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Research Article

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ANTI-DIABETIC ACTIVITY OF LEAVES EXTRACT OF *ZIZYPHUS NUMMULARIA* BY ALLOXAN INDUCED DIABETIC RAT MODEL

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Abstract The hypoglycemic effect of ethanolic leaves extract of *Zizyphus nummularia* was evaluated by alloxan-induced diabetic rats. Animals were induced alloxan for diabetes with (150 mg/kg bw i.p.) and treated orally with ethanolic leaves extract of *Zizyphus nummularia* (250 mg/kg & 500 mg/kg) and standard Glibenclamide (5 mg/kg). The extracts showed significant ($p< 0.01$& $p< 0.05$) anti-hyperglycemic activity as compared to diabetic control.

Keywords Hypoglycaemic, Ethanolic leaves extract, *Zizyphus nummularia*, Alloxan, Glibenclamide.

Introduction

According to WHO, the prevalence of diabetes is likely to increase by 35% by the year of 2025 currently there are over 150 million diabetics worldwide and this is likely to increase to 300 million or more. Statistical projection about India suggests that the number of diabetics will rise from 15 million in 1995 to 79.4 million by 2025, making it the country with the highest number of diabetics in the world [1-2]. Diabetes is a serious metabolic disorder with micro and macrovascular complication that results in significant morbidity and mortality [3]. Chronic hyperglycemia during diabetes causes glycation of body proteins that in turn leads to secondary complications affecting eyes, kidneys, nerves and arteries [4].

Ziziphus nummularia is a common plant of central India, its root, leaves and seed are used by tribes for curing different diseases like allergy, scabies, eczema and pyorrhea etc. The roots of *Ziziphus oxyphylla Edgew* and juice of fresh leaves of *Z. mauritiana L* are used for curing jaundice [5]. A cold suspension of dried roots powder of Ampelozyziphus amazonicus is used to prevent malaria [6]. Traditionally, *Origanum majorana L* is used in asthma, indigestion, headache, rheumatism and protect against hydroquinone induced cytogenesis and histological changes [7-8].

Material and Methods

Plant

Healthy and fresh leaves of *Z. nummularia* were collected from Mohan Lal Sukhadia University Campus, Udaipur (Raj). The collected leaves were washed with tap water to remove the dust particles. The leaves were shade dried for 10 to 15 days then powdered by electric grinder.

Extract preparation

The powder was passed through sieve no.30 and stored in a container. The powder of *Zizyphus nummularia* leaves were packed in a Soxhlet apparatus and extracted with distilled water for 18 hours. The obtained extract was dried at

45°C in hot air oven till solid/semisolid mass was obtained. Extracts were stored in air tight container in refrigerator below 10°C. The suspensions of aqueous and cold extracts were prepared by using normal saline as solvent for administration to experimental animals.

Animal selection

Healthy adult Wister rats of either sex weighing 150-180 g were selected for the study. The study was carried in accordance with the rules and regulations laid by the Institutional Animal Ethics Committee. The animals were housed with free access to food and water. Rats were starved 24 hr prior to the study.

Alloxan induced Anti-Diabetic Activity

Before starting the experiment, animals were separated according to their body weight. The animals were injected intra-peritoneally (i.p.) at a dose of 150 mg/kg b.w. alloxan monohydrate (S.D. Fine Chemicals Ltd., Boisar) freshly prepared in normal saline solution (Except normal control group i.e. Group I). After 4 hour of alloxan administration, animals were given feed *ad libitum* and 1ml of (100 mg/ml) glucose i.p. to combat ensuring severe hypoglycemia after 72 hr of alloxan injection; the animals were tested for evidence of diabetes by estimating their blood glucose level using glucometer (One touch, Johnson's & Johnson's) [9-11]. Diabetic animal selected for the experiment. And divided in four group. Group II (diabetic control), Group III (Extract treated 250 mg/kg) Group IV (Extract treated 500 mg/kg). Group V (standard treated**).** To the animals, the test extracts (250 mg/kg and 500 mg/kg b.w. orally) and standard drug glibenclamide tablets (5 mg/kg b.w. orally) were administered by dissolving in normal saline daily. The blood glucose level and body weight check on day 1^{st}, 3^{rd}, 7^{th} and 10^{th}.

Statistical Analysis

All the values of the experimental results were expressed as mean±SEM and analyzed for ANOVA followed by Dunnett's test.

Result and Discussion

Preliminary phytochemical screening

The preliminary phytochemical analysis of the extract of leaves of *Zizyphus nummularia* shows presence of flavonoids, saponins, alkaloids, mucilage, tannins and phenolic compounds.

Body weight

The table.1 shows the body weight of the normal and treated groups significantly differ from diabetic control on day 10. The treated groups animal body weight maintained throughout the experiment compare to diabetic control except.

Table 1: Effect of Ethanolic extracts of dried leaves of Zizyphus *nummularia* on body weight by Alloxan induced rats.

Treatment		**Body weight**			
		Day 1	Day 3	Day 7	Day 10
Group I	Normal Control	108.33+8.16	110.16±8.20	102.5±2.89	105.33±6.16
Group II	Diabetic Control	121.33±4.08	118±2.34	108.83±3.76	90.16+5.84
Group III	Glibenclamide (5 mg/kg)	131±6.32	121.66±4.36	114.17±3.76	110.83±3.76
Group IV	EtOH extract (250 mg/kg)	133.33±4.08	120±3.16	115±4.47	97.5±5.24
Group V	EtOH extract (500 mg/kg)	136.66±8.05	121.83±4.26	100.83±2.91	100.16±3.71

Blood glucose level

The hypoglycemic effect of the ethanolic extract of *Z. nummulari* leaves on the fasting blood sugar levels of diabetic rats is shown in the Tables 2.

Table 2: Effect of the *Z. nummulari* leaves EtOH extract on blood glucose level of alloxan-induced diabetic rats after s treatment.

Treatment		Blood glucose mg/dl			
		Day 1	Day 3	Day 7	Day 10
Group I	Normal Control	84.11±0.80	85.27±1.54	83.67±1.17	84.62±1.10
Group II	Diabetic control	188.74±1.50	190.04±1.20	192.31±1.42	193.88±1.38
Group III	Glibenclamide (5 mg/kg)	189.18±1.92	168.29±1.99**	172.16±2.22**	167.66±2.11**
Group IV	EtOH extract (250 mg/kg)	180.17±1.16	170.09±1.18	175.92±1.33*	173.34±1.09**
Group V	EtOH extract (500 mg/kg)	193.99±1.71	182.92±1.11**	170.68±1.63**	168.67±1.25**

Values are means±SEM; N=6. *P<0.05, **P<0.01 vs. diabetic control.

After treatment of 500 mg/kg showed a significant (P<0.01) reduction in the blood sugar level on day 3, where the extract at a dose of 250 mg/kg showed a significant (P<0.05) reduction in the blood glucose level on day 7 and showed a significant (P<0.01) reduction in the blood glucose level on day 10.

Conclusion

The present study demonstrated that the ethanolic leaves extract of *Zizyphus nummularia* could be useful in management of diabetes mellitus. Further study need to be isolate, identify the active compounds and find out the possible mechanism of actions**.**

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