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BLOOD GLUCOSE LOWERING EFFECT OF *Nigella sativa* IN ALLOXAN INDUCED DIABETIC RATS

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Research Paper

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ABSTRACT

Experimental study was carried out to investigate the blood glucose lowering effect of *Nigella sativa* in alloxan induced diabetic rats.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. 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 *Nigella sativa* (n=10), Group D: diabetics 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 *Nigella sativa* at the dose of 50g/kg. Data was analyzed on SPSS version 21.0. The continuous variables were analyzed by ANOVA with 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 *Nigella sativa* compared with alloxan (p=0.001), however , it was more compared to glimepiride group (p=0.001). The finding suggests that the *Nigella sativa* lowers blood glucose. The blood glucose lowering effect of *Nigella sativa* was inferior to glimepiride but it was observed. The blood glucose as high as ≥350mg/dl was noted in Alloxan group on days 7 and 14 (p=0.0001).

Key words: *Nigella sativa,* Alloxan, Diabetes mellitus,Glimepiride, Rats Sindh.

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INTRODUCTION

Nigella sativa is spicy herb belonging to a family Ranunculaceae and it is commonly as know as black cumin (Arayne et al., 2004). It is cultivated commonly in Europe, Middle East and Asia. In china it is called Hak jung Chou while in subcontinent, it is commonly called kalonji or kalajeera (Malviya et al., 2010). Recently, the pharmacological action and potential therapeutic activities of *Nigella sativa* have been proved for the management of many disease such as bronchitis, immumne disease , bacterial infection ,hypertension, liver disease, gastrointestinal disease and allergic condition (Zaoui et al., 2002; Kanter, 2007). In Islam it is well said that *Nigella sativa* can cure all diseases except the death (Paarakh, 2010). The many beneficial effects of *Nigella sativa* have not been satisfactorily scrutinized, but this plant possess many beneficial effects to avert many chonic diseases. Due to insulinotropic action (Farah et al., 2002 ; Rchid et al., 2004) and hepatic gluconeogensis (Farah et all.,2004) , *Nigella sativa* acts as antidiabetic agent. By the inhibition of eicosanoid generation and membrane lipid peroxidation *Nigella sativa* exhibits its antioxidative properties. The active compound in black cumin is thymoquninone which causes the antidiabtic action of *Nigella sativa (*Ilaiyaraja et al., 2010).

To confirm the effect of *Nigella sativa* on insulin sensitivity and release, many studies have already been conducted (Farah et al.,2004;Ilaiyaraja et al., 2010;Farah et al., 2002;Kanter., 2004). Recent studies have shown

Table1. Body weight (grams) in experimental animals (n=40).

	Mean±S.D		
	Day 0	**Day 7**	**Day 14**
Control	235.0±8.4	228.0±23	228.0±23
Alloxan control	225.4±10.8	225.8±42	172.2±17
Nigella Sativa	241.1±16.57	230.00±10.54	192.80±21.73
Glimepiride	241.1±16.5	239.9±24	223.5±30
p-value	p≥0.06	p≥0.07	p=0.001

that *Nigella sativa* prevents intensity of oxidative stress and improves insulin sensitivity (Bloch-Damti and Bashan, 2005). *Nigella sativa* increases the insulin sensitivity in peripheral tissues and enhances secretion of the β-cells of pancreas because it has been proposed that in pancreatic β-cells of STZ induced diabetic rats, the *Nigella sativa* has ability to restore its structural integrity. It is also observed that in the presence of 8.3mmol/L of blood glucose, the secretion of insulin is increased in the presence of *Nigella sativa* as has been checked in *in-vitro* isolated rat pancreatic islets (Rchid et al.,2004;Kanter et al.,2004). The reactive oxygen species (ROS) are generated by chronic exposure of hyperglycemia and are directly neurotoxic and promote neuronal apoptosis as it has been proposed from previous studies (Farah et al., 2002). *Nigella sativa* also have ability to delayed the complication related to the diabetes mellitus (Farah et al., 2010). The results of previous studies showed that through different mechanism, the *Nigella sativa* has anti diabetic properties (Kanter et al., 2004).

There are two important factors that contribute in the development of diabetic complication thay are hyperglycemia and dyslipidemia. *Nigella sativa* in various animal studies has shown beneficial effects in correcting both hyperglycemia and dyslipidemia (Kaleem et al., 2007). The present study was conducted to evaluate blood glucose lowering effect of *Nigella sativa* in alloxan induced diabetic rat model.

MATERIALS AND METHODS

Analytical and Experimental studies were 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 Nigella sativa (n=10), Group D: diabetic treated with Glimepiride (n=10).

Diabetes mellitus 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 2-3 ml 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. Diabetes mellitus (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 (Shukla et al.,). Nigella sativa was administered orally at the dose of 50g/kg (Mansi,2006). Data were analyzed on SPSS version 21.0. The continuous variables were analyzed by 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 1 and 2). Statistically significant differences were observed on day 14 for the body weight as shown in (Table 1), while days 0 and 7 were non-significant. Significant differences were observed for blood glucose among groups on different days. The blood glucose as high as 350mg/dl was observed in the alloxan treated group on days 7 and 14 with significant p-value (p=0.0001). The blood glucose was slightly more elevated in *Nigella sativa* compared to Glimepiride. The findings suggest that the *Nigella sativa* exerts glucose lowering effect, however, it was less effective compared to glimepiride.

DISCUSSION

Currently, obesity is an ever increasing issue of urban population. Obesity is one of the contributing factors of the metabolic disorders like dabetes mellitus, hence there is an urgent need to search into alternative molecules of herbal origin which may prove helpful.

The present study compared blood glucose lowering effects of *Nigella sativa* and glimepiride and conclusive results were observed. As reported previously, the

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

	Mean±S.D		
	Day 0	**Day 7**	**Day 14**
Control	88.70±12.80	88.70±12.80	82.40±14.50
Alloxan control	233.90±27.97	248.10±53.88	340.00±38.53
Nigella Sativa	211.3±49.9	224.3±58.5	231.2±59.4
Glimepiride	209.20±49.48	182.80±37.36	167.00±31.38
p-value	p=0.001	p=0.001	p=0.001

Nigella sativa may improve hyperglycemia and dyslipidemia through different mechanisms, similar findings have been observed in present study. (Rchid et al**.** 2004), reported that *Nigella sativa* stimulates β-cells of Islets of Langerhans of endocrine pancreas. Ali, (2004) reported that the *Nigella sativa* enhances partial regeneration and proliferation of β-cells of Islet of Langerhans.

The findings are consistent with present study as blood glucose lowering effect is confirmed. Another postulated mechanism of lowering of blood glucose is through reduced produciton of glucose from the liver, a mechanism called gluconeogenesis (Farah et al., 2002). Le et al. (2004), gave the opinion that the *Nigella sativa* reduces intestinal absorption of glucose from the lumen of gut. Ali, 2004 also reported that the *Nigella sativa* enhances the insulin effects on the target organs. The *Nigella sativa* has proved of lowering the blood glucose, however, the glimepiride was more effective. But again, the findings are of clinical importance as the *Nigella sativa* is a natural herb. The glimepiride is a potent antidiabetic drug. The present study concludes the role of herbs in lowering blood glucose.

The results of the present study are consistance with report (Zaoui et al.,2002) . Study proved the blood glucose lowering effect of *Nigella Sativa* and concluded that the *Nigella sativa* mediates its glucose lowering effect through enhancement of peripheral metabolism of glucose, an increase in insulin release and simultaneously a reduction in glucagon release or may be due to an intestinal reduction of absorption of glucose. The beneficial effects of *N. sativa* on diabetic control has been tested and proved in other animal studies (Altan et al.,2007;Kaleem et al.,2006).

The finding of blood glucose lowering effect of *Nigella Sativa* are consistent with previously studies as mentioned in literature. Kaleem et al., (2006) conducted study on 32 male Wistar albino rat model to compare the effects of *Nigella sativa* with *protamine zinc insulin* on blood glucose level and lipid peroxidation in Streptozocin induced rats. The study reported that the *Nigella sativa* reduces blood glucose level and exerts antioxidant effect in animal model. Thus it is suggested that the *Nigella sativa* exerts a blood glucose regulating effects comparable to drug molecule like glimepride in present study.

CONCLUSION

The present study concludes that the *Nigella sativa* shows blood glucose lowering effect in alloxan induced diabetic rat. However, the effect was less pronounced compared to glimepiride. Further studies are warranted to be conducted to elucidate the possible mechanisms of regulating the blood glucose.

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