tannins and saponins were detected in aqueous mango leaves extract with higher contents found in 70 mg leaves extract from these data; it could be observed that mango leaves are rich in total phenols and flavonoides. The values of tannins and saponins found in leaves extract are within the acceptable limits.

Ethanol fractions of plant materials usually extract tannins, polyphenols, flavonoides, terpenes, alkaloids and sterols if they are present the fraction of mango leaves used in the study of Irene and Ukweni,[68] and Rimi, S. *et al*.,[69] seen to be rich in alkaloids, flavonoides and tannins, but not saponins. These suggest that the medicinal properties attributed to mango leaves could be based on the antioxidant and antimicrobial effects of these phytochemical[70].

Phenolics compounds can play an important role in preventing body cells from injuries by hydrogen peroxide, preventing cells and the organs of man from damage by lipid peroxides and absorbing and neutralizing free radicals[64]. It has been reported that free radical scavenging and antioxidant activity of many medicinal plants are responsible for their therapeutic effect against cancer, diabetes, tissue inflammatory and cardiovascular disease[71].

Our findings were in accordance with the results mentioned by Buniyamin *et al*.,[72], Allam, Sahar O, *et al*.,[73] and Serraclara, A. *et al*.[74], and Nimenibo-Uadia, R.[75]. who found that the aqueous extract of mango leaves and fig leaves showed the presence of flavonoides, saponins and tannins, with no traces of alkaloids or anthraquinones. It was found that high total phenols content increases antioxidant activity and there was a linear correlation between phenolics content and antioxidant activity in mango leaves extract [76,77].

Table 4: Effects of aqueous mango leaves extract on liver functions in diabetic rats:

Group Time	Total protein (g/dl)		Albumin (g/dl)		Globulin (g/dl)		AST (LU/L		ALT (LU/L	
	point of start	End	point of start	End	point of start	End	point of start	End	point of start	End
Negative control	6.92 ^{A}	6.94^{A}	3.25^{A}	3.26 ^{A}	3.66^{A}	3.67^{A}	24.51^{A}	24.88^{A}	19.60^{A}	19.75^{A}
Positive control	6.22^{B}	6.34^{B}	2.73^{B}	2.76^{B}	3.48^{B}	3.57^{B}	30.10^{B}	31.44^{C}	24.40^{B}	24.93^{B}
Mango leaves extract (30 mg)	6.26^{B}	6.42^{C}	2.78^{B}	3.27^{C}	3.47^{B}	3.14^{C}	29.13^{B}	25.33^{D}	24.00^{B}	20.89 ^{AC}
Mango leaves extract (50mg)	6.31^{B}	6.71^{C}	2.74^{B}	3.50^{D}	3.55 ^{B}	3.22^{A}	28.75^{B}	25.00^{D}	23.55^{B}	19.33 ^{D}
Mango leaves extract (70 mg)	6.25^{B}	6.73^{A}	2.70^{B}	3.61^{A}	3.54^{B}	3.13^{A}	30.17^{B}	23.22^{A}	24.67^{B}	18.97^{D}
L.S. D.	01.401.4		0.42		0.10		3.55		2.66	

Table 5: Phytochemical constituents of mango leaves extract:

Extract	Total phenols (mg/g extract)	Total flavonoides (mg/g extract)	Tannins (%)	Saponins (%)
mango leaves extract (30mg)	3.06±0.03	0.23±0.02	1.89±0.03	0.08±0.02
mango leaves extract (50 mg)	6.12±0.05	0.46±0.04	2.83±0.03	0.13±0.01
mango leaves extract (70 mg)	9.15±0.08	0.68±0.05	3.95±0.03	0.18±0.02

From the Results Obtained in this Study: it could be observed that aqueous mango leaves extract had powerful antioxidants activity because of its high total phenols and total flavonoides contents. These antioxidant activities may be the factor responsible for lowering diabetic complications observed in the Streptozotocin –induced diabetic rat's accordance with the results mentioned by Esmaeili, M. A. and Yazdanparast, R.[78]. and therefore, this extract should be added to the natural products used for treating diabetes as hypoglycemic agent as neutracetical or functional foods.

Thus many different plants have been used individually or in formulations for treatment of diabetes and its complications[79]. One of the major problems with this herbal formulation is that the active ingredients are not well defined. It is important to know the active component and their molecular interaction, which will help to analyze therapeutic efficacy of the product and also to standardize the product.

In briefly, mango leaves extract increase peripheral utilization of glucose, increase hepatic and muscle glucagons' contents, promote B cells repair and regeneration and increase c peptide level. It has antioxidant properties and protects B cells from oxidative stress. It exerts insulin like action by reducing the glycated hemoglobin levels, normalizing the microalbuminurea and modulating the lipid profile. It minimizes long term diabetic complications. Efforts are now being made to investigate mechanism of action of some of these plants using model systems.

It is hoped that this study would lead to the establishment of some compounds that could be used to formulate new and more potent natural drugs of natural origin. Studies are in progress to further evaluate the mechanisms of action of *M. indica* extracts on some parameters and variables associated with human diseases. We need farther study to understand the mechanism of this antidiabetic drug using animal model on one hand and cultured islet cells on the other.

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