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Anti-Diabetic Activity of *Ferula assafoetida* Extract in Normal and Alloxan-Induced Diabetic Rats

Ahmed Saber Abu-Zaiton
Department of Biological Sciences, Al-Hussein Bin Talal University,
P.O. Box 20, Ma'an, Jordan

Abstract: The aim of the present study was to evaluate the possible anti-diabetic potential of *Asafetida* extract against the pancreatic β-cells damage from alloxan-induced diabetes in rats and some hormones related to diabetes mellitus. *Asafetida* induced significant reduction in blood glucose and increasing of serum insulin, our data indicate that the level of glucose in the animals that subjected with alloxan was 10.28 ±0.85 mmol L^{-1} $p<0.05$ comparing with control group 3.27±0.25 $p<0.05$, the level of blood glucose in diabetic group when subjected with *Asafetida* extract decreasing to 6.75±0.31 $p<0.05$. There was significant amount of insulin secretion in diabetic animals when subjected with *Asafetida* extract 0.48±0.05 $p<0.05$ in comparison with diabetic animal's 0.33±0.06 $p<0.05$. These findings suggested that *Asafetida* extract treatment exerts therapeutic protective effect in diabetes by preserving pancreatic β-cells integrity and significant activity extract, which supports traditional usage to prevent diabetic complications.

Key words: Alloxan, *Ferula assafoetida*, insulin, hypoglycemic agent, diabetes

INTRODUCTION

Diabetes is growing epidemic around the world which consider as chronic incurable condition due to insulin deficiency that effects 10% of the population (Doreen *et al*., 2006). The number of diabetic people is expected to rise from present estimate of 150 to 230 million in 2025 (Iraj *et al*., 2009).

Drug treatment is not completely successful in the people with diabetes and there is a compelling need for better prevention and treatment strategies (Baynes and Thorpe, 1996). Studies revealed that about 75% of patients use some of form of complementary and alternative medicine CAM (Balde *et al*., 2006) even though physician knowledge, regulatory strands and evidence of safety and benefit are often lacking (Alarcon-Aguilara *et al*., 1998).

Now day's herbal medicines are highly recommended for the treatment of diabetes (Sebbagh *et al*., 2009) in spite of the therapeutic options (Grover *et al*., 2002). In the search of new opportunities for treatment diabetes mellitus, researchers turn to the methods of popular medicine (Mansi and Lahham, 2008). Since, antiquity peoples used different medicinal herbs as antidiabetic remedy because its consider to be less toxic and induce fewer side effect than synthetic ones (Venkateshs *et al*., 2007). One of the most popular herbal supplements which used as antidiabetic phytotherapies is (*Ferula assafoetida*) *Asafetida*.

The plant also used as stimulant to the mucous membrane, especially to the alimentary tract and therefore, is a remedy of great value as a carminative in flatulent colic and a useful addition to laxative medicine (Pepato *et al*., 2002). There is evidence that the volatile oil is eliminated through the lungs, therefore, it is excellent for asthma bronchitis, whooping cough, etc. Owing to its vile taste, which usually taken in pill form, but it's often given to infants A per rectum in the form of an emulsion (Shane-Mcwhorter, 2001).

Farida *et al*. (1987) and Nammi *et al*. (2003) reported that *Asafetida* to possess antidiabetic effect and have been used in many countries of Eastern Mediterranean and central Asia as an herbal medicine for treatment of diabetes, asthma whooping.

MATERIALS AND METHODS

Plant extraction: Materials from *Asafetida* plant were purchased from a local herb store in Taif city, Saudi Arabia 2008, voucher specimens have been kept in central laboratory at the department of biological sciences, Taif University, Saudi Arabia. The extract prepared by powdered 5 g of resin in liter of boiling water for 5 min, allowing the decoction to stand for 30 min and filtering it through paper filter. The filtrate was adjusted to concentration of 10 mg mL^{-1} of *Asafetida*.

Animal experiments: All rats were fed normal laboratory chow diet containing (w/w) 16% protein, 66%

carbohydrates and 8% fat and were housed under a 12:12 h light and dark cycle at 25°C. Experiments were conducted on adult albino rats with the weights of 180-220 g. Forty animals were divided into four groups: first group were injected with physiological solution, second group injected with alloxan, third group injected with *Asafetida* extract and fourth group with alloxan +*Asafetida*.

The diabetes was artificially caused in rats by intraperitonially injection of a 5% alloxan solution at dose of 150 mg kg^{-1} (Prince and Menon, 2000). An experimental group of normal and alloxan-diabetic rats was subjected to daily injection of *Asafetida* extract at dose of 0.2 g kg^{-1} for 14 days while a control group of normal and diabetic rats received physiological solution for the same length of time.

Collection of blood and analytical procedure: By the end of each experiment, the rats were reweighed, starved for 24 h and sacrificed under chloroform anesthesia. Three milliliter of blood was collected from each animal by cardiac puncture. The blood sample was put into test tubes and allowed to clot for 30 min before centrifuging using a bench top centrifuge. They were stored at 4°C in refrigerator before the analysis of glucose by Nelson Somogyi's method (Howk *et al*., 1954) using a visible spectrophotometer. Serum Insulin were measured by radioimmunoassay methods (CEA-JRE-SORIN Firm, France).

Data and statistical analysis: The data were analyzed with one way ANOVA in SPSS 10. Duncan's test was used in all data appropriate. All data were expressed as Mean±SE. $p<0.05$ was considered significant.

RESULTS AND DISCUSSION

Use of herbal medicine is a common practice in many countries, particularly in Asia (Chacko, 2003), America (Poss *et al*., 2003) and Africa (Shapiro and Gong, 2002).

In present study, the results show that the baseline weights of the rats at the beginning of the study were similar in all groups at the end of experiment significant weight loss observed in alloxan induced diabetic rats than control normal rats. The finding of our study agrees to reports of study Giovanni and Marcelo (2006) that showed treatment with extract of *Asafetida* improved the weight gain compared to untreated diabetic rats (Table 1).

In this study, it is shown that the extract of *Asafetida* resulted in decreasing of blood glucose when subjected in diabetic animals 6.75±0.31 mmol L^{-1} $p<0.05$, in comparison with alloxanic group 10.28±0.20 mmol L^{-1}

Table 1: Mean values of body weights of the different groups of rats (g)

Parameters	Control	*Asafetida*	Alloxan	Alloxan+*Asafetida*
Initial body weight (g)	209±8	198±10	210±7	195±11
Final body weight (g)	205±6	209±8	186±9	196±6

Table 2: Concentration of serum glucose and insulin hormone in normal and diabetic rats in case of *Asafetida* administration

Parameters	Control	*Asafetida*	Alloxan	Alloxan+*Asafetida*
Blood glucose (mmol L^{-1})	3.27±0.25	4.23±0.33	10.28±0.20	6.75±0.31
Insulin (ng mL^{-1})	0.72±0.09	0.86±0.15	0.33±0.06	0.48±0.05

$p<0.05$. Numerous studies have found that the blood glucose level increased significantly in animals that injected with alloxan (Calca *at al*., 1983; Khosia *at al*., 1995; Szudelki, 2001).

At the end of experiments the level of insulin in group of alloxan subjected was decreased, reaching 0.33±0.06 ng mL^{-1}, $p<0.05$ in comparison with the control level of 0.72±0.09 ng mL^{-1}, $p<0.05$. At the same time in animals which were subjected to administration of *Asafetida,* the concentration of insulin increased (0.86±0.15 ng mL^{-1} $p<0.05$). However, extract of *Asafetida* produce clear effect on the level of insulin and blood glucose (Table 2).

Alloxan, abeta-cytotoxin causes a massive destruction of β-cells of the islets of Langherhans resulting in reduced synthesis and release of insulin (Szudelki, 2001). It is well established that sulphonylureas produce hypoglycemia by increasing the secretion of insulin from pancreas and these compounds are active in mild alloxan-induced diabetes whereas they are inactive in intense alloxan diabetes (Kameswara *et al*., 1997). The concentration of insulin and glucose in blood serves as the quantitative index in our study.

It is well known that during the evolution of diabetes mellitus in rats, after administration the alloxan, the function of the insulin system is suppressed, which is expressed by high level of hyperglycemia (Pepato *et al*., 2002). In animals, which were subjected to administration of alloxan, the capacity of pancreatic β-cells to adequately secrete insulin is being disturbed depending on the level of glycemia. Extract of *Asafetida* used traditionally by diabetic patients in Saudi Arabia and some Arab regions. Due to this reason, the extract evaluated and the data confirm the traditional indications.

We propose the following mechanism of *Asafetida* action on the normalization of blood glucose: it has proved that the effect of *Asafetida* on the secretion function of the pancreas is a result of their direction correlation with the cell membranes. By means of the carrier, Glut-2 the glucose enters the β-cells of the pancreatic Islets Langherhans, where during metabolism ATP created (Guyton and Hall, 2000). It is supposed that

ATP production stimulates the insulin secretion by changing the membrane potential, which finally ensures the Ca^{2+} ion flow into cytoplasm (Foster, 1994). The created ATP induces the closing of potassium canals it prevent the exit of K^+ from the cell, resulting in accumulation of positive charges within the cell and accordingly in depolarization of the membrane (Kennedy and Baynes, 1984). After reaching the limit, the potentially sensitive Ca^{2+} canals are opening ensuring the Ca^{2+} ion flow into the cells. The sensitive to Ca^{2+}, K^+ canals are opening according to the entering of Ca^{2+} into the cell, which causes the exit of K^+. Our extract of *Asafetida* has a high concentration of calmodulin which transports Ca^{2+} in β-cells. The sensibility of the β-cells to Ca^{2+} is increased by the action of other secondary messengers. Ca^{2+} stimulate the tyrosine kinase leading to activation of insulin and its secretion from the cell. Insulin is binding with the cell receptors, activating the transformation process ATP→AMP (Chacko, 2003; Guyton and Hall, 2000). The created energy ensures the entrance of glucose into the cell through the Glut-4 carrier, under this condition the content of glucose in plasma is normalizing.

CONCLUSION

From results, it was concluded that the *Asafetida* extract stimulate the changes of the functional state of pancreatic β-cells and may have beneficial effect by partly preserving or restoring pancreatic β-cells mass in the alloxan-induced diabetes rat model. At the same time the capacity of the organism to produce and secrete insulin is increasing, the glucose level in blood is decreasing. Our study clearly indicated a significant activity extract of *Asafetida* as antidiabetic and support traditional usage to prevent diabetic complications.

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