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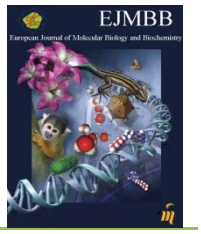

BLOOD GLUCOSE LOWERING EFFECT OF *CATHARANTHUS ROSEUS* IN ALLOXAN INDUCED DIABETIC RATS

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ABSTRACT
To investigate the blood glucose lowering effect of *catharanthusroseus* in alloxan induced diabetic rats. Study Design: Analyticals and Experimental study. Place and Duration: Animal house of Isra University, Hyderabad, Sindh from May to Novermber 2013. Forty male Wistar albino rats were selected according to inclusion and exclusion criteria. Animals were kept in separate stainless steel cages at normal temperature, 12 hour dark-light cycle and free access to chow and water. Rats were divided into four groups as; Group A: control (n=10), Group B: diabetic (alloxan treated control) (n=10), Group C: diabetics treated with *Catharanthus roseus* (n=10), Group D: diabetic treated with Glimepiride (n=10). Diabetes mellitus was induced by single intraperitoneal injection of Alloxan (Sigma Company) at the dose of 120mg/kg. Blood samples were taken on days 0, 7 and 14. Glimepiride was given orally at the dose of 0.1mg/kg and *Catharanthus roseus* at 125mg/kg. Data was analyzed on SPSS version 21.0. The continuous variables were analyzed by ANOVA and post Hoc Tukey-Cramer. The significant p-value was taken at ≤ 0.05. Significant differences were observed for blood glucose among groups on different days. The blood glucose was low in *Catharanthus roseus* compared with alloxan (p=0.001), however, it was more compared to glimepiride group (p=0.001). The finding suggests that *Catharanthus roseus* lowers blood glucose. The blood glucose lowering effect of *Catharanthus roseus* was inferior to glimepiride but it was observed. The present study concludes that the *Catharanthus roseus* shows blood glucose lowering effect in alloxan induced diabetic rat model.

INTRODUCTION

Worldwide, more than 1200 plants are available which are used for glucose lowering effect in Diabetes Mellitus (DM). The blood glucose lowering effects of these plants have been tested in experimental trials. These herbs are useful source of oral hypoglycemic compounds used as dietary supplements [1]. The herbs are less toxic and free of adverse effects compared to synthetic drugs [2].

The medicinal plants that have anti-hyperglycemic activity and commonly used for the treatment of DM include *Oivieri griseb* (Gentianaceae), *Bauhinia forficata koeingii* (Leguminosae), *Eugenia jambolana L.*(Myrtaceae), *Lactuca indica L.* Compositae), *Mucuna pruriens Bak. (*Leguminosae), *Tinospora cordifolia W.* (Menispermaceae), *Momordica charantia L.* (Cucurbitaceae), *Aporosa lindleyana* Baill

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(Euphorbiaceae), *Cogent db*, *Myrtus communis L.* (Myrtaceae), *Rhizoma Polygonati Odorati*(Liliaceae), *Terminalia pallida* Brand (Combretaceae), *Nigella sativa* L. 'Black cumin' (Ranunculaceae) and *Catharanthus roseus* (Apocynaceae). [3]. The development of complication of diabetes and metabolic abnormalities are delayed by the effects of these plants [4].

Cathranthus roseus (*C.roseus*) is commonly known as *Sadabhar* and in English called *Madagscar periwinkle*. Botanically, *C.roseus* belongs to the family Apocynaceae [5]. In Brazil, Cook Island, England, Pakistan, Taiwan, West indies and in Thailand the water decoction of the leaves and the whole plant is used for the treatment of diabetes mellitus [6]. This plant possesses wide range of pharmacological activities like anti-diabetic, anti-inflammatory, anti-hypertensive, anti-hypercholestesolemia, anti-malarial, anti-mutagenic, anti-oxidant, anti-viral, anti-diuretic, anti-fungal, anti-spasmodic, cardiotonic and anti-cancer activities [7].

Aqueous extract of *C.roseus* flowers and leaves are used to regulate blood glucose level in alloxan induced diabetic rats. In some studies, it is confirmed that the leaf juice of *Catharanthus roseus* has a more prolonged effect at the dose of 1.0 ml/kg than glibenclamide dose in the period of 24hr after treatment; this indicates prolonged antidiabetic action due to multiple sites of action exerted by *C.roseus*. In many studies, it is proved that *C.roseus* causes hypoglycemia due to its active principles like catharanthine, vindoline and vindolinine [8]. The rationale of present study was to evaluate blood glucose lowering effects of *C.roseus* in alloxan induced diabetic rat model.

MATERIALS AND METHODS

Analyticals and Experimental study was conducted on 40 male Wistar albino rats at the Animal house of Isra University, Hyderabad, Sindh from May to Novermber 2013. Normal healthy albino rats of 200-300 grams were selected, while female rats, sick and moribund animals were excluded. Animals were weighed and tagged, kept in separate stainless steel cages at normal temperature, 12 hour dark-light cycle and free access to chow and water. Forty rats were divided into four groups as; Group A: control (n=10), Group B: diabetic (alloxan treated control) (n=10), Group C: diabetic treated with *Catharanthus roseus* (n=10), Group D: diabetic treated with Glimepiride (n=10).

DM was induced in animals except the control group by single intraperitoneal injection of Alloxan (Sigma Company) at the dose of 120mg/kg dissolved in 0.5ml of acetate buffer. About 2-3ml of blood was drawn from the tail of rats, collected in vacutainers and centrifuged at 4000 rpm for 5 minutes to obtain serum. Blood samples were taken on days 0, 7 and 14. Body weight was measured simultaneously. The blood glucose test was performed on HITACHI ANALYZER 902. Hyperglycemia was confirmed by measuring random blood glucose after ten days by spectrophotometer. DM was defined as random blood sugar >200mg/dl on three successive days. Glimepiride 1mg tablet (Amaryl, Sanofi Aventis) was purchased from local pharmacy and administered orally at the dose of 0.1mg/kg [9]. The *C. roseus* were authenticated by the Botanist. Fresh flowers of *Catharanthus roseus* were administered orally at the dose of 125mg/kg [10]. Data was analyzed on SPSS version 21.0. The continuous variables were analyzed by ANOVA and post Hoc Tukey-Cramer. The significant p-value was taken at ≤ 0.05.

RESULTS

The results of body weight and blood glucose levels on Days 0, 7 and 14 are shown in tables I and II. Statistically significant differences were observed on day 14 for the body weight as shown in table I, while days 0 and 7 were non-significant. Significant differences for blood glucose levels were observed between groups on different days. The blood glucose levels as high as ≥350mg/dl were observed in the Alloxan treated group on day 7 and 14 with significant p-value (p=0.0001). The blood glucose levels were moderately elevated in *Catharanthus roseus* compared to Glimepiride group. The finding suggests that the *Catharanthus roseus* possess glucose lowering potential compared with Glimepiride. The blood glucose lowering effect of *Catharanthus roseus* was inferior than Glimepiride.

Table 1. Body weight (grams) in experimental animals (n=40)

Groups	Mean±S.D		
	Day 0	Day 7	Day 14
Control	235.0±8.4	228.0±23	228.0±23
Alloxan treated control	225.4±10.8	225.8±42	172.2±17
Catharanthus roseus	241.1±16.5	239.7±19	211.0±40
Glimepiride	241.1±16.5	239.9±24	223.5±30
p-value	p≥0.06	p≥0.07	p=0.001

Table 2. Blood glucose level (mg/dl) in experimental animals (n=40)

Groups	Mean±S.D		
	Day 0	Day 7	Day 14
Control	88.7±12.8	88.7±12.8	82.4±14.5
Alloxan treated control	233.9±27.9	248.1±53.8	340.0±38.5
Catharanthus roseus	204.5±40.5	192.6±41.2	191.2±49.4
Glimepiride	209.2±49.4	182.8±37.3	167.0±31.3
p-value	p=0.001	p=0.001	p=0.001

DISCUSSION

The present study is an original research work conducted on rat model at the animal house of Isra University. Currently the obesity is an ever increasing issue of urban population. As the obesity is one of the contributing factors of the metabolic disorders like DM, hence there is an urgent need to search into alternative molecules of herbal origin which may prove helpful in controlling DM.

The present study compared the blood glucose lowering effects of *Catharanthus roseus* with glimepiride. Alloxan was used to induce DM in rats. Alloxan-induced diabetes is one of the widely used models to study drugs in the experimental animals. Several studies had proved diabetogenic effect of alloxan in experimental animal [11].

The Natarajan et al studied effect of *Catharanthus roseus* on alloxan induced DM in a sample of 30 rats. The study reported positive effects on blood glucose and lipid levels. The findings of previous study are highly comparable to present study as blood glucose lowering potential of *Catharanthus roseus* is observed.

The study of Ibrahim et al aimed to evaluate anti-diabetic and anti-bacterial effects of whole plant extract of *Catharanthus roseus* in adult female Wistar albino rats. The previous study reported that the blood glucose was reduced with a concomitant increase in body weight in rats treated with *Catharanthus roseus* plant extract. The findings are highly in consistent with present study.

The Jayanthi et al [12] studied blood glucose lowering effects of *Catharanthus roseus* in alloxan induced diabetic rats. The body weight was increased while blood glucose reduced to normal in diabetic rats. The findings support the observations of present study. The Rajashree et al [13] proved that the blood glucose lowering effect of *Catharanthus roseus* results from an increase in glucose utilization by peripheral tissues or by enhanced secretion of insulin from the β-cells of Langerhans.

Another study by Mostafa et al [14] compared the blood glucose lowering effect of glimepiride with *Catharanthus roseus*, *Azadirachta indica*, and *Allium sativum*. Among herbs, the most potent glucose lowering agent was the *Azadirachta indica* which was as better as glimepiride. However, *C.roseus* exerted glucose lowering potential. Weight was maintained in present study in the glimepiride group, which is in agreement with the previous study [14].

The glimepiride is a potent anti-diabetic drug and present study has compared blood glucose lowering potential of *Catharanthus roseus* with glimepiride. The finding is of clinical importance as *Catharanthus roseus* may be used in treating DM, however further studies are warranted. The present study reports that the *Catharanthus roseus* shows blood glucose lowering potential in alloxan induced diabetic rat model. Further studies are recommended to be conducted in the future.

CONCLUSION

The present study concludes that the *Catharanthus roseus* shows blood glucose lowering effect in alloxan induced diabetic rat model, however, the effect was inferior to glimepiride. Further studies are warranted to be conducted to elucidate the possible mechanisms.

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