MANGIFERA INDICA LEAVES EXTRACT MODULATES SERUM LEPTIN, ASYMMETRIC DIMETHYLARGININE AND ENDOTHELIN-1 LEVELS IN EXPERIMENTAL DIABETES MELLITUS

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Received 2/9/2012– Accepted 3/10/2012

ABSTRACT

Diabetes is a chronic disease that is relatively common throughout the world. The present study was carried out in an attempt to investigate the possible antidiabetic activity of Mangifera indica (mango) leaves extract in streptozotocin (STZ)–diabetic rats. In addition, the effect of extract on diabetes complications as cardio, vascular and endothelial dysfunction was also studied. 30 male adult albino rats were divided to three groups (10 rats each) and were studied as following scheme for 42 days, group (1) normal control, group (2) diabetic control rats were given distilled water daily by gastric incubation, and group (3) diabetic rats were treated orally with Mangifera indica leaves aqueous extract. Blood samples were collected at 21st and 42nd day for different biochemical parameters estimations. The Mangifera indica extract administration to diabetic rats significantly decreased the level of blood glucose, leptin, asymmetric dimethylarginine and endothelin–1 as well as lactate dehydrogenase, creatine kinase and aspartate aminotransferase activities. The levels of insulin, C–peptide and nitric oxide were significantly increased. Further, the extract showed significant antihyperlipidemic activity. These findings demonstrated that Mangifera indica leaves extract possess antidiabetic and antihyperlipidemic properties thus suggesting its beneficial effect in the treatment of diabetes mellitus associated with hyperlipidemia and related cardiovascular complications.

Key words: diabetes, Mangifera indica, asymmetric dimethylarginine and endothelin–1

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INTRODUCTION

Diabetes mellitus is a metabolic disorder, characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, and/or insulin action (Wild et al., 2004). Although the link between diabetes and cardiovascular disease is not fully understood, loss of the modulatory role of the endothelium may be involved in the pathogenesis of diabetic vascular complications (Vehkavaara et al., 2000).

*Mangifera indica* L. (*M. indica*) is widely distributed in many tropical and subtropical regions; it is one of the most popular edible fruits in the world (Muruganandan et al., 2005). *M. indica* has been reported to have hypoglycemic effect in both experimental animals (Muruganandan et al., 2005) and human diabetic subjects (Mahabir and Gulliford, 1997).

Leptin, the adipocytic product of obese (ob) gene, signals the size of energy stores to the central nervous system, thus affecting hypothalamic centers involved in the regulation of food intake and energy balance (Campfield et al., 1995). Leptin resistance is related to the development of insulin resistance in individuals with type2 diabetes (Dagogo et al., 1996).

Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of endothelial nitric oxide synthase (eNOS) (Lin et al., 2002). Elevated ADMA levels have been detected in a large number of diseases associated with an impaired endothelial L-arginine–NO pathway, such as atherosclerosis, hypercholesterolemia, chronic heart failure, type2 diabetes mellitus, strok, hyperhomocysteinemia and hypertension (Cooke, 2004).

Endothelin–1 (ET–1), a vasoconstrictor peptide secreted from endothelial cells, is thought to play a role in a number of vascular diseases (Goto et al., 1996). ET-1 is stimulated by hypoxia, nor–epinephrine, vasopressin, and serotonin while vasodilators such as nitric oxide, prostaglandins E2 and I2, atrial and brain natriuretic factors inhibit ET-1 production and release (Shreenivas and Suzanne, 2007).

The aim of the present study was to investigate the antidiabetic effect of *M. indica* leaves water extract on streptozotocin diabetic rats and
also to investigate its ameliorative effects on cardiovascular and endothelial dysfunction.

MATERIALS AND METHODS

Chemicals: Streptozotocin (STZ) was purchased from Sigma-Aldrich chemicals, St. Louis, MO, USA. The analytical graded chemicals were used.

Tested plant and preparation of plant extract: The leaves of *M. indica* (Mango) were collected freshly from experimental station of Women’s College, Ain Shams University. The leaves were washed thoroughly with tap water, cut into small pieces; shade dried in air at room temperature and were crushed to powder with an electric grinder. 10g of powdered sample was added to 100ml already boiling distilled water and infused for 15 minutes with stirring and left overnight. Thereafter the infusion was filtered and the filtrate was freshly used (Nwinuka et al., 2008).

Experimental animals and diet: Thirty adult male Wistar albino rats with an initial weight between 180g to 220g were obtained from the Egyptian Organization for Biological Products and Vaccines, Helwan, Egypt. The rats were housed individually in plastic cages under controlled environment condition cycle. All rats were fed on basal diet prepared as nutrient requirements of laboratory animals (NRC, 1995) for one week (adaptation period) and also throughout the duration of the study (6 weeks), the diet and water were provided *ad libitum*.

Induction of experimental diabetes: Fasted twenty rats were rendered diabetic by a single subcutaneous (S.C.) injection of STZ (40 mg/kg body weight), freshly prepared in 0.1M ice–cold citrate buffer (pH 4.5), the injection was immediately within few minutes to avoid degradation of STZ (Junod et al., 1969). Normal control rats were injected S.C. with the appropriate volume of citrate buffer. During the first 24 hours of diabetes induction, STZ–treated rats were allowed to drink 5% glucose solution to overcome STZ–induced hypoglycemia. The development of hyperglycemia in rats was confirmed by the determination of fasting glucose concentration on the third day post STZ injection. Then the treatment was started on the fourth day after STZ injection and it was considered as first day of treatment.

Experimental design: Three groups of rats (10 rats each) were studied according to the following scheme for 42 days: (1) non
diabetic (normal control) rats were given distilled water daily by gastric incubation, (2) untreated diabetic (diabetic control) rats were given distilled water daily by gastric incubation and (3) diabetic rats orally treated with 1ml/100g body wt. of *M. indica* leaves water extract daily (diabetic + MLE) by gastric incubation (Nwinuka et al., 2008).

**Blood sampling:** At the middle (21st day) and by the end of experimental period (42nd day), blood samples of fasted rats were collected from the inner canthus of the eye under light ether anesthesia. The samples were collected in dry glass centrifuge tubes to obtain sera that stored at -20°C for subsequent biochemical analysis. Another blood sample was collected on sodium fluoride as anticoagulant for measuring of glucose.

**Biochemical assays:** Blood glucose was determined using the Trinder’s glucose oxidase method while serum insulin was determined using the rat insulin RIA kit (Millipore, USA). Serum C-peptide, leptin, asymmetric dimethylarginine and endothelin-1 were measured using commercially available kits specific for rat enzyme–linked immunosorbent assay (ELISA) as described by Finlay and Dillard (2007), Ducy et al. (2000), Böger et al. (1998) and Wakisaka et al. (1996), respectively. The method of Moshage et al. (1995) was used for assay the nitric oxide (NO).

Cardiac biomarkers as lactate dehydrogenase (LHD), creatine kinase (CK) and aspartate aminotransferase (AST) activities were determined using kits purchased from Randox, UK. Serum was analyzed for lipid triacylglycerols (TAG), total cholesterol (TC) and high density lipoprotein–cholesterol (HDL-C) levels by enzymatic colorimetric methods using assay kits (Analyticon, Germany) as described by Fossati and Prencipe (1982), Allain et al. (1974) and Lopes-Virella et al. (1977), respectively. Low density lipoprotein–cholesterol (LDL-C) was calculated using Friedwald et al. (1972) formula as following:

\[ \text{LDL–C} = \text{TC} - \left[ \text{HDL–C} + \left( \frac{\text{TAG}}{5} \right) \right] \]

**Statistical analysis:** The statistical analysis was applied in the present study by SPSS version 15. The present data were analyzed on the basis of one way analysis of variance (ANOVA) followed by Fisher’s LSD multiple–comparison test to evaluate the effect inbetween groups and give a chance of multiple comparisons between groups. Differences between the data in 21st and 42nd day were assessed by
two-tailed Student’s t-test. Results are expressed as mean ± standard deviations (S.D) and values of p<0.05 were considered statistically significant.

RESULTS

During the following 45 days after STZ injection, two STZ-diabetic untreated rats from group 2 died on the 12th and 18th day respectively, no death was seen in the normal control and STZ-diabetic treated with M. indica extract groups.

Serum levels of glucose and leptin were raised significantly (p<0.05), while insulin and C-peptide were significantly lowered in STZ-diabetic group compared to the control group. Whereas the administration of Mangifera indica leaves extract resulted in significant (p< 0.05) reduction in serum glucose and leptin levels accompanied with significant (P< 0.05) elevation in insulin and C–peptide levels at different periods in the experimental duration of 42 days in STZ-diabetic rats with the maximum percent reduction of glucose being 37.69, of leptin being 24.31 with the maximum percent elevation of insulin being 28.05 and of C–peptide being 24.00 on 42nd day of treatment (Table 1).

As compared to the normal control rats, diabetic condition caused significant (P< 0.05) increment in the values of ADMA and ET–1. On the other hand, there was a significant decrement in serum nitric oxide. The values detected being increased by 60.83 % and 65.79 % and decreased by 44.63%, respectively. These alterations were ameliorated by administration of Mangifera indica leaves extract (Table 1).

The data recorded in table (2) shows that, there was a significant (P< 0.05) increase in serum LHD, CK and AST activities of diabetic rats as compared with the normal control rats as noted at different periods of the study. As well as, the continuous administration of ML extract for 42 days caused a significant decrease in these activities at various time intervals with percentage changes 20.15 %, 35.00 % and 26.46 % at the end of experiment.

Data in table (3) revealed the effect of aqueous mango leaves extract on lipid profile in diabetic rats. There was a significant reduction in serum TAG, TC and LDL–C levels of diabetic rats treated with ML extract as comparable to non treated diabetic rats at
various time intervals. However, there was a significant (P<0.05) elevation in the HDL–C level in ML extract treated diabetic rats as compared to the diabetic control group.

**Table (1):** Effect of *M. indica* leaves extract on glucose, insulin, C-peptide, leptin, asymmetric dimethylarginine (ADMA), endothelin–1 (ET–1) and nitric oxide (NO) in diabetic rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Days</th>
<th>Normal Control</th>
<th>Diabetic Control</th>
<th>Diabetic + MLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl)</td>
<td>21</td>
<td>95.60± 1.47</td>
<td>258.45± 2.73</td>
<td>204.10± 4.27</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>98.30 ± 2.23</td>
<td>263.86± 10.61*</td>
<td></td>
</tr>
<tr>
<td>Insulin (ng/ml)</td>
<td>21</td>
<td>1.17 ± 0.12</td>
<td>2.00 ± 0.10</td>
<td>2.12 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>1.15 ± 0.11</td>
<td>0.82 ± 0.18**</td>
<td>1.05 ± 0.12</td>
</tr>
<tr>
<td>C-peptide (ng/ml)</td>
<td>21</td>
<td>0.040 ± 0.001</td>
<td>0.060 ± 0.005*</td>
<td>0.060 ± 0.001</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>0.040 ± 0.001</td>
<td>0.025 ± 0.002**</td>
<td>0.031 ± 0.001</td>
</tr>
<tr>
<td>Leptin (pg/ml)</td>
<td>21</td>
<td>212.48 ± 6.18</td>
<td>445.89 ± 6.45</td>
<td>440.39 ± 7.77</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>213.63 ± 3.36</td>
<td>451.03 ± 4.37**</td>
<td></td>
</tr>
<tr>
<td>ADMA (µmol/L)</td>
<td>21</td>
<td>1.18 ± 0.14</td>
<td>1.90 ± 0.26</td>
<td>1.85 ± 0.17</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>1.20 ± 0.15</td>
<td>1.93 ± 0.13*</td>
<td>1.53 ± 0.10**</td>
</tr>
<tr>
<td>ET-1 (Pg/ml)</td>
<td>21</td>
<td>0.37 ± 0.01</td>
<td>0.57 ± 0.02</td>
<td>0.51 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>0.38 ± 0.01</td>
<td>0.63 ± 0.02**</td>
<td>0.49 ± 0.01**</td>
</tr>
<tr>
<td>NO (µmol/L)</td>
<td>21</td>
<td>53.00 ± 1.08</td>
<td>31.61 ± 1.97</td>
<td>34.94 ± 3.07</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>52.36 ± 0.78</td>
<td>28.99 ± 0.70**</td>
<td>41.73 ± 2.14**</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D for 8-10 rats

* P < 0.05, diabetic control vs. normal control at 42nd day (ANOVA test).

** P < 0.05, diabetic + MLE vs. diabetic control at 42nd day (ANOVA test).

≠ P< 0.05, each group at 21st day vs. corresponding at 42nd day (t-test)
Table (2): Effect of *M. indica* leaves extract on cardiac biomarkers in diabetic rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Days</th>
<th>Normal Control</th>
<th>Diabetic Control</th>
<th>Diabetic + MLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDH (U/L)</td>
<td>21</td>
<td>221.44 ± 4.31</td>
<td>365.87 ± 4.57</td>
<td>323.59 ± 9.79</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>231.40 ± 3.00</td>
<td>374.24 ± 3.28*#</td>
<td>298.82 ± 8.45**#</td>
</tr>
<tr>
<td>CK (U/L)</td>
<td>21</td>
<td>92.88 ± 1.41</td>
<td>148.15 ± 3.32</td>
<td>134.58 ± 5.78</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>94.06 ± 2.27</td>
<td>158.96 ± 2.35*#</td>
<td>103.33 ± 3.58**#</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>21</td>
<td>33.88 ± 1.47</td>
<td>53.77 ± 1.74</td>
<td>50.23 ± 1.13</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>34.50 ± 1.89</td>
<td>61.48 ± 2.46*#</td>
<td>45.21 ± 1.59**#</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D for 8-10 rats.
* P < 0.05, diabetic control vs. normal control at 42\textsuperscript{nd} day (ANOVA test).
** P < 0.05, diabetic + MLE vs. diabetic control at 42\textsuperscript{nd} day (ANOVA test).
≠ P < 0.05, each group at 21\textsuperscript{st} day vs. corresponding at 42\textsuperscript{nd} day (t-test)

Table (3): Effect of *M. indica* leaves extract on lipid profile in diabetic rats.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Days</th>
<th>Normal Control</th>
<th>Diabetic Control</th>
<th>Diabetic + MLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAG (mg/dl)</td>
<td>21</td>
<td>92.60 ± 1.97</td>
<td>116.30 ± 3.59</td>
<td>106.60 ± 4.45</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>94.45 ± 2.25</td>
<td>130.47 ± 1.65*#</td>
<td>99.27 ± 1.41**#</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>21</td>
<td>78.03 ± 1.93</td>
<td>102.30 ± 2.89</td>
<td>94.10 ± 2.47</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>80.37 ± 3.00</td>
<td>107.95 ± 2.79*#</td>
<td>86.96 ± 1.32**#</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>21</td>
<td>35.64 ± 1.53</td>
<td>26.99 ± 2.03</td>
<td>30.04 ± 1.46</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>35.03 ± 1.90</td>
<td>23.87 ± 1.60*#</td>
<td>30.94 ± 1.23**</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>21</td>
<td>23.87 ± 2.31</td>
<td>52.06 ± 1.43</td>
<td>44.31 ± 2.03</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>26.45 ± 2.88*#</td>
<td>57.99 ± 2.16*#</td>
<td>36.17 ± 1.57**#</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D for 8-10 rats.
* P < 0.05, diabetic control vs. normal control at 42\textsuperscript{nd} day (ANOVA test).
** P < 0.05, diabetic + MLE vs. diabetic control at 42\textsuperscript{nd} day (ANOVA test).
≠ P < 0.05, each group at 21\textsuperscript{st} day vs. corresponding at 42\textsuperscript{nd} day (t-test)
DISCUSSION

An alternative strategy to treat diabetes is the use of various plant extracts or natural agents possessing hypoglycemic effect (Banerjee et al., 2005). The present study revealed a significant increase of serum glucose level after 6 weeks of STZ injection as compared with the normal control rats. These results are in accordance with the finding of several authors using STZ-diabetic animals (Abou El-Soud et al., 2007 and Bhowmik et al., 2009). On the other hand, the results obtained for serum insulin of STZ–diabetic rats showed low levels as compared with normal non-diabetic rats. Such results agree with that of Sellamuthu et al. (2009) and may be ascribed to the diabetogenic effect of STZ which lead to destruction of β-cells and decreased number of insulin–containing secretory granules.

The improvement with M.indica leaves extract administration in diabetic rats was evident by significant increases in insulin and in lowering glucose levels, and this correlates well with the observation of Aderibigbe et al. (2001) and Bhowmik et al. (2009) who demonstrated that the M. indica water extract may interfere with the intestinal glucose absorption by various mechanisms. This hypoglycemic effect may be due to the presence of flavonoids saponins, tannins, alkaloids and triterpenes. Muruganandan et al. (2005) suggested that both pancreatic and extra pancreatic mechanism might be involved in its antidiabetic or antihyperglycemic action. However, the extrapancreatic actions could consist of (i) a stimulation of peripheral glucose utilization, (ii) an enhancement of glycolytic and glycogen processes, and/or (iii) a glycemia reduction through the inhibition of glucose intake (Saxena and Vikram, 2004).

Aderibigbe et al. (1999) and Erato et al. (2005) have been reported that, the aqueous leaves extract of Mangifera indica possess antidiabetic properties.

C-peptide levels can be used to discriminate between type1 and type2 diabetes mellitus. Type1 diabetes mellitus (DM1) is characterized by β-cell destruction, which leads to very low or undetectable levels of C-peptide. In contrast, type2 diabetes mellitus (DM2) is associated with insulin resistance and typically initially has normal or elevated levels of C-peptide, which can decrease over the course of the disease (Kim...
et al., 2006). The previous report run parallel with our finding where as there was a significant elevation in C-peptide level at 21st day of the experiment and there was a significant decrease of this level at the end of the experiment.

Regarding to the effect of STZ–injection on serum leptin there was a significant increase in diabetic group as compared to normal control one, while the administration of *M. indica* leaves extract resulted in significant decrement. Kiess et al. (1998) stated that, plasma leptin levels are elevated in obesity and type2 diabetes mellitus, while they are decreased in DM1 and are positively associated with body mass index.

It is widely recognized that patients with diabetes mellitus are at high risk of developing micro-and macroangiopathic complications and the diabetic state is considered a major cardiovascular risk factor (Anderssohn et al., 2010).

The results concerning the effect of *M. indica* leaves extract on endothelial dysfunction was manifested by significant decrease in ADMA and ET-1 along with significant increase in NO levels that shown in diabetic rats, such results was in harmony with that obtained by Makino and Kamata (1998) and Lin et al. (2002) who observed an elevation of ADMA and ET-1 with reduction of NO levels in diabetic rats.

The results demonstrated that serum ADMA concentration was significantly increased in parallel with the elevation of blood glucose levels in diabetic rats. In addition, exposure of endothelial cells to a high glucose concentration has been found to enhance ET-1 secretion. After rats were administered *M. indica* extract, glycemic control was remarkably improved and serum ADMA concentration was decreased. The mechanisms of increasing ADMA levels associated with diabetes or in the context of insulin resistance are not well understood. However, in diabetic rats, the activity of dimethylarginine dimethylaminohydrolase (DDAH), that metabolize ADMA and produce citrulline and dimethylamine, was significantly reduced and was found to be negatively associated with plasma ADMA concentrations (Lin et al., 2002). ADMA inhibits eNOS by competitive displacement of physiological substrate, L-arginine, from the enzyme. The inhibition leads to decrease NO production in the endothelium of vessel walls. Thus, when ADMA levels are elevated, endothelial dysfunction may result (Böger et al., 1998).
Impaired glucose tolerance and diabetes mellitus specifically caused impaired NO production or NO bioavailability in the endothelium. Metabolic abnormalities found in diabetes such as hyperinsulinemia, hyperglycemia and dyslipidemia along with oxidative stress were all shown to contribute to endothelial dysfunction (Umpierrez et al., 2009). In turn, endothelial dysfunction was also shown to be present in very early stages of atherosclerosis, suggesting that endothelial dysfunction may be a phathophysiological link explaining the high rate of vascular complications in diabetes (Davignon and Granz, 2004).

Tissue damage is usually associated with the release of enzymes to the affected organ or tissue into circulation (Sroka and Cisowski, 2003). The present data indicated significant increases in LDH, CK and AST activities of STZ-diabetic animals which are concomitant with Sellamuthu et al. (2009) and Rawi et al. (2011). High AST levels in diabetic rats are thought to be consistent with its greater need for gluconeogenic substrate. The present study revealed that treatment of STZ–diabetic rats with the tested plant extract caused a detectable decrease of these enzyme activities this may be attributed to the good cardio-protective and antioxidant activity which due to the presence of a number of constituents, the major ones are flavonoids, tannins, saponins, polyphenols and triterpenes, since antioxidants are known to reduce the development of chemically induced organ damage (Chen and Yen, 2007).

Lactate dehydrogenase and aldolase are the bifunctional enzymes involved in the glycolytic pathway. The lactate dehydrogenase system reflects the NAD+/NADH ratio indicated by the lactate/pyruvate ratio of hepatocyte cytosol. The mangiferin and glibenclamide treated diabetic rats were reversible to near normal LDH activity. This may be regulated by NAD+/NADH ratio (Sellamuthu et al., 2009). Improvement in lipid profile following M. indica extract administration in diabetic rats was similar to that previously reported by Muruganadan et al. (2005) and Rawi et al. (2011). The hypertriglyceridemia observed in patients with DM2 originates from (i) lipolysis of TAG store from adipose tissue that causes elevated free fatty acid flux to the liver and hence, increased hepatic TAG synthesis and (ii) inhibition of lipolysis of chylomicrons and VLDL due to decreased lipoprotein lipase activity (Lann and Le Roith, 2007).

Our present study indicated that mango leaves extract administration
MANGIFERA INDICA LEAVES EXTRACT MODULATES …….

in diabetic rats could curb such development. These results suggest the presence of some compounds in the aqueous mango leaves extract that influence lipid catabolism indicating its potent antihyperlipidemic and antiatherogenic activity.

More importantly, ML extract induced a significant increase in HDL-C levels in the diabetic rats. Elevating HDL-C may serve as a more attractive treatment alternative instead of lowering LDL-C. Furthermore, the improvement with *M. indica* administration is in agreement with Dineshkumar et al. (2010) who reported marked decrease in lipid variables after treatment with *M. indica* and its polyphenol compound mangiferin which may be ascribed to lipid lowering activity of mangiferin or due to its influence on various lipid regulation systems.

Several studies on different parts of *M. indica* have demonstrated the presence of phenolic constituents, triterpenes, flavonoids, phytosterols and polyphenols, which are known to possess antioxidant properties (Selles et al., 2002 and Singh et al., 2004). The role of antioxidants in preventing various human diseases by preventing oxidative stress and damage in biological tissues has been demonstrated in many experiments (Repetto and Llesuy, 2002).

It could be conceived that the plant extract may also contain some biomolecules that may sensitize the insulin receptor to insulin or stimulates the β-cells of islets of Langerhans to release insulin which may finally lead to improvement of carbohydrate metabolizing enzymes towards the re-establishment of normal blood glucose level.

In conclusion, our results demonstrate that an elevation in the level of the endogenous inhibitor of NOS in rats with STZ–induced diabetes is closely related to glycemic control of the disease. *M. indica* extract treatment may be an effective pharmacologic approach to prevent the elevation of ADMA concentration and this normalization of serum ADMA and ET-1 concentration may contribute to the benefit effect of the phytochemicals, that possess antioxidant properties, on the impairment of endothelium–dependent vasodilatation, preventing damage in biological tissues and may be subsequent to the correction of metabolic abnormalities.
REFERENCES


MANGIFERA INDICA LEAVES EXTRACT MODULATES


المملوک الفكري

مستخلص أوراق المانجو يعد مستويات العسل من هرمون الليبتين، داي ميثيل أرجنين غير المتماثلة و الانتهالين-1 في مرضى البوال السكري

نورا محمد الشيخ

قسم الكيمياء الحيوية والتغذية
كلية النباتات - جامعة عين شمس - القاهرة - مصر

مرض السكري هو مرض مزمن شائع نسبياً في جميع أنحاء العالم. وقد أجريت هذه الدراسة في محاولة لتحقيق من قدرة مستخلص أوراق المانجو المضادة لمرض السكر المحدث بالاستروجين في الجرذان. بالإضافة إلى ذلك تم دراسة تأثير المستخلص على مضاعفات مرض السكري مثل اعتلال القلب والأوعية الدموية والبترائية.

تم تقسيم 30 جذر من الجرذان البيضاء البالغة إلى ثلاث مجموعات (10 جذر لكل مجموعة) وتم نسيجهم على النحو التالي لمدة 42 يوم. المجموعة الأولى ضبطت صمامات، المجموعة الثانية ضبطت مصابة بداء السكري ومجمعة الثالثة ضبطت مصابة بداء السكري، وتم إعطاءها عن طريق الاستروجين المعدل المستخلص المانجو. تم تجميع عينات الدم في اليوم الحادي والعشرين واليوم الثاني والأربعون لتقييم القياسات البيوكيميائية المختلفة.

اشترطت النتائج أن إعطاء مستخلص أوراق المانجو للجرذان مصابة بداء السكري داي ميثيل أرجنين غير المتماثلة، الانتهالين-1 بالإضافة إلى تأثير مضادات الأكسدة النازعة للهيدروجين، الككرياتين كينز، والاسبابيات النازعة لمجموعة الأمين. وارتبطت مستويات الأسولفين والسي-بيتيد وأساس التردد معها. علاوة على أن المستخلص أظهر تأثير مضاد لارتفاع دهون الدم، وتمكّن له أن يكون له فعّالة في علاج مرضى السكري المرتبطة بمضاعفات القلب والأوعية الدموية والبترائية.

الكلمات المفتاحية: مرض السكري–أوراق المانجو– داي ميثيل أرجنين غير المتماثلة– الانتهالين-1