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THERAPEUTIC EFFECT OF MANGO SEED EXTRACT IN DIABETES MELLITUS.

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ABSTRACT… Objectives: Diabetes mellitus is very common disease; the oral hypoglycemic drugs are utilized for diabetes. In Asia therapeutic plants are extensively used for cure of widespread variation of illnesses. **Objectives:** To study the Therapeutic effect of mango seed extract on diabetes Mellitus. **Study Design:** A prospective study and longitude. **Setting:** This study was conducted at Jinnah Post graduate Center, Karachi. **Period:** From June 2016 to June 2017. **Material and Methods:** Mango seeds were taken out with ethanol and used for study. The antidiabetic action of mango seeds extracts were well-thought-out at 100 and 200 mg/kg b.wt. The antidiabetic effect of mango seeds extracts were matched with tolbutamide 500 mg/kg b.wt. **Result:** The ethanolic extract of mango seeds (200 mg/kg) revealed major ($p < 0.01$) hypoglycemic outcome in fasted diabetic rats, when matched with normal control group. The mango seed extracts were significantly increased insulin level and decreased HbA1c levels at the dose level (100, 200 mg/kg) in alloxone encouraged diabetic rats. **Conclusion:** The ethanolic extract of mango seeds ensuring important antidabatic outcome compared to aloxone tempted diabetes in albino rats and its stimulating insulin production in pancreas of albino rats.

Key words: Alloxane, Diabetes Mellitus, Mango Seed, Tolbutamide.

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INTRODUCTION

Diabetes mellitus (DM), commonly known as Diabetes, is collection of metabolic diseases in which there are increased levels of sugar in blood for prolonged time. Diabetes is either caused due to insufficient release of insulin by pancreas or Beta cell does not react effectively to the insulin.[1]

The total number of peoples having diabetes have been increased from 108 million in 1980 to 422 million in 2014.[2] The worldwide prevalence of diabetes amongst adults over 18 years of age have risen from 4.7% in 1980 to 8.5% in 2014.[2]

In 2015, about 1.6 million deaths were directly caused by diabetes. Another report showed 2.2 million deaths were due to high blood glucose in 2012.[2] According to WHO diabetes will be the seventh leading cause of death in 2030.[2]

Pakistan is the 7th in the world, according to WHO estimates, with 7 million people with Diabetes and is expected with 15 million people per year until 2025.[2] Type 2 Diabetes makes up to 85-90% of all diabetes cases.[2]

Type 2 Diabetes is one of main fear to human health because of increasing prevalence, lifelong problems related to longer duration, involving various disabilities. Conventional therapies available for Diabetes: stimulus for endogenous insulin secretion, enhancing insulin effect on target tissues and uses of oral hypoglycemic agents.[3]

Although Biguanides and Sulfonylureas are important for treatment of type 2 DM, the value of these drugs are limited by their inadequate

action, pharmacokinetic properties, their failure rates and associated side effects.[4]

In place of the existing hypoglycemic management, have opposing adverse effects, there is an increasing demand of natural sources for treatment diabetes and its complications. Medicines from plant sources are broadly used in almost all over the world to treat diabetes. So, plant are considered as another sources of antidiabetic agents.[5]

Mango is beneficial tropical fruit.[6] The main constituents of mango seed are starch, fat and protein. Mango seed consists of about 52-56% stearic unsaturated fatty acids and 44-48% saturated fatty acids. Mango seed have low protein content, having most of the essential amino acids, with higher values of lysine, valine and leucine and also a good source of phytochemicals such as polyphenols and carotenoids.[7]

Mangiferin promotes the utilization of glucose, increased uptake of glucose by cell is attributed to the enhanced surface expression of GLUT4 transporters. In a dose-dependent manner, mangiferin negatively regulates exhibition of main enzyme of the gluconeogenesis pathway, namely fructose-1,6-bisphosphatase (FBP). Inhibition of gluconeogenesis in the liver reduces the production of hepatic glucose and therefore reduces blood glucose levels.[8]

Complex carbohydrate molecules are broken down into glucose in the intestine by a class of glucosidase enzymes such as sucrase, isomaltase and maltase. Mangiferin has also been shown to reduce glucose uptake through its inhibitory effect on α-glucosidase enzymes in experimental rats. This extra pancreatic action of mangiferin reduces glucose uptake and subsequent decrease in blood glucose levels.[8]

It has been established that mangiferin derivatives inhibit the activity of protein tyrosine phosphatase 1B (PTP1B) and inhibition of PTP1B is considered a potential target for the treatment of Diabetes mellitus.[8]

MATERIAL AND METHOD

There were selected 50 diabetic rats of either sex, (female ensured to be non-pregnant weighing 160-175 grams to compare the hypoglycemic effects of Tolbutamide and Ethanol extract of Mango seed. Study animals were divided into 5 groups with 10 rats in each group. All animals were selected from the animal house of BMSI, JPMC, Karachi. Group I: Normal control (without diabetes), Group II: Diabetic control (without treatment), Group III: Diabetic rats treated with Tolbutamide 500 mg/kg body weight and Group IV: Diabetic rats treated with ethanol extract of mango seed 200 mg/kg. Tablet: Alloxan monohydrate 120mg/kg was given as single dose as intraperitoneally in 18 h fasted animals for induction of diabetes.

Preparation of Extract of Mango Seed

The fresh ripe mangoes without bruises, weighing 200-250 grams were purchased from local market. Pulp was removed from fruit and seed were selectively separated and washed with distilled water to remove pulp traces. Seed kernel was separated from seed coat, shed sun-drying for 4 days, powdered in an electrical grinder and subjected for extraction with ethanol until 72 hours.

Preparation of Extract

The mango seed powder was extracted with 80% ethanol, extract obtained was filtered through Whatman No.1 filter paper, filtrate obtained was concentrated under reduced pressure using a rotator evaporator at 40°C, and was lyophilized. The lyophilized powder was stored at 4°C until further use. The seed extract powder was dissolved in distilled water and used for in vitro and in vivo studies.[7]

Statistical Analysis

Statistical software SPSS version 21.0 was used for data feeding and analysis. A descriptive statistical analysis of continuous variables was performed. Data on continuous parameters were presented as Mean + standard deviation (SD) + standard error of mean (SEM). Descriptive statistics were calculated using SPSS version 21. Quantitative variables were presented in term

of mean and standard deviations. ANOVA, was applied to compare mean as appropriate P value ≤ 0.05 was considered.

RESULTS

Effect of Ethanol Extract of Mango Seed on Mean Fasting Glucose Levels in Alloxan Induced Diabetic Rats

The Ethanol Extract of Mango Seed showed significant reduction in fasting blood sugar levels at 200 mg/kg ($p < 0.01$) on 7th, 14th and 21st days of drug administration, when compared to control group. The standard drug Tolbutamide (500 mg/kg) also produced Significant ($p < 0.01$) decrease in fasting sugar levels. Results are shown in Figure-1.

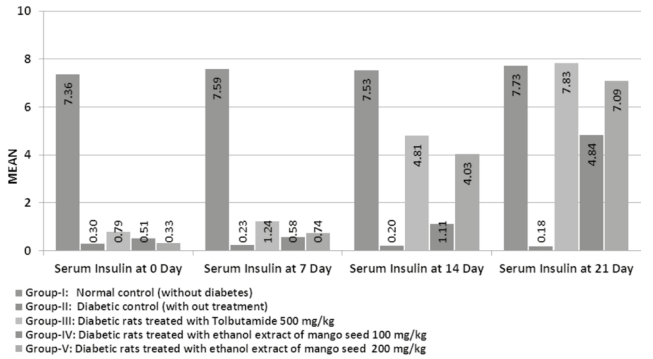

Figure-1. Comparison of mean fasting blood sugar according to days

Effect of Ethanol Extract of Mango Seed on Hb1Ac in Alloxan Induced Diabetic Rats

The Ethanol Extract of Mango Seed (200 mg/kg) produced significant ($p < 0.01$) antidiuretic activity is indicated by reduction in glucose levels and Hb1Ac level throughout treatment for 21 days as standard drug tolbutamide (500 mg/kg) decreases the Hb1Ac level. Results are shown in (Figure-2).

Effect of Ethanol Extract of Mango Seed on Body Weight in Alloxan Induced Diabetic Rats

There was a significant weight loss in the tolbutamide treated diabetic rats, whereas animals treated with Ethanol Extract of Mango Seed at the doses of 200 mg/kg presented the significant increase in weight 14th day onwards, showing that the Ethanol Extract of Mango Seed had valuable effects in avoiding reduction of body weight of diabetic rats. Results are shown in (Figure-3).

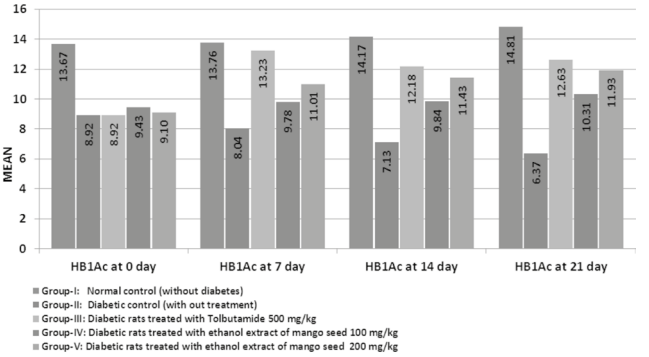

Figure-2. Comparison of mean HbA1c level according to days

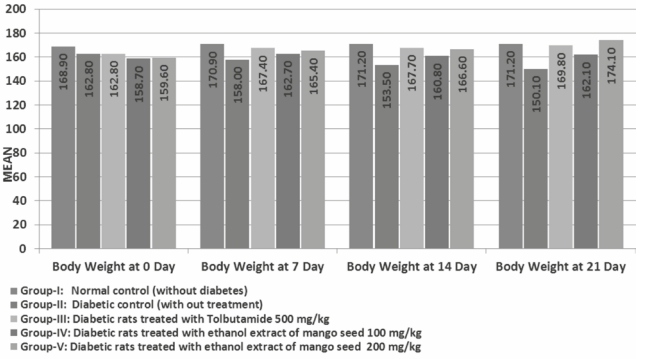

Figure-3. Comparison of mean body weight

Effect of Ethanol Extract of Mango Seed on Insulin Level in Alloxan Induced Diabetic Rats

The Ethanol Extract of Mango Seed (200 mg/kg) produced sustained and significant ($p < 0.01$) antidiabetic activity against alloxan induced diabetics and significantly increased insulin level. The standard drug tolbutamide (500 mg/kg) elevated the insulin level to the normal. (Figure-4)

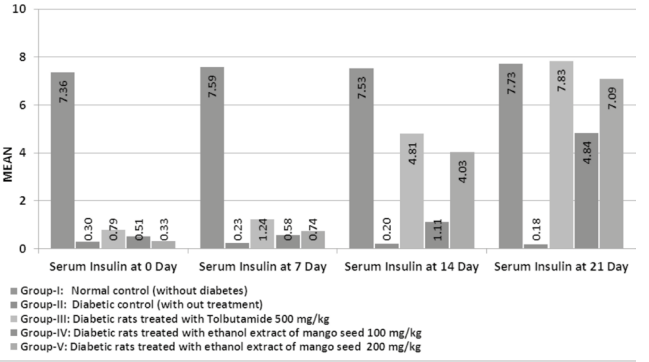

Figure-4. Comparison of mean insulin level according to days

DISCUSSION

In our study, we observed the anti-diabetic effect of ethanol extract of mango seed in rats, having described in another study that mango seed is main basis of significant flavonoids in addition to phenolic acids, the ethanolic extract prevents approximately important enzymes (α amylase, α glucosidase, and aldose reductase) associated towards the pathology and problems of T2D in vitro.[9]

In sight of opposing effects and expensive price of artificial antidiuretic medicines, investigation has been done on substitute methods of inhibiting T2D that might be further effective, harmless and reasonable. Nutritional mediation has established as an alternative way (10) usage of flavonoids rich diets has been labelled as protective in contrast to growth of deteriorating syndromes together with diabetes.[11]

The use of alloxan model for induction of diabetes in rats has been stated by earlier studies.[12,13,14] The lethal effect of Alloxan on pancreatic Beta cells were illustrated several years ago by Dunn et al.[15], it is the addition of some processes: oxidation of essential (-SH) groups, reserve of glucokinase, production of free radicals and conflicting with calcium homeostasis, these all processes are leading to induction of diabetes, so that Alloxan is diabetogenic.[16]

The decrease in the body weight of the diabetic rats could be because of lack of fluids and greater than before muscle wasting[17]; and continuing gluconeogenesis, where in fats and proteins are broken down.[18]

The better significance of ethanol extract of mango seed on the hyperglycemic rats were experimented in study might be due to flavonoids and phenolic acids existing in mango seed.[9] These phenolic mixtures are famous to apply their antidiuretic activity by some different mechanisms, inhibition of carbohydrate hydrolyzing enzymes.[19] The rise in FBG levels of diabetic rats were just because of decrease in the liver glycogen concentration, comparative to the normal control group. Underneath regular metabolic and physiological conditions, insulin increases cellular glycogen stores through exciting actions of glycogen synthase and preventing glycogen phosphorylase.[20]

It is suggested that mango seed extract in diabetic rats causes the release of insulin, synthesis of glycogen synthase and inhibition of its inactivation.[21] Other researchers have also been reported that persistent management by mangiferin dropped the plasma glucose level in diabetic rats. Likewise, different extracts of stem bark were described to have antihyperglycemic activity.[23,24]

Glycosylated hemoglobin (HbA1c) is predictable measure of diabetes, as an important tool for detecting diabetic hyperglycemia.[25] The HbA1c follows gradually and conclusively throughout the 90–120 days period of RBCs.[26] Hence it is an additional inclusive measure for total glycemic exposure than FBG as marker for levels of blood glucose in both post-prandial and fasting state.[27] The rise in HbA1c detected in diabetic rats comparative with normal control rats may be greater level of glycation of hemoglobin under hyperglycemic state achieved by alloxan administration. This is correlated with the evidences of raised HbA1c in diabetic rats by other researchers.[28] Conversely, ethanol extract of mango seed, decreases HbA1c levels of diabetic rats, when matched with control group; this provides an additional credibility to the hypoglycemic influence of ethanol extract of mango seed.[29]

The overall antidiabetic effect of ethanol extract of mango seed may possibly be due to flavonoids and phenolic acids polyphenols.[9] Furthermore, controlling carbohydrate breakdown by preventing α glucosidase and α amylase enzymes as well as decrease intestinal concentration of dietary carbohydrate, enhancement in function of β cells, stimulation of insulin release, antioxidative and anti inflammatory belongings.[30,19]

CONCLUSION

The Ethanolic Extract of Mango Seed possesses

normoglycemic activity to alloxan treated diabetic rats, is a restoration in blood glucose level and insulin. Moreover it showed reduction in hemoglobin and increase in body weight by stimulating the insulin production from pancreas, extra pancreatic action and effective in controlling the diabetes and related complications.

Hence mango seed extracts possess marvelous potential as a food and medicine. Mango seed can therefore be a gifted natural cure in controlling of Type 2 Diabetes and its accompanying pathologies.

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3	Farah Asad	Data analysis.	
4	Hamid Ali Kazi	Research review & Study design.	
5	M. Umair Farooqui	Writing & review.