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EVALUATION OF ANTI-DIABETIC EFFICACY OF MANGOPULP IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT

Background: Diabetes mellitus is a most common endocrine disorder acquiring 4-5% of the world population, characterized by hyperglycemia, hypoinsulinaemia or insulin resistance, leading to increased morbidity and mortality. Though several anti-diabetic drugs are available in the market some have adverse side effects. *Mangifera indica* have been used in traditional medicine and possess anti-diabetic, hypoglycemic, hypolipidemic and hypertension.

Objective: The present study was taken up to evaluate the anti-diabetic activity of mango pulp in streptozotocin (STZ) induced diabetic rats.

Method: Male wistar albino rats were divided in to four groups. 5g/kg/day of mango pulp was orally administered for 8 weeks to see the efficacy of anti-diabetic activity of mango pulp in STZ induced rats and non- diabetic rats.

Results: Glucose, lipid profile, insulin resistance, AST and ALT biochemical parameters were analyzed after administration of mango pulp at 5g/kg/day in all the experimental groups. From the results data it is shown that mango pulp possess anti-diabetic activity.

Key words: *Mangifera indica*, mango pulp, diabetes, insulin resistance

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INTRODUCTION

Diabetes mellitus (DM), a metabolic disorder characterized by hyperglycemia insulin resistance or relative lack of insulin, acquires 4-5 % of the total world population, resulting in significant financial burden causing morbidity and mortality (Ley, et al., 2014). DM is considered to be a major global health problem and successful treatment is yet to be discovered for the management of diabetes. It is associated with an increased risk of coronary heart diseases (CHD) by alteration in plasma lipids, triglycerides and lipo protein profile (Manjunath, et al., 2013). Interruption in carbohydrate, lipid and protein metabolism results insulin secretion deficiency. Non-Insulin dependent and Insulin dependent diabetes mellitus both are characterized by chronic hyperglycemia associated with the pathogenesis of diabetic dyslipidemia, micro and macro vascular complications (Seki et al., 2004).

Drugs such as insulin, biguanides, thiazolidinediones etc are used for the treatment of diabetes, but exert severe side effects (Ansari et al., 2004). At present, the use of medicinal plant/herbal medicine for treating various disorders and diseases is rapidly progressing and also presumed to have no side effects (Hymavathi, et al., 2017; Rao, P,S., and Prasad, M,N,V, 2013). The active components in these Medicinal /herbal plants have been shown to efficiently slow down the disease symptoms in a synergistic manner (Rao, P, S., and Prasad, M, N, V.2008).

The active components from these plants may be polysaccharides, pigments, steroids, terpenoids, flavonoids and alkaloids etc; moreover these medicinal/herbal plants extracts and purified molecules have been demonstrated significant role in controlling various diseases and disorders. In spite of therapeutic potential of Medicinal plant/herbal plants, its effect on DM are poorly understood (Satyanand, et al., 2013). A number of plant crude extracts and active biological compounds were tested as alternative source in the treatment of diabetes mellitus (Grover et al., 2002).

Mangifera indica L. is a perennial arboreal tree, belong to the genus Mangifera of the family Anacardiaceae and consist of 40 species distributed in tropical and sub-tropical parts of South East Asia, Africa and Latin America (Masud Parvez, 2016). *Mangifera indica*, a common garden tree throughout the world tropics. Several research studies focused on the importance of *Mangifera indica* as an Herbal drug, and using in the treatment of diabetes (Afifa et al., 2014; Guevara Garcia et al., 2004). Diabetes is an important human ailment afflicting many, from various occupations in different countries. Previous investigations of the biological properties of *Mangifera indica* have found that this plant has antiviral, antibacterial, analgesic, anti-inflammatory, immune- modulatory response and antioxidant activities (Jahurul et al., 2015). The present study is to evaluate the anti-diabetic efficacy of mango pulp in streptozotocin induced diabetic rats.

MATERIALS AND METHODS

Experimental design

Healthy male wistar albino rats weighing between 180-200 g were selected and used for the present study. Animal studies were carried out at Animal house, Naryana Medical College & Hospital, Nellore, A.P., India. Animals were procured from National Institute of Nutrition, Hyderabad, India. All animal experiments were in accordance with CPCSEA guidelines and with the approval of Institutional Animal Ethical Committee. Animals were allowed free access to food and water. Induction of diabetes was done by streptozotocin procured from Sigma, USA. Intraperitoneal administration at a dose of 60 mg/kg.bd wt of streptozotocin dissolved in 0.9% w/v of saline was inducted into the rats. Mango pulp (Banginapalli variety) was obtained from the local market area. The rats were divided into four groups of six rats per group, maintained under standard conditions (12h light/ 12h dark cycle, 25 ^{0}C and 30-35% humidity).

Group-1: Control.

Group-II: Rats fed with Group I diet and Mango pulp 5g/kg bd. wt /day orally administrated.

Group-III: Rats were fed with Group I diet and 60mg/kg bd. wt STZ induced by intraperitoneal injection method to the rats (non-treated only Diabetic rats).

Group-IV: 60mg/kg bd. wt STZ induced diabetes rats with standard pellet diet plus Mango pulp 5g/kg/day administrated.

Collection of blood and preparation of serum

Blood samples were collected following an overnight fast and were collectively analyzed in 4 groups of animals. Blood samples were collected after 48 hr of STZ injection and glucose levels were determined. At the end of the 8week period of mango pulp administration, blood samples were collected directly into anticoagulant containers and later plasma was collected after centrifugation. Blood was collected into two polypropylene tubes, one for serum and then one for plasma. The blood for plasma was collected in heparin, serum was prepared by allowing the blood to clot at 37 °C and centrifuged at 3000 RPM for 10 min. Samples were stored in a freezer at -20 degree centigrade for further biochemical analysis.

Biochemical analysis

Blood samples were analyzed for fasting glucose, serum Creatinine, Total cholesterol, LDL-cholesterol, Triglycerides, analyzed by utilizing Humastar 300 (GmBh) Autoanalyser. Serum insulin level was determined by using Chemiluminescence immunoassay replica (Beckmann Coulter, USA). The homeostatic model assessment (HOMA) index was used to estimate insulin resistance and calculated as fasting insulin (µU/mL) × fasting plasma glucose (mM)/22.5 High sensitive-reactive protein levels (hsCRP) were estimated by turbidometry method using Humalyzer 3000 chemistry analyzer.

Statistical analysis

All the data value of variables explicitly in the mean and standard deviation (Mean±SD). Statistical analysis was done by using Instat Graph Pad Prism.

RESULTS

Blood glucose levels higher than 250 mg/dL were considered diabetic in the STZ induced rats. Statistically significant difference major changes in the biochemical parameters notably fasting blood sugar, total cholesterol, triglycerides, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), high density lipoprotein (HDL) and insulin were observed (Table 1). Weight loss was observed in STZ induced group (group III) when compared to other control and treated rats.

Plasma lipid levels (Plasma Total cholesterol LDL-Cholesterol and Triglycerides) decreased in group-IV when compared to group-III & group-I after the experiment (Table 1). Creatinine, AST, ALT levels, and insulin resistance decreased significantly in group-IV when compared to Group-III.

Table1. Effect of mango pulp on biochemical parameters of serum in control and experimental induced STZ Wistar albino rats

S.No	Group I	Group II	Group III	Group IV
Body weight (g/kg)	192±6.2	186±3.2*	182±1.5	196±2.9**
Glucose (mg/dL)	128±11	130.6±14*	351.6±54**	160.3±8.6*
Serum HDL-Cholesterol (mg/dL)	18.7±1.7	22±2.8	20.7±0.4	18.2±1.0
Serum LDL-Cholesterol (mg/dL)	43.3±4.1	50.8±6.4*	46.4±1.1**	42.1±2.4**
Serum triglycerides (mg/dL)	60.5±1.4	70.1±4.2*	107.8±9.4**	81.5±5**
Serum creatinine (mg/dL)	1.3±0.18	1.2±0.08*	2.27±0.8**	1.62±0.4*
Serum AST (IU/L)	26±1.6	26±0.18*	36±2.1**	28±0.81
Serum ALT (IU/L)	32±2.4	31±1.6*	46±1.8**	31.3±1.2
Insulin (mIU/mL)	1.06 ±0.02	2.2±0.21*	0.9 ±0.02**	1.1±0.12
Insulin resistance (IU/mL)	0.69±0.2	0.71±0.4*	1.9±0.4**	0.86±0.1*

Values expressed were mean±SD. * indicates value is significantly different from the control value at $p<0.05$ while ** indicates significance different at $p<0.001$.

DISCUSSION

Mango fruit is rich nutrient and possess phenols, flavonoids, minerals, fibre and other biological active compounds (Severi, et al., 2009). Many experimental studies suggest that mango pulp treated diabetic rats might protect the prevention of liver and kidney tissue dysfunction against the cytotoxic action of STZ (Liu, et al., 2013). Muruganandan, et al., 2005 investigated the effect of *Mangifera indica* on hyperglycemia, atherogenicity, and oxidative damage to cardiac and renal tissue in streptozotocin- induced diabetic rats. The reported pharmacological activities of *Mangifera indica* include antioxidant, antidiabetic, radioprotective, antitumor, anti-inflammatory, which may support the numerous traditional therapeutic uses of the plant (Severi, et al., 2009).Both animal and human studies suggest that mango pulp maintains some glucose-lowering properties. The possible mechanism mango pulp hypoglycemic action may be through potentiating the plasma insulin effect by increasing either pancreatic secretion of insulin from regenerated β-cells. Moreover, it has decreased from bound insulin response in type 2 diabetic patients also suggests that mango is well tolerated in diabetics (Corrales –Bernal, et al., 2014).

Streptozotocin (STZ) exerts selective toxicity related to pancreatic β cells. STZ administration causes reduction in the number of β-cells and induces hyperglycemia (Kaleem, et al., 2006). The STZ-induced diabetes is associated with the chronic hyperglycemia be able to cause oxidative stress (Gondi & Prasad, 2015), which lead to the cellular tissue damage and excess production of reactive oxygen species (ROS) especially to cytotoxicity in β-cells, thus decreasing the synthesis and release of insulin and also affecting the pancreas. Kakkar, et al., 1984 reported that streptozotocin induced diabetes rats was being reduced SOD and GSH activity observed in the liver and kidney with progression of diabetes may be due to non enzymatic glycosylation of the enzyme, which happens in a diabetic state. Mango pulp has been decreased the levels of the pancreas thiobarbituric acid reactive substance (TBARS) could be due to the increase in free radicals and decrease in non enzymatic antioxidants.

Lipid abnormalities play a muscle auxiliary with atherosclerosis is the major cause of cardiovascular disease in diabetes. The atypical in lipid metabolism lead to an elevation in the levels of serum lipid and lipoprotein that in turn play a vital role in an event of premature and severe atherosclerosis, which affects patients with diabetes (Saleh, et al., 2014). These results indicate the presence of some compounds in the Mango pulp that influence lipid catabolism. Further, the studies suggested that triglycerides itself are independently regulated to coronary heart disease (Pardo-Andreu, et al., 2008). In our study, the reduction of triglycerides following administration with mango pulp would also make possible the glucose oxidation and utilization and subsequently the reduction of hyperglycemia.

Insulin resistance and type II diabetes are associated with a decrease in mitochondrial function that contributes to the ectopic fat accumulation in muscle and fat fibber. Petersen et al., (2003) found that several insulin resistances are associated with significantly higher levels of triglycerides in both muscle and liver in the elderly. These alterations were accompanied by decreases in both mitochondrial oxidative energetically and mitochondrial ATP synthesis, both indicative of a decrease in mitochondrial function.

In addition, recent studies has investigated "insulin resistant" glucose transport of the fat cell in animal model of insulin-dependent diabetes mellitus can be explained by a reduction in the number of glucose transport systems appear in the plasma membrane in response to insulin. Insulin as the effect of a depletion of these glucose transport mechanisms in the cell's intracellular pool (Gonzalez et al., 1989).

High levels of free fatty acids are also associated with insulin-receptor dysfunction leading to insulin resistance, hyperglycemia, and increased hepatic gluconeogenesis. Our study showed that after supplementation of mango pulp there are increasing pancreatic β cell activity and decrease insulin resistance, and hypolipidemic effect.

Systemic long-term inflammation has been suggested to have an important role in the pathogenesis of obesity related insulin resistance. It has been shown that biomarkers of inflammation, such as TNF, IL-6, and C-reactive protein (CRP), are present at increased concentrations in particular that are insulin resistant and obese, and these biomarkers predict the development of type II diabetes (Mortensen, R.F, Duszkiewicz , J.A, 1997). CRP is one of the most frequently quantified molecules in clinical medicine. CRP enhances the generation of oxygen free radicals by monocytes and neutrophils directly. Oxygen radicals have been implicated in the pathophysiology of diabetes, atherosclerosis and other cardiac diseases. The oxidative hypothesis of diabetes depends upon the oxygen radicals. The increased level of serum CRP in obese individuals is due to increased substances is produced of interleukin-6 and tumor necrosis factor in adipocytes, which regulate CRP production in hepatocytes and induce a chronic inflammatory state (Kailash, P.C, 2003). Administration of mango pulp has shown potent anti-inflammatory, insulin resistance and hypolipidemic activity. These activities may be due to the phenols and flavonoids compounds present, and responsible for lowering diabetic complications observed in the Streptozotocin-induced diabetic rats (Masud Parvez, 2016; Shahidi, et al., 1992).

CONCLUSION

From the results it is concluded that mango pulp has effect in reducing the hyperglycemic condition

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Conflict of interest

None

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