The Professional Medical Journal
www.theprofesional.com

ORIGINAL PROF-2833

HYPERGLYCEMIA;
CATHARANTHUS ROSEUS & NIGELLA SATIVA AMELIORATE IN ALLOXAN INDUCED DIABETIC RATS

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Article received on:
28/02/15
Accepted for publication:
07/05/2015
Received after proof reading:
08/08/2015

ABSTRACT…Objectives: To investigate blood glucose regulaitng effects of Catharanthus Roseus (C.roseus) and Nigella sativa (N.sativa) in alloxan induced diabetic rats. **Study Design:** Experimental study. **Place and Duration:** Animal house Isra University Hyderabad. From April to Novermber 2013. **Methodology:** 50 male rats were housed at normal température, 12 hour dark - light cycle with free access to chow and water. A single intraperitoneal bolus of alloxan (120 mg/kg) was given to induce diabetes mellitus. Glimepiride, C. roseus and N. Sativa were administered at doses of 0.1 mg/kg, 125 mg/kg and 50 g/kg respectively. Data was analyzed on SPSS version 21.0. Significant P - value was defined at ≤ 0.05. **Results:** C.roseus ad N.sativa showed blood glucose lowering potential but the effect was less when compared to glimepiride (P = 0.001). However, C. roseus was more effective compared to N.sativa (P = 0.001) in reducing blood glucose. Findings suggest that both C. roseus and N. sativa possess glucose regulating potential. **Conclusion:** It is concluded that the C. roseus and N. sativa exert blood glucose regulating effects in alloxan induced diabetic rat model.

Key words: Catharanthus roseus, Nigella sativa, Alloxan, Rats

Article Citation: Abbasi P, Memon AR, Abbasi ST, Kazi S, Siddiqui S. Hyperglycemia; catharanthus roseus & nigella sativa ameliorate in alloxan induced diabetic rats. Professional Med J 2015;22(8):1048-1052.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia caused by defective insulin secretion or its physiological function. Insulin deficiency disturbs metabolism of glucose, proteins and fats equally. World over, DM is the 5th leading cause of death. DM causes microvascular complications and increases mortality and morbidity due to complications.[1]

Many plants have been used for controlling hyperglycemia in diabetics. Reported herbs and plants include; Nigella sativa, Terminalia-pallida, Cogent db, Myrtus communis, Mucuna pruriens, Eugenia jambolana, Bauhinia forficata koeingii, Tinospora cordifolia, Lactuca indica, Momordica charantia, Oivieri-griseb and Aporosa lindleyana Baill. C. roseus has also been reported for lowering of blood glucose in diabetics.[2,3] Previous studies had reported that these herbs and plant inhibit and delay the complications of DM also.[3]

In English, C. roseus is known as Madagscar periwinkle while in Southeast Asia, it is famous as Sadabhar. Previous studies had reproted anti-hypertensive, anti-mutagenic, anti-fungal, anti-spasmodic, anti-cancer, anti-malaria, and lipid lowering effects of C. roseus. Anti-diabetic acivity

has also been attributed to C. roseus.[4] A previous study reported anti-hyperglycemic activity of C. roseus in alloxan induced diabetic rat model.[5] Studies had reported that the leaf juice of C. roseus exerts more prolonged glucose lowering than glibenclamide at a dose of 1.0 ml/kg and multiple cellular mechanisms had been proposed for its glucose lowering effects. Glucose lowering effects are exerted by its active ingredients like, vindoline, vindolinine and catharanthine.[5,6]

N. sativa belongs to Ranunculaceae family and is strong spicy herb. It is commonly known as black cumin.[7] Previous studies had reproted N. sativa as remedy for many disease such as acute bronchitis, auto-immumne disease, bacterial infection, hypertension[8], liver ailments, gastrointestinal disorders and allergic disease.[9] It is honored say of Holy Prophet (SAW) that the N. sativa cures all diseases except the death.[10] Beneficial effects of N. sativa had never been fully scrutinized, as it showed multiple beneficial effects to avert many chonic diseases. N.sativa is claimed of exerting insulinotropic action[11,12] and inhibiting liver gluconeogensis.[13] Anti-oxidative properties of N. sativa are produced by inhibition of eicasonoid synthesis and lipid peroxidation of membrane phospholipids. Thymoquninone is though to be the active ingredient of N.sativa and anti-hyperglycemia activity is attributed to it.[14] The rationale of present study was to evaluate blood glucose lowering effects of C.roseus and N.sativa in alloxan induced diabetic rats in comparison to glimepiride.

MATERIALS AND METHODS

An experimental study was conducted at the Animal house of Isra University, Hyderabad, Sindh from April 2013 to November 2013. A sample of 50 male Wistar albino rats was selected. Male Wistar Albino rats of 200 - 300 grams were included, while female rats, sick and moribund animals were excluded. Animals were weighed, tagged, and 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 five groups as ; Group A: control (n = 10), Group B: diabetic (alloxan treated control) (n = 10), Group C: diabetic was treated with C. roseus (n = 10), Group D : was treated with N. sativa (n = 10), Group E: diabetic rats 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 120 mg/kg dissolved in 0.5 ml of acetate buffer. 2 - 3ml of blood was drawn from the tail vein. Blood was collected in gel tubes 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 level was checked on HITACHI 902 CHEMICAL ANALYZER (Hitachi, Roche, USA). 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 (1).C.roseus was authenticated by the Botanist. Fresh flowers of C.roseus were given orally at the dose of 125mg/kg[15] and N.sativa at dose of 50g/kg.[16] Data was analyzed on SPSS version 21.0. (IBM, incorporation, USA) Normality of data was checked by Shapiro Wilks test. The continuous variables were analyzed using ANOVA and post Hoc Tukey-Cramer tests. 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. Body weight showed significant difference on day 14th ($P = 0.001$) on day 14th, but not on Days 0 and 7 as shown in table-I ($P > 0.06$ and > 0.07 respectively). Significant differences for blood glucose were observed among groups on different days ($P = 0.001$) as indicated by F – ratio and p – value of analaysis of variance. Blood glucose as high as ≥ 350mg/dl was noted in the alloxan treated rats on days 7 and 14 with significant P - value ($P = 0.0001$). Both C.roseus ad N.sativa showed blood glucose lowering potential but this effect was less when compared to glimepiride ($P = 0.001$). However, C. roseus was more effective compared to N.sativa

(P = 0.001) in reducing blood glucose. Findings suggest that C. roseus and N. sativa possess glucose regulating potential.

In summary, the glimepiride was most effective in lowering blood glucose levels compared to C. roseus and N.sativa, but later also showed blood glucose lowering effects.

	Mean±S.D (grams)		
	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
Nigella Sativa	241.1 ± 16.5	230.0 ± 10.5	192.8 ± 21.7
Glimepiride	241.1 ± 16.5	239.9 ± 24	223.5 ± 30
p-value	P ≥ 0.06	P ≥ 0.07	P = 0.001

Table-I. Body weight in experimental animals (n = 40)

	Mean ± S.D (mg/dl)		
	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
Nigella Sativa	211.3 ± 49.9	224.3 ± 58.5	231.2 ± 59.4
Glimepiride	209.2 ± 49.4	182.8 ± 37.3	167.0 ± 31.3
p-value	P = 0.001	P = 0.001	P = 0.001

Table-II. Blood glucose level in experimental animals (n = 40)

DISCUSSIONS

The present study is an original research work conducted at the animal house of Isra University. Currently, obesity is projecting as multiplying concern of ubran population. Obesity is one of the risk factors for DM, and is a metabloic disorder primarily of glucose metabolism. There is an urgent need to search into alternative molecules of herbal origin which may prove helpful in controlling obesity and diabetes mellitus both.

The oral antidiabetic drugs provide good glycemic control along with beneficial effects on dyslipidemia,[17] however, few studies indicated that these drugs are associated with risk of ischemic heart disease[18] and cardiac failure.[19] Thus, achievement of better glycemic control with minimal side effects is still a challenge of modern therapeutics.[20] The present study provides an insight into new herbal remedy for controlling hyperglycemia. Present study compared the blood glucose lowering effects of C. roseus and N.sativa compared with glimepiride.

A previous study of Kaleem, et al[21] reported the effects of N.sativa to protamine zinc insulin for blood glucose lowering and lipid peroxidation in streptozocin induced diaebtic rats. It was reported[21] that the N.sativa reduced blood glucose and exerted antioxidant effect in animal model.

The Natarajan, et al[22] studied effect of C. roseus in alloxan induced diaebtic rats. The study reported positive effects on blood glucose and lipid levels. The findings of previous studies are comparable to present study.

The study of Ibrahim, M. et al[23] aimed to evaluate antidiabetic and antibacterial effects of whole plant extract of C. roseus in adult female Wistar albino rats, and reported that the blood glucose was reduced with a concomitant increase in body weight in rats. The findings are in agreement with present study.

The Jayanthi, et al[24] studied blood glucose lowering effects of C. roseus in alloxan induced diabetic rats. The body weight was increased and blood glucose reduced to normal. The findings of present study also parallel to above mentioned report.

The Rajashree, et al[25] reported that the blood glucose lowering effect of C. roseus results through an increase in glucose utilization by peripheral tissues or by enhanced secretion of insulin from the β-cells. The findings are also comparable to present study.

Another study by Mostafa, et al[26] compared the blood glucose lowering effect of glimepiride with C. roseus, azadirachta indica, and allium sativum. Among herbs, the most potent glucose lowering agent was the azadirachta indica which was as better as glimepiride followed by C. roseus.

On the basis of witnessed observations of present study, it is reported that the C. roseus and N.sativa regulate and reduce blood glucose in alloxan induced diabetic rats. Further studies are recommended to be conducted in the future.

CONCLUSIONS

The present study concludes that the Catharanthus roseus and Nigella sativa regulate blood glucose in alloxan induced diabetic rat. Further studies are recommended to confirm the finidngs of present study.

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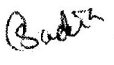
4	Dr. Sadia Kazi	Concept of study, data collection, data analysis and manuscript writing and checking	
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