EFFECTS OF NIGELLASATIVA AND ALLIUM SATIVUM ON TYPE 1 DIABETES

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Abstract:

Allium sativum (Garlic) and Nigella sativa (Black cumin) are widely used as food seasoning or traditional medications in many countries. Their effects on STZ induced type 1 diabetes in rats were compared.Type 1 diabetes induced to rats by injecting STZ. The oil extracts of A. sativum and N. sativa were peritoneally injected daily at concentrations of 10 mg/kg, 20 mg/kg for A. sativum and 7 mg/kg or 14 mg/kg for N. sativa. Compared to the untreated group, the two groups treated with A. sativum and the two groups treated with N. sativa showed marked recoveries in some physiological aspects. The data showed marked improvements in body weights for all treated groups especially the groups treated with A. sativum, and after four weeks body weights were improving whereas body weights for untreated group were decreased. FBG levels in the group treated with 10mg/kg A. sativum showed the best improvement, but by the end of the month all treated groups FBG levels were less than half of the blood glucose levels for untreated group but still about twice of that in the normal animals in the control group. Blood insulin levels in the group treated with 20 mg/kg A. sativum was 81% of the control, but all the other groups were also higher than that of the untreated group. In fact, A. sativum showed better results compared to N. sativa but both plants showed improving of the conditions of type 1 diabetes.

Key words: Nigella sativa, Allium sativum, diabetes, STZ, FBG, Insulin

Introduction

Diabetes mellitus (DM) is a very common endocrine disorders accompanied by metabolic disorders. This chronic system disorder characterized by hyperglycemia and metabolic abnormalities including carbohydrates, proteins and lipids metabolisms resulting from defects in insulin secretion, insulin action, or both [1]. Type1 Diabetesmellitus is a chronic disease occurs when the immune system attacks and destroys the insulin-producing ß-cells in the islets of Langerhans of the pancreas [2]. Insulin is considered to be the only treatment for Type1 Diabetesmellitus patients, and as it is a biochemical agent it causessome side effects [3]. Diabetes mellitus could be induced in experimental animals by administering Streptozotocin (STZ) to the animals which will be transported into pancreatic beta-cells through glucose transporters in the cell membranes and attacks mitochondria [4]. It is clearly confirmed that streptozotocin is widely used to induced type 1 diabetes in animal models such as rats and mice[5].

Allium sativum is known by many common names such as Softneck Garlic, Hardneck Garlic, and Rocambole [6]. Allium sativum originated in central Asia and spread to Southwest Asia and the Mediterranean region also used for human consumption more than 10 million years ago [7]. Allium sativum has been used in herbal medicine for centuries for various ailments such as diabetes and cardiovascular risk factors. The essential of Allium sativum was recognized many centuries in early Chinese, Egyptian and Indian civilization as herbal or traditional medicinal agent [8].

The seeds of Nigella sativa are known by many different names like black seeds or black cumin[9,10]. In Arabic it is called ‘HabbahSawda’ or ‘Habbat el Baraka’ translated as ‘seeds of blessing’ while in old Latin, it is known as ‘Panacea’ meaning ‘cure all’. It is also a famous saying by the Prophet Muhammad (SAW) "Hold on to use of the black cumin seed, for it has a remedy for every illness except death" [11].

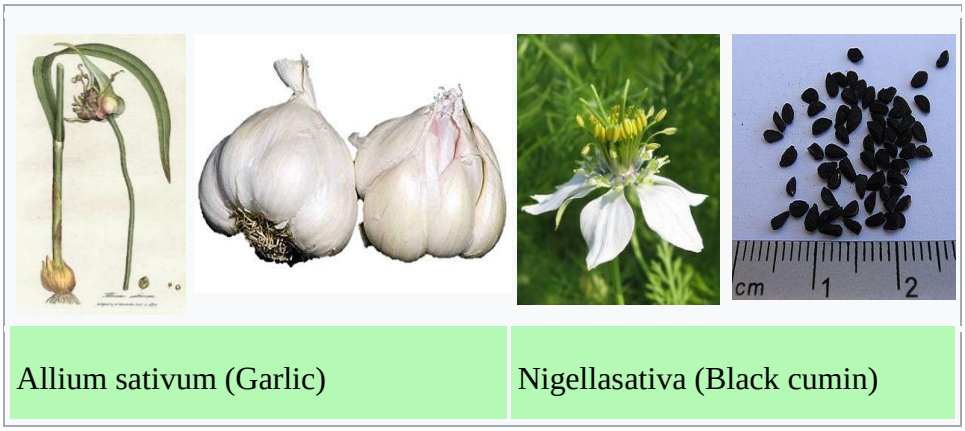

Figure1: The A. sativum and N. sativa plants.

The aim:

The aim of our project is to investigate the effects of A. sativum and N. sativa on body weight, blood glucose levels and blood insulin levels in type 1 diabetic rats. This investigation will compare the effects of the extracts of these two plants on these three parameters.

The experiment

This study was designed to compare the effects of A. sativum and N. sativa extracts on rat model. A total of 36 rats were divided into six groups. The first group was used as a negative control and was not treated with any substances. The other five groups were injected with a single dose of 65 mg/kg body weightStreptozotocine (STZ) to induce type 1 diabetes. The first group was kept as a positive control with no further treatments. The second and third groups were treated with interperitoneallyinjection of A. sativum (10 mg/kg for the second group and 20 mg/kg for the third group)for 30 days. The fourth and fifth groups were interperitoneally injection withN. sativa (7 mg/kg for the fourth group and 14 mg/kg for the fifth group) for 30 days. Body weights and blood glucose levels were recorded at day zero and every week for all groups. By the end of the experiment, the animals were killed and blood was harvested to measure insulin levels. The data were collected and analyzed.

Results

The effect of A. sativum and N. sativa on body weights:

The changes in body weights were expressed as percentages of the weightin day zero as illustrated in figure 2. As can be seen in the figure the body weights in the control group had an increase of 7% at the end of the first week and 31% at the end of the month. Untreated diabetic rats had a decrease of 7% at the end of the first week and 10% at the end of the month. The diabetic group that was treated with 10 mg/kg with A. sativum oil had a 5% increase of body weights at the end of the first week and a 17% increase of body weights at the end of the month. The diabetic group that was treated with 20 mg/kg with A. sativum oil had an initial 2% decrease of body weights at the end of the first week and a 20% increase of body weights at the end of the month. The diabetic group that was treated with 7 mg/kg with N. sativa oil had a 7% decrease of body weights at the end of the first week and an improvement of 5% but did not reach the original weight at the end of the month. The diabetic group that was treated with 14 mg/kg with N. sativa oil had a 15% decrease of body weights at the end of the first week and an improvement of 10%but did not reach the original weights at the end of the month.

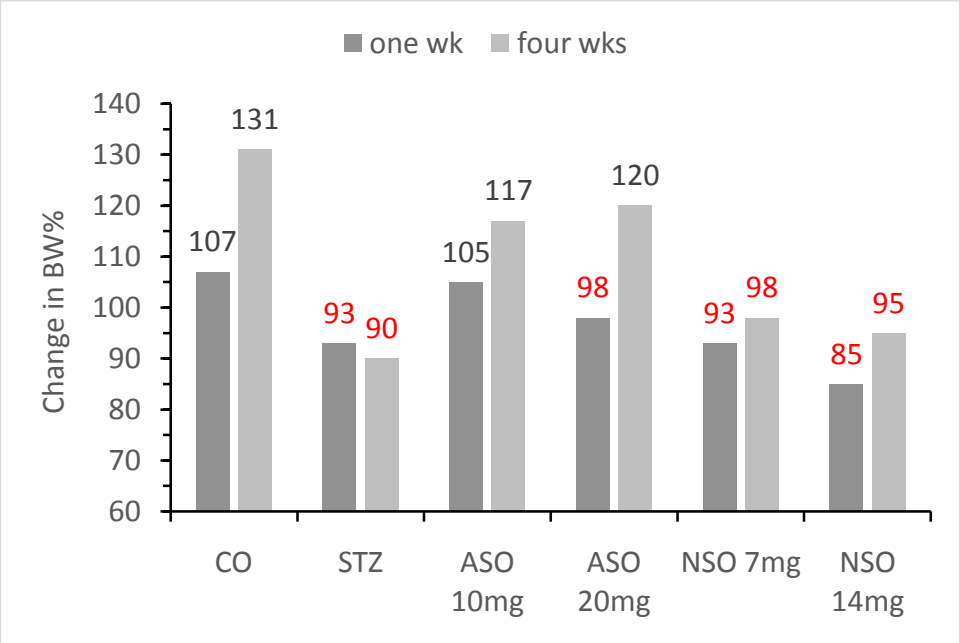

Figure2: The effects of A. sativum and N. sativa on body weights, As can be seen in this figure the body weights in the control group had an increase of 7% at the end of the first week and 31% at the end of the month. By the end of the first week, the only treated group that showed an increase in body weight was the 10mg/kg A. sativum treated group. By the end of the month the 20 mg/kg A. sativum treated group showed the best results with 20% increase in body weight.

The effect of A. sativum and N. sativa on FBG levels:

The glucose levels were expressed as mmol/l as illustrated in figure 3. As can be seen in this figure the FBG levels in the control group was within the normal range (5.5 and 5.3 mmol/l) at the end of the first week and at the end of the month. Untreated diabetic rats had very high FBG levels (23.5 and 24 mmol/l|) at the end of the first week and at the end of the month which is more than four times the FBG levels for the control group. The diabetic group that was treated with 10mg/kg with A. sativum oil had an initial increase of FBG levels (10.6 mmol/l) at the end of the first week and then a decrease of FBG levels (7 mmol/l) at the end of the month. The diabetic group that was treated with 20mg/kg with A. sativum oil had an initial increase of FBG levels (13.4 mmol/l) at the end of the first week and then a slight decrease of FBG levels (11.3 mmol/l) at the end of the month. The diabetic group that was treated with 7 mg/kg with N. sativa oil had an initial increase of FBG levels (14 mmol/l) at the end of the first week and then a slight decrease of FBG levels (11 mmol/l) at the end of the month. The diabetic group that was treated with 14 mg/kg with N. sativa oil had an initial increase of FBG levels (18 mmol/l) at the end of the first week and then a decrease of FBG levels (10.5 mmol/l) at the end of the month.

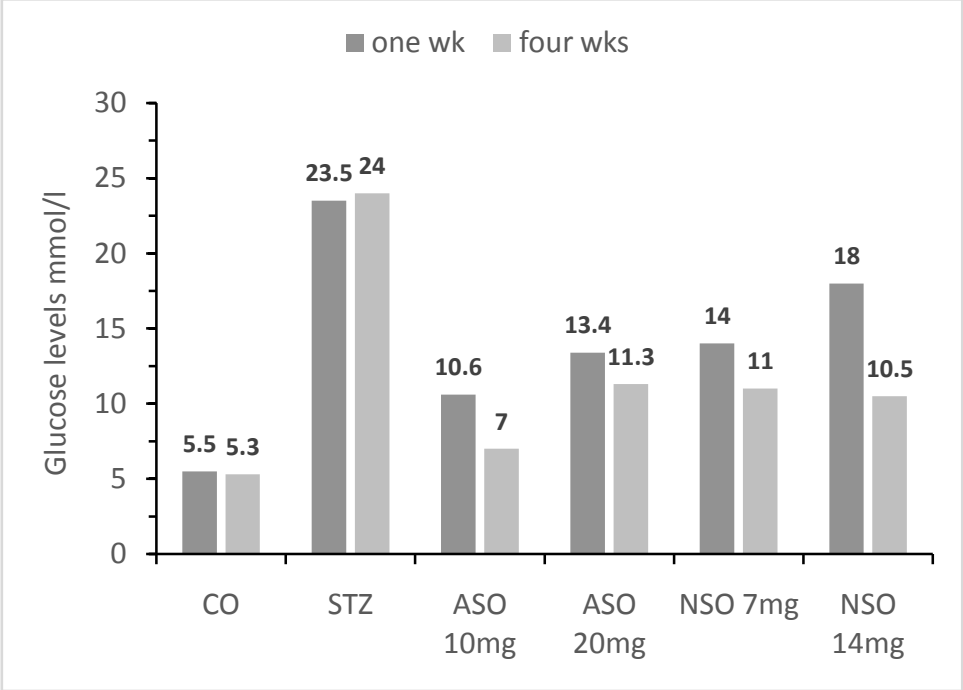

Figure 3: The effects of A. sativum and N. sativa on FBG levels.As can be seen in this figure the FBG levels in all A. sativum and N. sativa treated groups were much lower compared to the diabetic untreated group. The best result was obtained by the 10 mg/kg A. sativum oil treated group whereas all the three other groups showed very close results by the end of the month.

The effect of A. sativum and N. sativa on blood insulin levels:

The blood insulin levels were expressed as percentages of the control as illustrated in figure 4. As can be seen in the figure the blood insulin levels in the control group were expressed as 100%. Untreated diabetic rats had blood insulin levels of 41% compared to the control. The diabetic group that was treated with 10 mg/kg with A. sativum oil had blood insulin levels of 62% compared to the control. The diabetic group that was treated with 20 mg/kg with A. sativum oil had the highest blood insulin levels of 81% compared to the control. The diabetic group that was treated with 7 mg/kg with N. sativa oil had blood insulin levels of 54% compared to the control. The diabetic group that was treated with 14 mg/kg with N. sativa oil had blood insulin levels of 53% compared to the control.

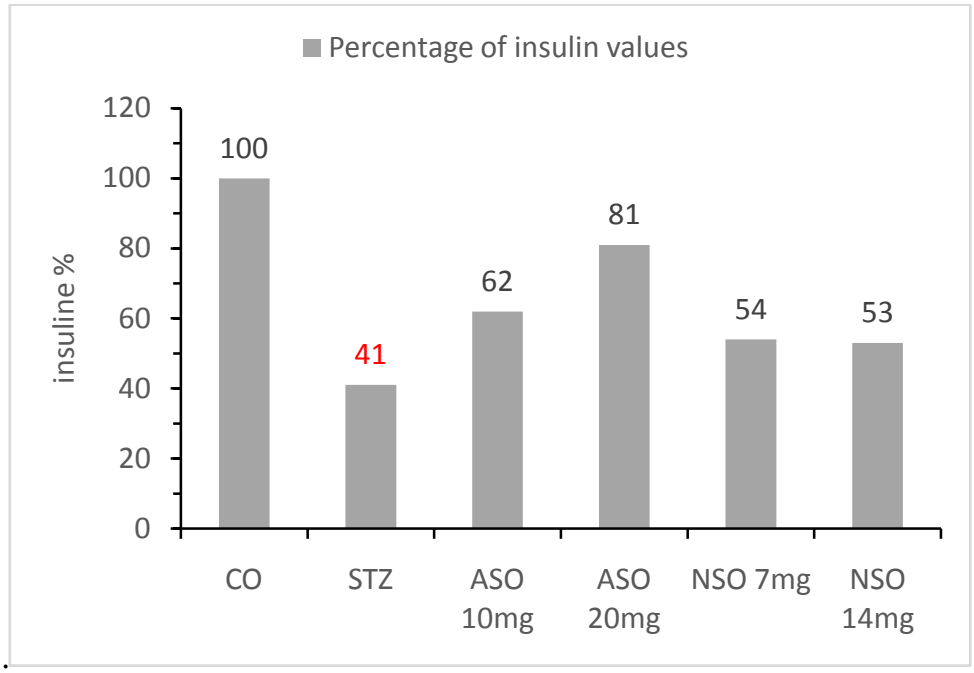

Figure 4: The effects of A. sativum and N. sativa on blood insulin levels. As can be seen in this figure the blood insulin levels in all A. sativum and N. sativa treated groups have higher blood insulin levels compared to the diabetic untreated group. The best result was obtained by the 20 mg/kg A. sativum oil treated group where the insulin levels were restored by 81% compared to the control, whereas all the three other groups showed very close results by the end of the month.

Effect of N. sativa on Pancreatic islets

The control rats (A) showed normal pancreatic structure. The islet of Langerhans appeared regular in shape surrounded by a thin capsule of connective tissue. The clusters of cells are embedded in the pancreatic exocrine tissue. The cells are polygonal cells on shape and have regular nuclei. In STZ diabetic rats (B), the pancreatic tissues have degenerative, necrotic changes, and shrinkage in the islets of Langerhans. The islets were relatively small and atrophied.

In diabetic animals treated with 7 mg N. sativa oil (group C), the histological sections showed that the islets were relatively small in size and irregular in shape compared tothe normal control group. There were less hydropic degeneration, degranulation, and necrosis in the islet cells. More viable polygonal islet cells were observed compared to group B (STZ only treated group).The islets of Langerhans of rats treated with 14 mg of N. sativa oil (group D), showed similar appearance as in group C, there were more viable cells present, and less hydropic degeneration, degranulated and necrosis compared to group B as can be observed in figure 5.

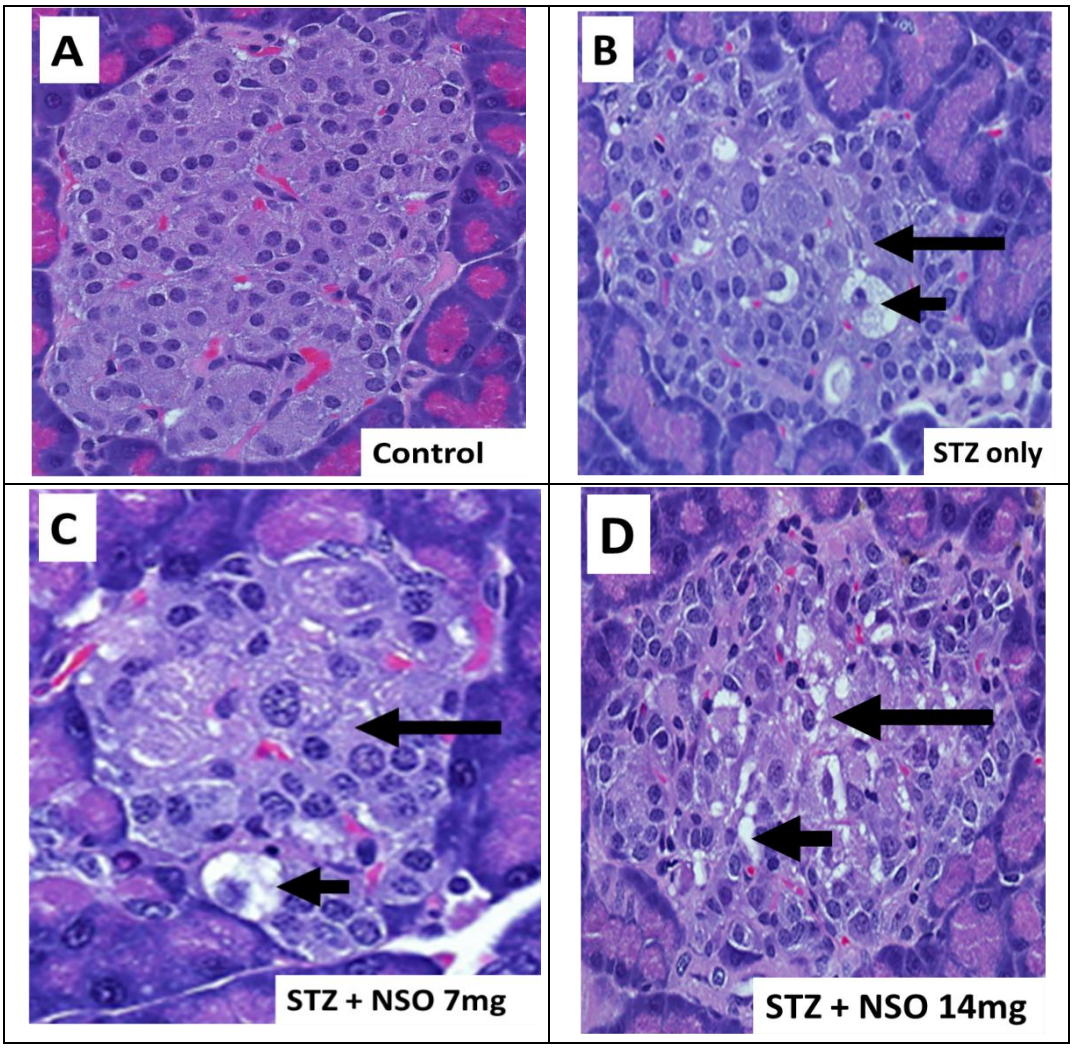

Figure 5: The effects of N. sativa on pancreatic islets. As can be seen in this figure the pancreatic islets in the control group (A) have normal structure, whereas the STZ only group (B) suffered from degenerative necrosis (small arrow) and shrinkage (long arrow). Both of the N. sativa treated groups (C & D) showed improvement compared to the STZ group (B) as can be seen in the histological sections where less degenerative necrosis and cell shrinkage were observed but did not reach full recovery (compared to the control group.

Effect of A. sativum on Pancreatic islets

The control rats (A) showed normal pancreatic structure. The islet of Langerhans appeared regular in shape surrounded by a thin capsule of connective tissue. The clusters of cells are embedded in the pancreatic exocrine tissue. The cells are polygonal cells in shape and have regular nuclei. In STZ diabetic rats (B), the pancreatic tissues have degenerative, necrotic changes, and shrinkage in the islets of Langerhans. The islets were relatively small and atrophied.

In diabetic animals treated with 10 mg A. sativum extracts (group C), the histological sections showed that the islets were relatively small in size and irregular in shape compared to normal control group. There were less hydropic degeneration, degranulation, and necrosis in the islet cells. More viable polygonal islet cells were observed compared with group B (STZ only treated group). In the islets of Langerhans of rats treated with 20 mg of A. sativum extracts (group D), a similar appearance as in group C can be observed, there were more viable cells present, and less hydropic degeneration, degranulated and necrosis compared to group B (Figure 6).

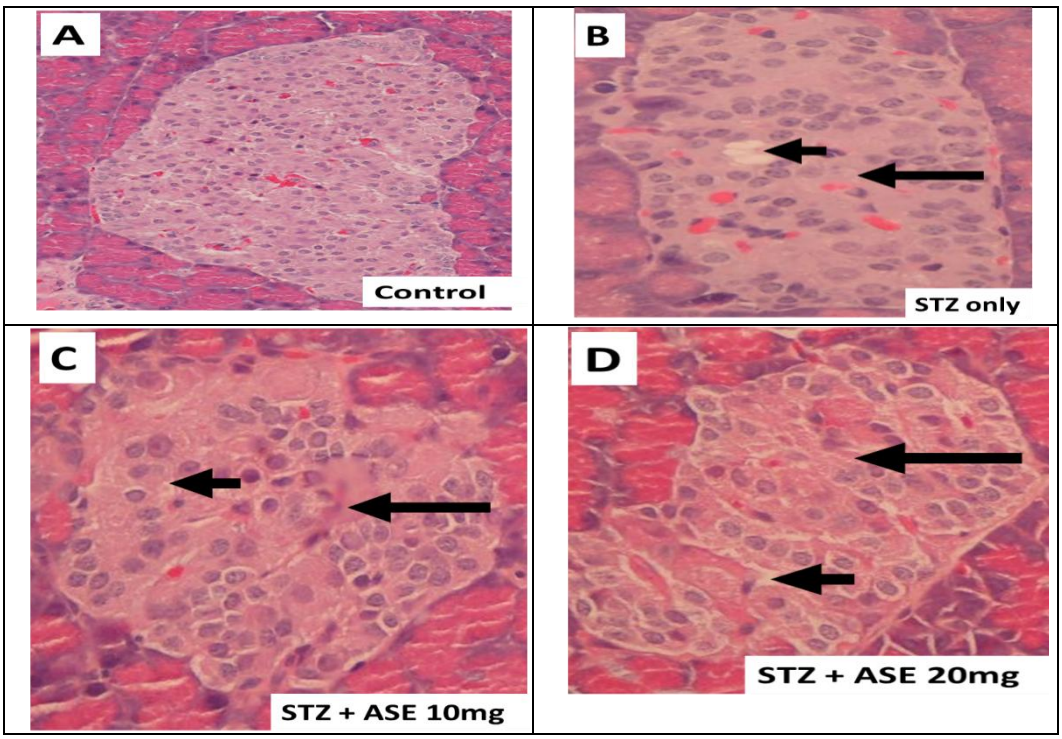

Figure 6: The effects of A. sativum on pancreatic islets. As can be seen in this figure the pancreatic islets in the control group (A) have normal structure, whereas the STZ only group (B) suffered from degenerative necrosis (small arrow) and shrinkage (long arrow). Both of the A. sativum treated groups (C & D) showed improvement compared to the STZ group (B) as can be seen in the histological sections where less degenerative necrosis and cell shrinkage were observed but did not reach full recovery (compared to the control group.

Discussion and Conclusion:

This study was conducted to investigate the effects of A. sativum and N. sativa on type 1 diabetes. The effects of these two plants on body weight, FBG levels and blood insulin levels were obvious, however, differences between the effects of these two plants and also between the two concentrations that were used from each plant were considerable. Compared to the untreated diabetic group where the weight loss continued throughout the month, the only group who gained weight at the first week was the group treated with A. sativum 10mg/kg who had an increase of 5% of body weight and all the other three treated groups have an initial decrease of body weight from 2% to 15%.By the end of the month all the treated groups have improvements in their body weights but the group that was treated with 20mg/kg A. sativum showed the best result with 22% increase after the first week, the group that was treated with A. sativum 10mg/kg had an increase of 15% after the first week. The groups that were treated with N. sativa 7 mg/kg and 14mg/kg on the other hand have weight increase of 5% and 10% respectively after the weight loss of the first week. These results are supported by other studies showed improvements of body weights after A. sativum and N. sativa treayments[12–14]

The effects of the two plants on FBG levels were also obvious, however the group that was treated with 10mg/kg A. sativum showed the best results either by the end of the first week where it was less than half of the diabetic untreated group but still about twice the normal level or by the end of the month where it was only slightly higher the normal levels. The group that was treated with 14mg/kg N. Sativa had the highest FBG levels among the treated group (18 mmol/l) in the first week but FBG levels decreased by the end of the month to 10.5mmol/l). the other two groups however have slight decreases at the end of the month but still about twice the normal levels. Other studies showed similar results of the effects of A. sativum and N. sativa on reducing FBG levels in diabetic animals[1516].

The effects of the two plants on blood insulin levels were also obvious, however the group that was treated with 20mg/kg A. sativum showed the best results with about 81% insulin levels restoring and the group that was treated with A. sativum was the second with 62% restoring of insulin levels. The groups that were treated with 7mg/kg N. Sativa and 14mg/kg N. Sativa had only slight improvements. The blood insulin levels improvements by using A. sativum and N. sativa were also reported by other researchs[1718]

The histological sections of the pancreatic islets of the animals at the end of the experiment showed that animals treated with extracts from both plants were improved and less damaged, however none of the treated groups reached full recovery suggesting that one month is not enough to reach full recovery. Moreover, there might be a better improvement with A. sativum

treatment than the N. sativa treatment. More time periods might be needed to observe the full recovery of the pancreatic islets damaged by STZ.

As a conclusion, comparing the effects of both A. sativum and N. sativa plant extracts on diabetic rats suggest that A. sativum had a better effect on diabetes than N. sativa. Even though using a dose of 20mg/kg gave the best results on body weight and insulin levels, but using the 10mg/kg gave a bitter initial effect on body weight at the first week and on the glucose levels by the end of the month. These results suggest that using a dose of 15mg/kg of A. sativum might give better results in reducing the effect of type 1 diabetes.

References

1. Ashraf R, Khan RA, Ashraf I. Effects of garlic on blood glucose levels and HbA1c in patients with type 2 diabetes mellitus. J Med Plants Res. 2011;5(13):2922-2928. https://www.researchgate.net/publication/261277383. Accessed December 22, 2019.

2. Hober D, Alidjinou EK. Enteroviral pathogenesis of type 1 diabetes: Queries and answers. Curr Opin Infect Dis. 2013;26(3):263-269. doi:10.1097/QCO.0b013e3283608300

3. Heinemann L. Variability of insulin absorption and insulin action. Diabetes Technol Ther. 2002;4(5):673-682. doi:10.1089/152091502320798312

4. Roy K. K, Harris F. F, Dennison S.R. SR, Phoenix D.A. DA, Singh J. J. Effects of streptozotocin-induced type 1 diabetes mellitus on protein and ion concentrations in ocular tissues of the rat. Int J Diabetes Metab. 2005;13(3):154-158. doi:10.1159/000497584

5. Arora S, Ojha S, Vohora D. Characterisation of streptozotocin induced diabetes mellitus in swiss albino mice. Glob J Pharmacol. 2009;3(2):81-84.

6. Al-Zahim M, Newbury HJ, Ford-Lloyd B V. Classification of genetic variation in garlic (Allium sativum L.) revealed by RAPD. HortScience. 1997;32(6):1102-1104. doi:10.21273/hortsci.32.6.1102

7. ETOH T. Fertility of the Garlic Clones Collected in Soviet Central Asia. J Japanese Soc Hortic Sci. 1986;55(3):312-319. doi:10.2503/jjshs.55.312

8. Mahesar H, Ma B, Aa K, Nt N. GARLIC USED AS AN ALTERNATIVE MEDICINE TO CONTROL DIABETIC MELLITUS IN ALLOXAN-INDUCED MALE RABBITS. Vol 6.; 2010. http://www.pps.org.pk/PJP/6-1/Mahesar.pdf. Accessed December 22, 2019.

9. Yimer EM, Tuem KB, Karim A, Ur-Rehman N, Anwar F. Nigella sativa L. (Black Cumin): A Promising Natural Remedy for Wide Range of Illnesses. Evidence-based Complement Altern Med. 2019;2019. doi:10.1155/2019/1528635

10. Ahmad A, Husain A, Mujeeb M, et al. A review on therapeutic potential of Nigella sativa: A miracle herb. Asian Pac J Trop Biomed. 2013;3(5):337-352. doi:10.1016/S2221-1691(13)60075-1

11. Mohammad MY, Yaheya M, Ismail M. Therapeutic Role of Prophetic Medicine

Habbat El Baraka (Nigella sativa L.)-A Review. World Appl Sci J. 2009;7(9):1203-1208.

12. Kanter M, Coskun O, Korkmaz A, Oter S. Effects ofNigella sativa on oxidative stress and ?-cell damage in streptozotocin-induced diabetic rats. Anat Rec. 2004;279A(1):685-691. doi:10.1002/ar.a.20056

13. Amagase H. BLP. Allium sativum - an overview | ScienceDirect Topics. In: Encyclopedia of Food Sciences and Nutrition (Second Edition). ; 2013:11. https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/allium-sativum. Accessed December 7, 2019.

14. Masjedi F, Gol A, Dabiri S. Preventive effect of garlic (Allium sativum L.) on serum biochemical factors and histopathology of pancreas and liver in streptozotocin-induced diabetic rats. Iran J Pharm Res. 2013;12(3):325-338. doi:10.22037/ijpr.2013.1322

15. Fararh KM, Atoji Y, Shimizu Y, Shiina T, Nikami H, Takewaki T. Mechanisms of the hypoglycaemic and immunopotentiating effects of Nigella sativa L. oil in streptozotocin-induced diabetic hamsters. Res Vet Sci. 2004;77(2):123-129. doi:10.1016/j.rvsc.2004.03.002

16. Thomson M, Al-Amin ZM, Al-Qattan KK, Shaban LH, Ali M. Anti-Diabetic and Hypolipidaemic Properties of Garlic (Allium Sativum) in Streptozotocin-Induced Diabetic Rats. Vol 15.; 2007.

17. Al-Hader A, Aqel M, Hasan Z. Hypoglycemic effects of the volatile oil of nigella sativa seeds. Pharm Biol. 1993;31(2):96-100. doi:10.3109/13880209309082925

18. Eidi A, Eidi M, Esmaeili E. Antidiabetic effect of garlic (Allium sativum L.) in normal and streptozotocin-induced diabetic rats. Phytomedicine. 2006;13(9-10):624-629. doi:10.1016/j.phymed.2005.09.010

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