

EFFECT OF AQUEOUS EXTRACT OF *EUPHORBIA HETEROPHYLLA* ON BLOOD GLUCOSE LEVELS OF ALLOXAN INDUCED DIABETIC RATS

A. Annapurna and Ketan Hatware

A.U. College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, Andhra Pradesh, India.

ABSTRACT

The present study was undertaken to evaluate the effect of, aqueous extract of *Euphorbia heterophylla* on alloxan induced diabetic rats. Diabetes was induced in healthy albino wistar rats by administering freshly prepared Alloxan monohydrate in normal saline solution at a dose of 150mg/kg intraperitoneally. As Diabetes mellitus is a chronic disorder, leads to an increased concentration of glucose in the blood (hyperglycemia), we checked the blood glucose level in different groups of rats, Group I (received 1% Sodium CMC Orally), Group II (received 10 mg/kg Glibenclamide Orally), Group III (received 150 mg/kg Aq. Extract of *Euphorbia heterophylla* Orally), and Group IV (received 300 mg/kg Aq. Extract of *Euphorbia heterophylla* Orally). After administration of all the drugs blood glucose level was estimated by using "One Touch Horizon Glucometer", at 0 hr, 1sthr, 2ndhr 4thhr, 8thhr and 12th hr. The aqueous extract of *Euphorbia heterophylla* has shown significant blood glucose lowering effect on Alloxan induced rats.

Keywords: Alloxan, Blood Glucose, *Euphorbia heterophylla*, etc.

INTRODUCTION

Diabetes mellitus is a chronic disorder, which has affected about 171 million people around the globe and is spreading at an alarming rate¹. Diabetes is a condition where the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces. This leads to an increased concentration of glucose in the blood (hyperglycemia)². Traditional medicines all over the world have advocated the use of herbs to treat diabetes since time immemorial. Many Indian plants have been investigated for their beneficial use in different types of diabetes and wide array of plant-derived active principles demonstrated consistent hypoglycemic activity.

There are 2000 species of euphorbia, out of which some are having many pharmacological activities such as analgesic, anti inflammatory,

anti oxidant, anti bacterial, hypoglycemic, anti diabetic (*Euphorbia balsamifera*) etc; *Euphorbia heterophylla* belongs to Euphorbiaceae family and it is a annual herb which is abundantly found in India, Africa, America, south and southeast Asia etc³. It consists of mainly methyl esters and derivatives, diterpene polyesters, sesquiterpenes, a small percentage of monoterpenes and aliphatic compounds, quercetin and other bioflavonoids, etc; and it is having anti bacterial, anti-inflammatory and anti oxidant activity. As mentioned above our interest is to evaluate the effect of *Euphorbia heterophylla* on blood sugar level of diabetic rats⁴⁻⁹.

MATERIALS AND METHODS

Plant material

Fresh leaves of *Euphorbia heterophylla* used for the study were collected from several crop

fields near to Hyderabad. Dirt was removed from the plant by rinsing in clean water and used for extraction.

Animals

Healthy female Albino Wistar rats weighing 180-200gms, procured from Mahaveer enterprises, Hyderabad, India were used for the study. The animals were kept and maintained under standard conditions (12h light and dark cycle and room temperature at 25^o C) and were fed with standard pellet diet and water *ad libitum*. They were housed in polypropylene cages. The rats were used after an acclimatization period of seven days to the laboratory environment.

Acute toxicity study

Healthy adult wistar albino rats of either sex starved overnight, were divided into four groups (n=6) and were orally fed with aqueous extract of *Euphorbia heterophylla* in increasing doses of 100, 500, 1000, 3000mg/kg body weight where the rats were observed continuously for 2hr for behavioral, neurological and autonomic profiles, and then at 24 hr and 72 hr for any lethality.¹⁰

Chemicals

Alloxan monohydrate was purchased from Qualikems, New Delhi, India. Sodium CMC was purchased from Merck Chemicals, Mumbai, India. Glibenclamide was purchased from Orchid labs, Chennai, India. All other chemicals used for the study were of analytical grade.

Instruments

One Touch Horizon glucometer (Johnson & Johnson).
One Touch Horizon glucose strips.

Methodology

Preparation of plant extract

Aqueous extract of *Euphorbia heterophylla* was used for the study. Fresh leaves of *Euphorbia heterophylla* were boiled in water for about 15-20 minutes. The boiled drug-water mixture is cooled and filtered. The total extract obtained was concentrated under vacuum and dried completely. A yellowish brown powder of characteristic smell was obtained. The powder was stored at cool temp. (4^oC).

Induction of diabetes

Diabetes was induced in healthy albino wistar rats by administering freshly prepared Alloxan

monohydrate in normal saline solution at a dose of 150mg/kg intraperitoneally.

The animals were fasted overnight before the administration of Alloxan.

One hour after alloxan administration each rat was given 2.5 ml of 2% glucose solution orally and standard pellet diet was provided after that.

48 hours after alloxan administration fasting blood glucose levels of all the rats was estimated by using Glucometer. Animals with blood glucose levels above 200 mg/dl were selected for study.

Drug treatment

Animals whose fasting blood glucose levels are ≥ 200 mg/dl were divided into five groups of six animals each.

On the day of experiment over night fasted rats were taken and drugs were administered to each group in the following manner.

Group I

Animals in this group served as **diabetic control** and received 1ml of 1% sodium CMC (vehicle) orally.

Group II

Animals in this group received **Glibenclamide** at a dose of 10mg/kg orally.

Group III

Animals in this group received aqueous leaf extract of *Euphorbia heterophylla* at a dose of 150mg/kg orally.

Group IV

Animals in this group received aqueous leaf extract of *Euphorbia heterophylla* at a dose of 300mg/kg orally.

1% sodium CMC is used as vehicle for all the drugs and extract.

All drugs were administered orally by using oral feeding tubes.

Blood glucose level determination

Blood glucose level was estimated by using One touch horizon glucometer. Initial or 0 hr blood glucose levels were determined before the administration of drugs and extract. After drug administration blood glucose level was determined at intervals of 1sthr, 2ndhr, 4thhr, 8thhr and 12thhr of drug administration. Blood was collected from the tail by Tail snipping method. All the animals were fasted throughout the experiment (i.e. till the end of 12th hr blood glucose level estimation)

RESULTS AND DISCUSSION

Group I animals received 1% sodium CMC orally. There was no significant decrease in blood glucose levels when 1% sodium CMC was administered orally. The percentage reductions in blood glucose levels at 0hr, 1st

hr, 2nd hr, 4th hr, 8th hr and 12th hr were found to be 0%, 2.42%, 4.65%, 11.47%, 12.84% and 14.86% respectively. The peak reduction in blood glucose level was observed at 12th hr. This suggests that 1% sodium CMC, which is used as vehicle, has no hypoglycaemic activity. Glibenclamide, which is a chemically a sulfonylurea has been proved to have hypoglycaemic activity and has been used as a standard drug in Group II animals. The percentage reductions in blood glucose levels at 0hr, 1st hr, 2nd hr, 4th hr, 8th hr and 12th hr were found to be 0%, 30.15%, 40.3%, 62.78%, 46.48% and 41.74% respectively. The peak reduction in blood glucose level was observed at 4th hr. aqueous leaf extract of *Euphorbia heterophylla*, which is our test drug, was administered orally to Group IV animals at a dose of 150 mg/kg. The percentage reductions in blood glucose levels at 0hr, 1st hr, 2nd hr, 4th hr, 8th hr and 12th hr were found to be 0%, 13.08%, 28.5%, 49.7%, 61.6% and 56.75% respectively. The peak reduction in blood glucose level was observed at 8th hr. Aqueous leaf extract of *Euphorbia heterophylla*, which is our test drug, was administered orally to Group IV animals at a dose of 300 mg/kg. The percentage reductions in blood glucose levels at 0hr, 1st hr, 2nd hr, 4th hr, 8th hr and 12th hr were found to be 0%, 31.36%, 41.18%, 54.58%, 59.1% and 45.64% respectively. The peak reduction in blood glucose was observed at 8th hr. As *Euphorbia heterophylla* consists of mainly methyl esters and derivatives,

diterpene polyesters, sesquiterpenes, a small percentage of monoterpenes and aliphatic compounds, quercetin and other bioflavonoids, etc; it may be responsible for the anti hyperglycemic activity.

CONCLUSION

From the results obtained it is observed that aqueous leaf extract of *Euphorbia heterophylla* when administered orally to Group III and IV at a dose of 150 mg/kg and 300 mg/kg respectively, it has shown significant reduction in blood glucose levels of diabetic rats. This reduction seems to be dose dependent as it has shown more reduction in blood glucose levels in-group IV than group III. From the above data we conclude that *Euphorbia heterophylla* possess significant anti-hyperglycemic activity.

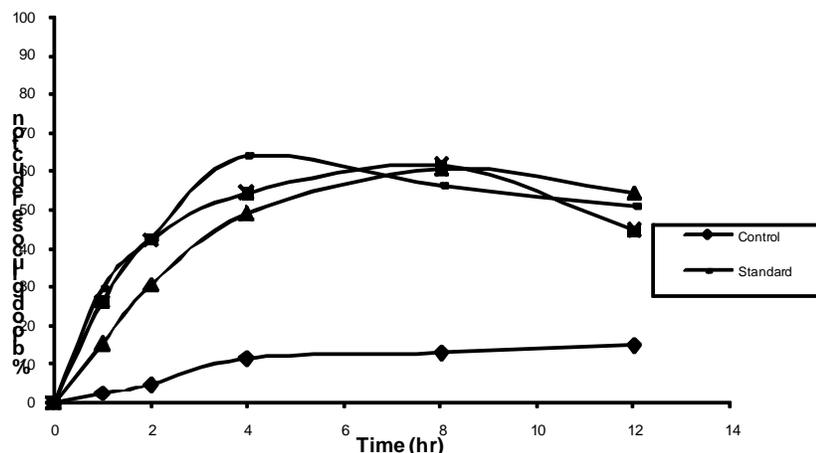
Future scope of the study: Significant research work is going on in diabetes research. Many active principles of plants which possess antidiabetic property came into limelight because of this. But research work on *Euphorbia heterophylla* did not receive much attention. The present work may be helpful in gaining attention towards *E. heterophylla*. Extension of our study in areas like, Effect of *E. heterophylla* on lipid levels, Insulin levels, Blood Glucose levels in normal and diabetic rats, Mechanism of Antidiabetic action etc, may produce valuable information that will be helpful in the field of diabetes research.

Table I:

Time (hr)	Blood glucose levels & % reduction in Alloxan induced diabetic rats							
	Vehicle (1% sodium CMC) mean \pm SEM mg/dl	% Red	glibenclamide (10mg/kg) mean \pm SEM mg/dl	% Red	<i>Euphorbia heterophylla</i> (150 mg/kg) mean \pm SEM mg/dl	% Red	<i>Euphorbia heterophylla</i> (300 mg/kg) mean \pm SEM mg/dl	% Red
0	329.6 \pm 5.1	0	323.8 \pm 24.6	0	351.5 \pm 18.4	0	354.5 \pm 28	0
2	321.5 \pm 4.1	2.42	226.16 \pm 20.2	30.15	305.5 \pm 21.1	13.08	243.3 \pm 23.9	31.36
4	314.3 \pm 4.9	4.65	193.3 \pm 17.4	40.3	251.1 \pm 17.6	28.5	208.5 \pm 11	41.18
6	291.8 \pm 15.2	11.47	120.4 \pm 7.69	62.78	176.6 \pm 16.8	49.7	161 \pm 9.6	54.58
8	287 \pm 15.1	12.84	173.3 \pm 5.37	46.48	134.6 \pm 8.4	61.6	144.8 \pm 9.3	59.1
12	280 \pm 14.83	14.86	188.6 \pm 6.5	41.74	152 \pm 13.5	56.75	192.6 \pm 22.7	45.64

Table II:

Time (hr)	% reduction in Alloxan induced diabetic rats			
	Vehicle (1% sod. CMC) Orally (A)	glibenclamide (10mg/kg) Orally (B)	Euphorbia heterophylla (150 mg/kg) Orally (C)	Euphorbia heterophylla (300 mg/kg) Orally (D)
0	0	0	0	0
2	2.42	30.15	13.08	31.36
4	4.65	40.3	28.5	41.18
6	11.47	62.78	49.7	54.58
8	12.84	46.48	61.6	59.1
12	14.86	41.74	56.75	45.64



Graphical Representation of % Blood Glucose Reduction in Rats

REFERENCES

1. Wild S, Roglic G, Green A, Sicree R and King H. Global prevalence of diabetes: estimates for 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047-53.
2. Rother KI. Diabetes treatment—bridging the divide". *The New England Journal of Medicine* 356 (15):1499-501. L M Tierney, S J McPhee, M A Papadakis (2002). *Current medical Diagnosis & Treatment*. International edition. New York: Lange Medical Books/McGraw-Hill. 2007;1203-15.
3. Bremer K. *Asteraceae cludistics and classification*, Timber press Portland ,Oregon, 1994.
4. Omale James and Emmanuel T. Phytochemical composition, bioactivity and wound healing potential of euphorbiaheterophylla (euphorbiaceae) leaf extract.
5. Department of Biochemistry, Kogi State University, PMB 1008, Anyigba, Kogi State ,Nigeria.
6. Vamsidhar I, Mohammed AH, Nataraj B, Rao CM and Mullangi R. Antinociceptive activity of Euphorbia heterophylla roots. *Fitoterapia*. 2000;71(5):562-563.
7. Falodun A, Okunrobo LO and Uzoamaka N. Phytochemical and Anti-inflammatory evaluation of Methanolic extract of Euphorbia heterophylla Linn (Euphorbiaceae). *Afri J Biotech*. 2006;5(5):529-531.
8. Falodun A, Agbakwuru EOP and Ukoh GC. Antibacterial activity of Euphorbia heterophylla L. (Family - Euphorbiaceae). *Pakistan Journal of Scientific and Industrial Research*. 2003;46(6):471-472.
9. Falodun A and Agbakwuru EOP. Phytochemical analysis and laxative activity of the leaf extracts of Euphorbia heterophylla L. (Euphorbiaceae). *Pakistan Journal of Scientific and Industrial Research*. 2004;47(5):345-348.
10. Turner MA. In *Screening methods in pharmacology*. New York: Academic Press,1965;26.