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PROTECTIVE EFFECT OF *AEGLE MARMELOS* EXTRACTS IN ALLOXAN INDUCED TYPE I DIABETIC RATS

Aarti Verma[1], Shiv Kumar Jayant[1], RB Raipuriya[2*]

[1]Govt. SMS Modal Science College, Gwalior.

[2]Govt. KRG Post Graduate (Autonomous) College, Gwalior

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***Correspondence for Author**
R B Raipuriya
Govt. KRG Post Graduate (Autonomous) College, Gwalior.

ABSTRACT

Reactive oxygen spaces (ROS) are common by product of many oxidative biochemicals, metabolic and physiological process. ROS increased blood glucose, lipid profile and decrease antioxidant defence system in experimental animals. The present studies clearly showed a dose and exposure dependent increase in the levels of blood glucose, serum glutamate oxaloacetate transaminase **(**SGOT), serum glutamate pyruvate transaminase (SGPT), Creatinine, billirubin and urea in diabetic rats. Diabetic rats treated with *Aegle marmelos* extract decrease in the levels of blood glucose, SGOT, SGPT, Creatinine, billirubin and urea in diabetic rats.

KEYWORDS: Alloxan, Diabetes, Herbal drugs, Oxidative stress.

INTRODUCTION

Diabetes mellitus is a chronic disease that occurs either when the pancreas does not produce enough insulin or body cannot effectively use the insulin it produces. Hyperglycemia is a common effect of uncontrolled diabetes and over time leads to damage of biological macromolecules such as lipid, protein and DNA [1]. A WHO fact sheet stated that, 346 million people worldwide have diabetes. WHO demonstrated that diabetes death will double between 2005 and 2030. The total number of persons with diagnosed and undiagnosed diabetes in Egypt will increase from 3.80 million in 2000 to 8.80 million by the year 2025.[2]

Medicinal plants are widely used in management of diseases all over the world. There are about 800 plants which have been reported to show anti-diabetic potential.[3] A wide

collection of plant derived active principles representing numerous bioactive compounds has established their role for possible use in the treatment of diabetes.[3]

The aim of the present study was designed to investigate the potential of an aqueous extract of *Aegle marmelos* in controlling blood glucose and decreased in the level of Creatinine, Bilirubin, Urea, SGOT and SGPT in alloxan induced diabetic rats, compared to normal control and diabetic untreated rats. Insulin stimulates muscle and fat cells to remove glucose from the blood and stimulates the liver to metabolize glucose, causing the blood sugar level to decrease to normal levels.

MATERIALS AND METHOD

PLANT MATERIAL: The fresh leaves of *Aegle marmelos* (bael) were collected from botanical garden in school of studies in Botany, jiwaji University, Gwalior.

EXPERIMENTAL ANIMAL

Male albino rats of Wistar strain (weight 120 ± 20g) was used in the proposed study. Animals were obtained from the animal facilities of Defence Research and Development Establishment, Gwalior, India, and were maintained under controlled conditions of temperature ($25^0 \pm 2^0$C), relative humidity of (50 ± 15%), and normal photoperiod (light-dark cycle of 12 hrs) in the animal room of our department on standard pellet diet and tap water *ad libitum*. Animals were housed throughout the experiment in polypropylene cages (with each cage housing six animals) containing paddy husk as bedding and allowed to acclimatize to the environment of animal room for 7 days before the start of experiment.

EXPERIMENTAL DESIGN

Twenty four rats were randomly divided into four groups of six rats each. Animals were divided into four groups and were given following treatments:

Group 1 : Normal control

Group 2 : Normal control + extracts of *Aegle marmelos*

Group 3 : Diabetic control (I.V. injection of alloxan 85 mg/kg body weight).

Group 4 : Diabetic control + extract of *Aegle marmelos*

INDUCTION OF EXPERIMENTAL DIABETES AND PLANT EXTRACT TREATMENT

Type I diabetes was induced by giving single intravenous injection of alloxan monohydrate 85 mg/kg body weight, dissolved in 0.9% solution of sodium chloride. The animals were

checked for blood glucose level 48 h after alloxan injection, and blood sugar level above 180 mg/dl was used for the experiment.

Aegle marmelos (bael) leaves were obtained from botanical garden of jiwaji university gwalior, cleaned and Aqueous extract of *Aegle marmelos* was prepared and 2 mg/kg body weight was given orally to the rats of group 2 and 4 with the help of cannula, daily for two weeks.

Rats were humanly killed 24 h after the last treatment by cervical dislocation; different tissues were excised off, washed with 0.9% NaCl and used for different estimations. Animals were handled, ethically treated and humanly killed as per the rules and instructions of Ethical Committee of Animal Care (Ref No. IAEC/JU/2012/01) of Jiwaji University, Gwalior, India, in accordance with the Indian National law on animal care and use.

ASSAY OF BIOCHEMICAL PARAMETERS

FBG levels were estimated by glucose oxidase peroxidase reactive strips [4] (Accu-Chek, Roche Diagnostics, USA). The biochemical parameters evaluated were Creatinine [5], Bilirubin [6], Urea [7], SGOT and SGPT [8], using diagnostics kits.

STATISTICAL ANALYSIS

Results are expressed as mean ± S.D. of four different sets of observation taken on different days. All the statistical analyses were performed using one-way analysis of variance (ANOVA) with *post hoc* Dunnett's multiple comparison test applied across treatment groups for each tissue. Significance level was based on $p < 0.05$.

RESULT AND DISCUSSION

The association of elevated serum uric acid, urea and creatnine and higher urinary albumin excretion rate with advanced impaired renal function prompts an examination of its role in early renal function decline in patients with type 1 diabetes before proteinuria develops [9], Serum uric acid levels are a strong predictor of cardiovascular disease mortality in healthy aged men, independent of variables commonly associated with gout or the metabolic syndrome. Serum uric acid has been recently associated with insulin resistance.

The blood glucose level of all the rats was tested by taking the blood from the tail vein and using electronic glucometer. The anti diabetic effects of the extracts on the fasting blood sugar levels of diabetes (Table 1) and administration of alloxan (85 mg/kg, i.v) led to 3 fold

elevation of fasting blood glucose levels, which was maintained for period of 14 days. It was observed that oral administration of *Aegle marmelos* extracts significantly decreased the blood glucose levels in diabetic rats. The present study results showed that oral administration of *Aegle marmelos* extracts daily for 14 days, to the diabetic rats caused 34.9% decrease on 7th day and 58.3% decrease in the blood glucose level on 14 days of the start of treatmet (Table 1). The results clearly showed the hypoglycemic potential of *Aegle marmelos* extracts.

Table-1: Effect of oral treatment of *Aegle marmelos* extracts for 14 days on glucose concentration levels in alloxan induced diabetic rats.

SNo.	Group	0days	7days	14days
1.	Control	102±2.65	106.33±2.4$^{\#}$	110.33±3.53$^{\#}$
2.	Control + Aegle marmelos	97±3.46$^{\#}$	95±2.08*	91±1.73**
3.	Diabetic	368±3.53***	376±2.65***	380.33±2.33***
4.	Diabetic + Aegle marmelos	363±1.15***	244.67±3.18***	158.67±2.96***

Glucose concentration is expressed as mg/dl.

Results are expressed as mean ± S.E. of four set of observation.

Significance is based on p>0.05 #, p<0.05 *, p<0.01 **, p<0.001 ***

Table 2: Effect of *Aegle marmelos* extracts for 14 days experimental rats on SGOT, SGPT, ALP and bilirubin levels in alloxan induced diabetic rats.

SNo.	Group	Creatinine	Billirubine	Urea	SGOT	SGPT
1.	Control	0.62±0.04	0.29±0.02	12.53±0.29	13.63±0.5	8.93±0.45
2.	Control + Aegle marmelos	0.53±0.07$^{\#}$	0.21±0.01*	10.77±0.26*	11.87±0.22*	7.7±0.29$^{\#}$
3.	Diabetic	1.52±0.04***	1.63±0.03***	21.07±0.47***	29.03±0.41***	18.77±0.26***
4.	Diabetic + Aegle marmelos	0.80±0.06***	0.45±0.04***	13.53±0.29***	16.30±0.64***	11.9±0.4***

Creatinine, Bilirubin, Urea, SGOT and SGPT concentration are expressed as mg/dl.

Results are expressed as mean ± S.E. of four set of observation.

Significance is based on p>0.05 #, p<0.05 *, p<0.01 **, p<0.001 ***

The levels of Creatinine, Bilirubin, Urea, SGOT and SGPT were significantly increased in alloxan induced diabetic rats. These adverse changes were reversed to near normal values in extracts of *Aegle marmelos* treated. In the present study indicates the increase in the levels of Creatinine, Bilirubin, Urea, SGOT and SGPT in serum when compared with control rat. The levels of Creatinine, Bilirubin, Urea, SGOT and SGPT were increase 145.2%, 462%, 68.2%,

113% and 110.2% increase in alloxan induced diabetic rat as compared with control rats (Table 2). Oral administration of *Aegle marmelos* extracts for 14 days, showed 47.4%, 72.4%, 35.8%, 43,9% and 36.6% decreased in the level of Creatinine, Bilirubin, Urea, SGOT and SGPT in rats when compared with diabetic rats (Table 2).

CONCLUSION

Diabetes showed the changes in the level of Creatinine, Bilirubin, Urea, SGOT and SGPT in normal and experimental groups of rats. Diabetes mellitus was a significant increase in Creatinine, Bilirubin, Urea, SGOT and SGPT in rats when compared to control rats. Diabetic rats treated with oral administration of *Aegle marmelos* extracts decrease in Creatinine, Bilirubin, Urea, SGOT and SGPT levels as compared with diabetic control rats. Further human studies are necessary to found the role of these herbal drugs in controlling type I diabetes and its complications.

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