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The effects of Anderoctonus Crassicauda scorpion venom in the treatment of Diabetes Mellitus type 1 in Animal models

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ABSTARCT

Diabetes Mellitus is one of the most prevalent endocrine disorders in the world [4]. The symptoms include polydipsia and polyuria [11,14]. Scorpion venom contains various proteins including phospholipase A2, which has been extensively studied secondary to its presumptive medical effects [12]. In the following research, the effects of Anderoctonus Crassicauda scorpion venom in diabetic rats was studied. Diabetes was induced in rats by using alloxan monohydrate. In this study, Wistar rats with a mean body weight of 220 ± 30 gr were randomly selected. Twenty five rats were divided into five groups including the control(non diabetics) , Diabetic control, and three treatment groups and underwent observation for a period of 8 weeks. Blood samples were taken on schedule, and blood glucose level was measured using Glucometer. At the end of the 8-week period, significant difference was found between the treatment group receiving a higher dose of scorpion venom and Analysis of variance (ANOVA) was applied in our statistical data with a P value of <0.05 . Hence, it can be concluded that scorpion venom is effective in treating the pancreatic Beta cells.

Key words: Scorpion venom, Alloxan monohydrate , Rat, Diabetes

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INTRODUCTION

Diabetes is a prevalent illness in Iran. According to the latest statistics of the World Health Organization, there is a daily worldwide growth of this disease, particularly in Asia[2 , 4] Diabetes manifests in two types: type 1 and type 2. In type 1, there is destruction of pancreatic Beta cells, which leads to the inability to synthesize insulin. The major symptoms include polydipsia and polyuria [11]. Type 1 Diabetes is treated by administering exogenous insulin. Animal models have been used in scientific and medical researches for a long time. In recent years, much attention has been given to the venom of some animals in development of new treatments for various diseases including Diabetes. Such as, bee venom has been previously shown to have therapeutic effects in diabetic rats. Recently, scorpion venom has also been found to be effective in treating diabetes [3,12]Scorpion is one of most primitive creatures on earth, which has existed since more than 300 million years ago. Scorpion is not only the oldest member of the Arachnidas class, but also one of the oldest Arthropoda on earth. The conventional use of animal toxins by humans is rooted in the far past, and among all, the scorpion venom has a special place [5,16].The black Anderoctonus crassicauda scorpion (olivier 1807) belongs to the Buthideae family. The scorpion venom is soluble in water, with a pH of neutral to alkaline. It is composed of oligopeptides, nucleotides, amino acids, and other organic compounds. It also contains enzymes such as phospholipases, hyaluronidase, and low-molecular weight compounds such as serotonin, histamine, protease inhibitors and histamin releasers [1,18]. The components of scorpion venom which contain a high molecular weight stimulate an immune response. hyaloronidase and phospholipase A2 are among such compounds.[1,5] .Based on previous studies pertaining to the therapeutical properties of scorpion venom, the following research was conducted to examine the effects of scorpion venom in the treatment of adult Wistar rats in which diabetes was induced by suing alloxan monohydrate.

MATERIALS AND METHODS

The scorpions were collected in the cities of Omidieh and Aghajari in the province of Khuzestan, Iran. They were captured at nights by using flashlights known as the Black Light. After separating the Anderoctonus Crassicauda scorpions, electroshock devices were used to extract and produce pure venom. To extract the venom, an electrode is connected to the body of the scorpion, and another electrode is connected to the poison gland. Then the scorpion is briefly shocked by passing a weak wave of electricity through the electrodes. As a result, venom is released and collected in the fang tubes. A voltage of between 6 to 10 was used for this purpose. After venom was extracted, it was dried by using a freezedryer and then was refrigerated with a temperature of 2-4 degrees of Celsius [16] .In this study, 25 male Wistar rats with a body weight of between 220 ± 30 grams were used. These rats were purchased from the Institut Pasteur tehran, and were kept in the animal laboratory of the Sciense and Research University branch of Tehran. The animals were kept under a 12-hour light and 12-hour dark schedule in a temperate of 22 degrees of Celsius with optimal humidity. They were allowed to freely feed on typical rat food and water [7]. Alloxan monohydrate (sigma-Aldrich, Germany) was used to induce diabetes in rats with a dosage of 180 mg per kilogram rat body weight. It was introduced into the body of rats through intraperitoneal injections. 72 hours after injecting rats with 180 mg/kg of alloxan monohydrate, the diabetes criteria which includes a blood glucose level of above 280 mg/dl [14]appeared in rats, as well as the typical diabetic symptoms of polydipsia, polyuria, and weight loss [14,11] , Median level of blood glucose in Diabetic rats were between 650-700 mg/dl. The therapeutic process was conducted by using the venom of Anderoctonus crassicauda and redistilled water, which were injected into rats intraperitoneally daily in sub-lethal doses of 0/1, 0/01 , 0/05 mg/kg [13]

The experimental rats were randomly divided into 5 groups, each consisting of 5 rats:
1) The control group: healthy rats which received distilled water
2) The diabetic control group: rats in which diabetes was induced by intraperitoneal injections of 180 mg/kg of alloxan monohydrate. redistilled water was used as a solvent.
3) The diabetic treatment group: rats which received 0/1 mg/kg dose of scorpion venom
4) The diabetic treatment group: rats which received 0/01 mg/kg dose of scorpion venom
5) The diabetic treatment group: rats which received 0/05 mg/kg dose of scorpion venom

RESULTS

1) The result of the impact of intraperitoneal injection of 180 mg/kg alloxan monohydrate on rat blood glucose level measured in mg/dl is shown in figure 1. Blood glucose level is significantly increased in the diabetic placebo group (576/2 ± 21/24) in comparison with the control group (92/6 ± 3/974) with p<0/05.

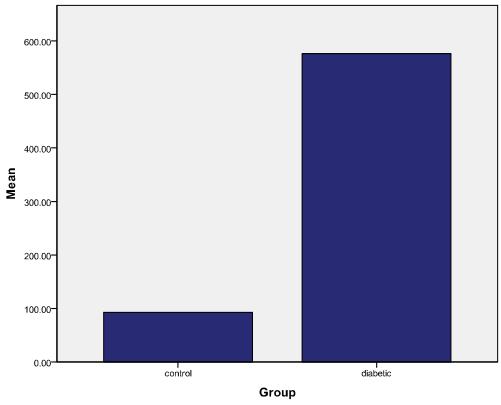

Figure 1: Comparison chart of blood glucose control and diabetic groups after injection of alloxan monohydrate . Results as (Mean ± SEM) are reported.

2) The result of using three different doses of scorpion venom through a 8-week treatment period and the subsequent effects on blood glucose level in mg/dl is demonstrated in table one. The blood glucose level in the diabetic placebo group was(576/2 ± 21/24) in comparison to the control group which had a blood glucose level of(92/6 ± 3/974). The difference was statistically significant with p<0/05. Furthermore, comparing the blood glucose level of the diabetic control group and the diabetic treatment groups indicated that there is a significant decrease in blood glucose in the diabetic treatment groups which received sub-lethal doses of scorpion venom.

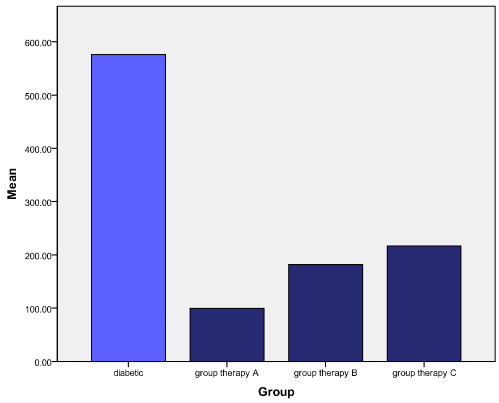

Figure 2:The effect of scorpion venom Anderoctonus Crassicauda on blood Glucose level after 8 weeks of treatment in the treated group compared with Diabetic control group shows.Results as (Mean ± SEM) are reported.

3) The result of the impact of injecting 3 different doses of scorpion venom (groups A, B, and C) on rat blood glucose level after a treatment period of 8 weeks is shown in figure 3. Groups A, B, and C received scorpion venom in the dosages of 0/1, 0/01, and 0/05 mg/kg respectively. There was a significant decrease in blood glucose level in group A (99/06 ± 5/504) compared to group B (182/0 ± 54/49). However, there was not a significant difference between group B and group C (216/6 ± 57/55).

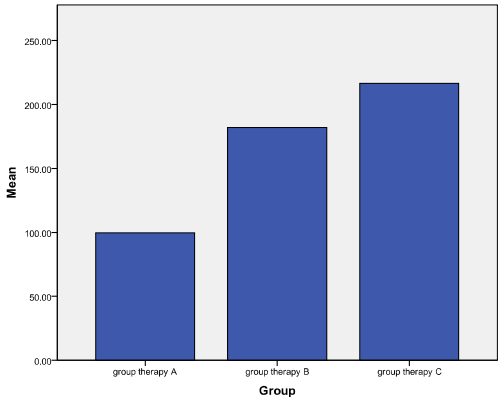

Figure 3: Comparison chart of blood glucose in group treated with three doses of 0/1 ,0/01 ,0/05 mg/kg after injection of scorpion venom. .Results as (Mean ± SEM) are reported

DISCUSSION

In this study, the destruction of pancreatic Beta cells by alloxan monohydrate, and the subsequent increase in blood glucose was demonstrated. This was similar to the findings of [27]

Diabetes was induced in rats by using intraperitoneal injections of 180 mg/kg alloxan monohydrate (sigma-Aldrich Germany), which is soluble in physiological serum, or redistilled water [25, 26]

In a study in 2011, components of scorpion venom elicited new anti-diabetic activities in rats in which diabetes was induced by using streptozotocin. In this study, the diabetic rats received 0/2 mg/kg of scorpion venom daily for a period of 5 weeks. Subsequently, weight loss, decrease in the level of blood glucose and fat, and an increase in insulin was observed in diabetic rats. Furthermore, there was a significant increase in the number and volume of Beta cells [12]

The result of researches conducted by Weidong xie et.al confirms our study in that scorpion venom could be used in treating diabetes. Also, the dosages used in our study were less than those in the Weidong study. Hence, it can be concluded that even smaller doses of venom can produce therapeutic effects.

As phospholipase A2 is the main component of scorpion venom, we conclude that this enzyme provides important therapeutic effects in treating diabetes. [12]

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