

Investigating the effects of noise exposure on intensification of diabetes mellitus, serum glucose, cortisol level and body weight of the male mice

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ABSTRACT

Noise is considered as one of the harmful factors at industrial environments. It affects human health in different aspects including harmful influences on auditory, vision, neurological and psychiatric systems, hormones, physiological and mental systems. Paying attention to the importance of hormonal effects on human body seems to possess crucial importance. The aim of the present study is to investigate the effects of noise exposure on variation of serum levels of glucose and cortisol at Syrian adult male mouse. 36 Syrian male adult mice were randomly categorized into two experiment and control groups. Garlic powder was added to the mice pelleted food meal (equal to 1% of their daily diet) to study its effect on the cortisol and glucose serum levels. The mice pelleted food contains starch, glucose, isolated soya protein, etc., which are the rich resources of A, C, B1, B2 and B6 vitamins. Streptozotocin (60mg/kg) was injected to the mice at experiment group which were under noise exposure with intensity of 90dB in frequency range of 700-5700Hz. Noise were generated using CoolEdit software and distributed to the fabricated box for 30 days (8h/d). Fasting cortisol and glucose serum levels were measured for mice of both groups 24h after finishing the exposure period. Results indicated that the glucose serum level in non-diabetic and diabetic subjects under noise exposure had significant difference ($p<0.002$) with the subjects at control group. Also, cortisol level in non-diabetic and diabetic subjects under noise exposure indicated significant difference ($p<0.002$) with the subjects at control group. Exposure to noise with intensity of 90dB at frequency range of 700-5700Hz increases the glucose and cortisol serum levels.

Keywords: Cortisol; Glucose; Mouse; Noise.

INTRODUCTION

Diabetes Mellitus is defined as group of metabolic disorders that is accompanied by high blood sugar which is induced by deficiency at production insulin or insulin resistance (IR) [1, 2]. It has been estimated that the quantity of people who have diabetes will increase from 171 million at 2000 to 366 million at 2030 [3]. Similar to other countries, diabetes tends to run rampant in Iran. According to the epidemiologic studies performed at the last decade in Iran, diabetes outbreak rate has been estimated as 1.5 million people [4]. Also, statistics published by world health organization (WHO) at the world health day (2016) revealed that about 422 million adult people have diabetes worldwide which is going to

be more than doubled at the next 20 years [5]. Also, the results of WHO's investigations indicated that diabetes was the direct cause of 1.5 million deaths in Iran at 2012 [5]. The outbreak rates of diabetes type 2 have been evaluated as 5.5%, 5.7% and 6.8% in Iran at 1995, 2000 and 2025, respectively. The diabetic population of the country was about 1.70, 1.98 and 5.12 million people at the mentioned years [6]. Diabetes is usually accompanied by high risk levels of vascular, renal, ocular and neuropathic complications which induce to the early incapability and even death [7]. Likewise, it has been revealed that stress is one of the factors that may induce to diabetes in the people who are prone to diabetes [8]. Noise can be considered as

a physical stressful factor at the work environments which stimulates the worker's body and results in different stress responses [9-11]. This harmful occupational factor is one of the environmental parameters which activate the nervous-hormonal paths in the person's body [12]. In this regard, Cortisol is the hormone that is released to make body cope with the external stressful conditions [13]. Cortisol is the main Glucocorticoid in body that is the final product of the Hypothalamus-Pituitary-Adrenal (HPA) function [14]. After Cortisol secretion, it sits on the GLUT-4 receptors and blocks the glucose transfer system from blood to cells which induces to the high blood sugar. This mechanism is defined as the counterbalance of insulin [15, 16]. In a research conducted by Monsefi et al, it is concluded that the noise pollution can increase the stress hormone levels and induce to increase at the volume of the adrenal glands in rats which is related to the noise effects at the Hypothalamus-Pituitary-Adrenal [17]. In the study conducted on 100 workers, chronic exposure to noise with intensity above 80dB resulted at an increase in blood sugar and Cortisol level [18]. Herbs and their derivatives have been considered as treatments to diabetes and its side effects; nevertheless, research-based and confirmed pieces of evidence have not been found on their definite efficiency [19]. There are several evidence for the beneficial effects of garlic herb on diabetes. Garlic (with scientific name *Allium Sativum*) is a species from Liliaceous genus and is classified in the onion family [20]. This herb has special properties in reducing Cholesterol and Triglyceride levels, blood pressure, prevention of the blood platelet mass formation. It also contains antibacterial, anti-diabetes and anti-oxidation properties [21]. Garlic herb has pharmaceutical materials such as Alliin, Allysine, Alliinase enzyme, Inulin, Vitamin groups A, B and C [22]. In this regard, it has been confirmed that the pure garlic extract reduces the levels of lipid peroxidation indices such as MDA, superoxide and hydroxyl radicals and increases the levels of tissue protection enzymes with antioxidant properties such as Superoxide Dismutase, Catalase, Peroxidase and Glutathione peroxidase [23]. On the other side, the protective properties of the wild garlic herb have been confirmed on

blood circulation system and antiplatelet concentration similar to the garlic herb, [24]. The medicinal properties of garlic herb are related to the presence of Sulfur compounds such as Allysine. The conducted researches indicated that oral consumption of garlic herb has anti-hyperglycemic effect on diabetic rats in experimental model of diabetes mellitus [25]. Literature published for investigating the effects of noise on Cortisol hormone and blood sugar levels have been concentrated on noises with specific fixed frequencies; such as the occasion in which workers are in exposure to varying noise with different frequency spectrum. Also, most of the published researches have concentrated on the garlic extract and its beneficial properties. Few researches have been conducted for studying the effects of the powder form of garlic herb, its oral consumption and its effects on the glandular endocrines. So, the main aim of present study is to investigate the effects of noise with intensity above the allowed limits (90dB) in frequency range 700-5700Hz on the Syrian adult male mice. Also, the efficiency of the oral consumption of garlic powder has been studied on the Cortisol hormone and blood sugar levels at the Syrian male mice.

MATERIALS AND METHODS

Animals

In this research, 36 male adult mice (of NMRI race) weighing 25-35g and age of 7 to 8 weeks were chosen for the experiments [26]. They were transferred to the university animal house for a week before tests to cope with the environment. At the animal house, they were exposed to weather conditions with temperature range of 20-25°C and humidity of 40-50%. They were also kept at daylight for 12h and night time for 12h. They were fed by the mouse food with enough water. At the exposure time, they were fully adult, with age range of more than 56 days. The work has been approved by the Ethical committee of the university where the study has been performed. Also, ethical standards in working with animals were considered according to the university guideline considerations. Mice were first weighted and labelled with specific IDs.

They were randomly categorized into six groups each containing six animals as:

1. Control group
2. Control group with garlic consumption equal to 1% of their daily diet
3. Non-diabetic group with noise exposure
4. Non-diabetic group with noise exposure and garlic consumption equal to 1% of their daily diet
5. Diabetic group with noise exposure
6. Diabetic group with noise exposure and garlic consumption equal to 1% of their daily diet

The mice quantities were determined as six at each group according to the previous researches and preliminary experiments [27].

Noise exposure room

A small box was built in dimensions of $80 \times 60 \times 30\text{cm}$ as noise exposure room (Fig. 1). A perforated meshed metal plate with 5mm thickness was installed at the box floor that had exact distance of 26cm to the box roof ($80 \times 60 \times 26\text{cm}$). A sliding drawer was installed with distance of 4cm from box floor to collect animal wastes and transfer them into the waste pot. Holes were created on the center of side walls with distance of 3cm to the mice positioning plate (the approximate position of the mice heads) to measure and monitor the room conditions [28].

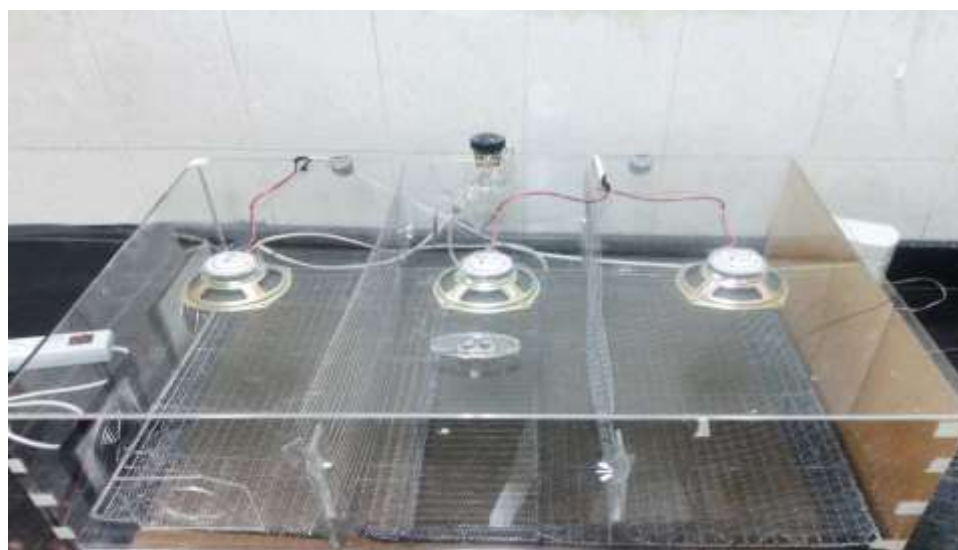


Figure 1. The noise generation and monitoring system at the exposure room (before noise exposure)

According to the suggested condition for keeping mice during noise exposure, room temperature was adjusted at 25°C using temperature control device. If temperature was raised from the adjusted value, two fans (that were installed near the box) were turned on and worked until temperature reached to the adjusted value and were then turned off automatically. Noise with average intensity of 90dB within the mentioned frequency range was run on computer using Cool Edit software and distributed to the room from its center points by the installed speakers to determine the effects of noise variance inside the constructed box (Fig. 2). Noise intensity was then measured at 12 points inside the box that were

chosen at two levels with heights of 3cm and 10cm from the mice keeping metal plate. Six points were selected at each of the mentioned level. Measurements were performed using Casella sound level measurement device model Cel-490. The mentioned model was chosen for measurement purposes because of its flexible microphone enabling the sound level measurement at the closed boxes. The results of measurements indicated that the noise intensity was $90 \pm 1^{\circ}\text{C}$ at different points of the constructed box. This result revealed that the noise variance was trivial in different parts of the box and noise up and down intensity was very low at the fabricated box.

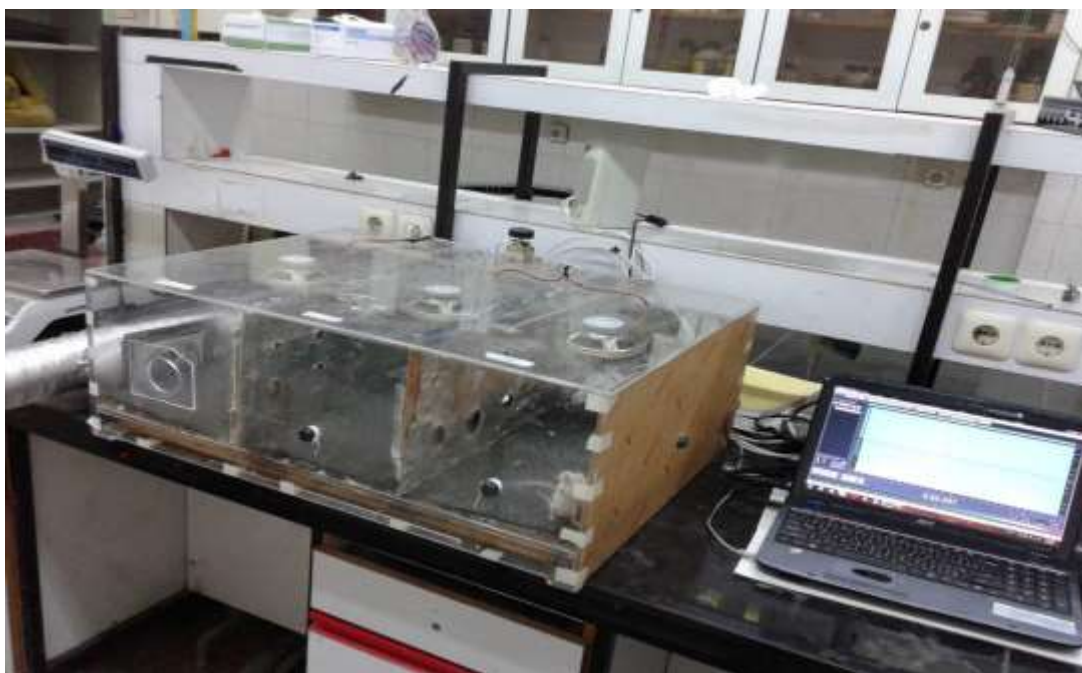


Figure 2. The noise generation and monitoring system at the exposure room (during the noise exposure)

Garlic powder

The required garlic for test performance were grained and divided into two equal parts. The first part was put at oven with temperature of 60°C within two days for grains to dry and then, the dried garlic grains were milled into the powder form. Mice don't tend to eat garlic, inherently. So, garlic powder (equal to 1% of their daily diet) was mixed with the pelleted food meal and prepared as dough. The prepared mix was molded in shape of the pelleted food considering the average daily diet of Syrian mouse as 5-10g [29]. For example, pellet containing 1% of garlic consisted of 0.1g garlic powder and 9.9g of the standard food with 5ml of water. Diabetogenic effect: For making the samples diabetic, 60mg of Streptozotocin (STZ) per 1kg of the body weight were injected to the mice through Intraperitoneal (IP) method. For preparation of the injection solution, Streptozotocin was solved in Citrate buffer (0.1 molar with PH=4.5). Mice were considered as diabetic if their fasting blood sugar was above 200mg/dl [30]. Urinary glucose test strips were used for ensuring the non-diabetogenic effect. Mice were mildly anesthetized by chloroform at 9-11AM of the 30th days after an overnight fasting for measurement of their fasting glucose [31]. They were fixed at the autopsy table and after

opening their chest, bloodletting was directly performed from the right ventricle. The blood samples were then centrifuged with speed of 5000rpm in about 20min to prepare the required serums. Serums were kept at temperature of -20°C until the hormonal evaluation tests were performed. The glucose oxidase enzyme method was incorporated for the glucose measurement [32, 33] and the Radioimmunoassay (RIA) method was employed for measurement of Cortisol serum level [31].

STATISTICAL ANALYSIS

Data analysis was performed using SPSS v.21 software. All of the obtained data were expressed as mean value $\pm$ standard deviation. Finally, data were analyzed through incorporation of the one-way Anova tests followed by Turkey method. Results with $p < 0.05$ were considered as statistically significant.

RESULTS

The variation of the glucose level, cortisol serum level and weight difference between the diabetic and non-diabetic samples under noise exposure are presented in Table 1. Also, comparison between these parameters has been

presented in Figs. 1, 2 and 3 for the different studied populations.

Glucose level variation in diabetic and non-diabetic rat serums

The results of present study indicated no significant difference between the glucose levels at different groups at the week before starting investigation. After 30 days of noise exposure (at the fourth week), glucose serum levels were increased significantly ($p<0.002$) at non-diabetic group and non-diabetic group under treatment by garlic herb in comparison to the week before investigations. At the last day of noise exposure (30th day), glucose serum level for the non-

diabetic group under treatment by garlic herb was significantly ($p<0.001$) more than its level at the week before starting the investigation. Nonetheless, glucose level in this group was significantly lower than the non-diabetic group during the experiment weeks. In this regard, glucose level indicated significant difference ($p<0.002$) in both diabetic and non-diabetic group with garlic herb treatment in comparison with the glucose level in the control group. Also, control group under treatment by garlic herb didn't indicate significant reduction of glucose serum level, compared to the simple control group (Table 1 and Fig. 3).

Table 1. The mean value and standard deviation of glucose serum level, Cortisol level and body weight variation at the diabetic and non-diabetic Syrian male mice under noise exposure.

Groups	Quantity	Glucose (mg/dl)		Cortisol ($\mu\text{g/dl}$)		Weight variation (g)	
		Before exposure	After exposure	Before exposure	After exposure	Before exposure	After exposure
Control	6	105.2 $\pm$ 6.4	105.4 $\pm$ 5.8	1.1 $\pm$ 0.02	1.1 $\pm$ 0.04	32.0 $\pm$ 1.0	39.0 $\pm$ 2.2
Control + Garlic	6	106.2 $\pm$ 6.4	106.4 $\pm$ 5.8	1.1 $\pm$ 0.02	1.1 $\pm$ 0.04	32.0 $\pm$ 1.0	41.4 $\pm$ 3.6
Non-diabetic subjects	6	105.6 $\pm$ 6.3	169.7 $\pm$ 7.8	1.1 $\pm$ 0.02	3.1 $\pm$ 0.04	32.0 $\pm$ 1.0	35.0 $\pm$ 3.2
Non-diabetic subjects + garlic	6	105.2 $\pm$ 4.3	148.7 $\pm$ 6.1	1.1 $\pm$ 0.02	3.0 $\pm$ 0.02	32.0 $\pm$ 1.0	38.0 $\pm$ 3.2
Diabetic subjects subject	6	202.2 $\pm$ 10.3	412.7 $\pm$ 16.8	1.1 $\pm$ 0.02	5.3 $\pm$ 0.08	32.0 $\pm$ 1.0	29.40 $\pm$ 2.2
Diabetic subjects + Garlic	6	204.2 $\pm$ 12.6	369.2 $\pm$ 17.8	1.1 $\pm$ 0.02	5.1 $\pm$ 0.06	32.0 $\pm$ 1.0	30.4 $\pm$ 3.4

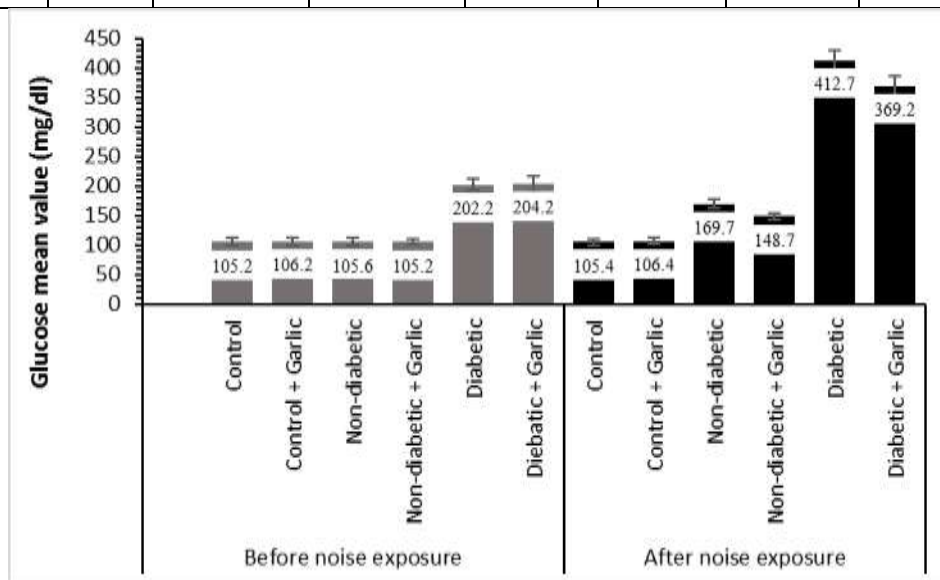


Figure 3. Glucose serum level at diabetic and non-diabetic Syrian male mice (both graphs drawn in Mean $\pm$ SEM)

Cortisol level variations in diabetic and non-diabetic rats

Investigation of Cortisol level at diabetic and non-diabetic groups indicated significant difference ($p < 0.002$) between non-diabetic samples under noise exposure and non-diabetic samples with garlic treatment. Also, significant increase ($p < 0.002$) was observed for Cortisol level between the diabetic group samples under

noise exposure and diabetic samples with garlic treatment. At the last day of noise exposure (30th day), the Cortisol level was significantly increased ($p < 0.001$) in non-diabetic and diabetic groups with garlic treatment in comparison with the week before starting the investigation. Nevertheless, Cortisol level at this group was significantly lower than the non-diabetic and diabetic groups during the experiment weeks (Fig. 4).

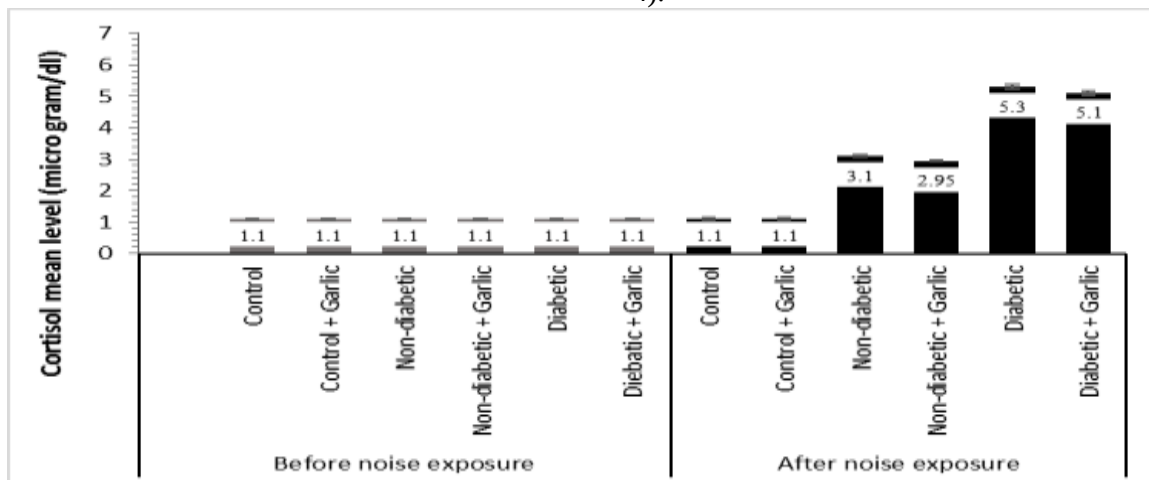


Figure 4. Cortisol level at diabetic and non-diabetic Syrian male mice (both graphs drawn in Mean ± SEM)

Weight variation in diabetic and non-diabetic rats

Despite trivial weight variation in the control group with garlic treatment compared to the control group, these variations were not statistically significant. Weight difference between non-diabetic group under noise exposure and control group indicated significant reduction

($p < 0.001$); however, no significant reduction was observed between the weights of non-diabetic group with garlic treatment and control group. Also, weight difference between both diabetic samples under noise exposure and diabetic samples with garlic treatment represented significant reduction ($p < 0.002$) in comparison to the control group (Fig. 5).

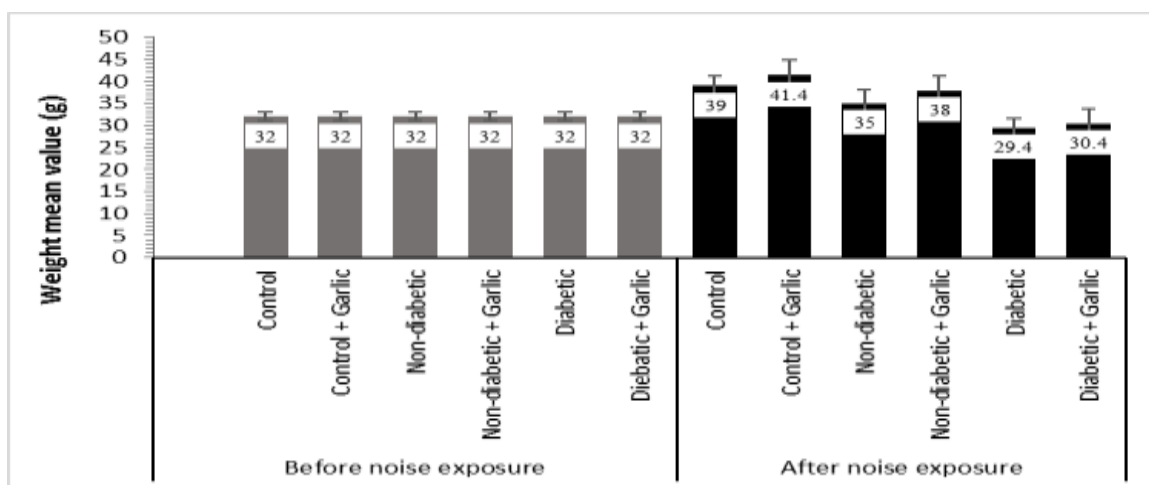


Figure 5. Weight variation at the diabetic and non-diabetic Syrian male mice (both graphs drawn in Mean ± SEM)

DISCUSSION

Results of the present study revealed that the measured parameters for non-diabetic and diabetic control groups (that have not been under noise exposure) didn't have significant effects on the levels of Cortisol and blood sugar (glucose). Glucose serum level was considerably increased under noise exposure. Nevertheless, the considered noise exposure time didn't induce to the real diabetes and a pre-diabetes condition was only prepared for the exposed mice. So, noise exposure (as a cause to the psychological stress) can be a risk factor of diabetes for people who are prone to this disease or those with an inherited predisposition to diabetes. Results indicated that the glucose serum level increased for the non-diabetic and diabetic mice that were exposed to the noise with the specified intensity and frequency. The noise waves induced by noise exposure activates the hypothalamic-pituitary-adrenal function of the mice through the mutual relationship existed between the sub-cortical central nervous system and mice auditory system. This activation increases the Cortisol hormone level [34]. The hypothalamic-pituitary-adrenal route is activated when human or animal is in stressful conditions and releases Cortisol from the adrenal glands as a response to the stressful stimuli [35]. Cortisol prevents the appropriate efficiency of insulin on GLUT-4 by keeping the blood sugar at high levels which cuts glucose transfer from blood to the cells, stirring up to the high blood sugar [16]. These results confirm the reality that Streptozotocin enters the Pancreas beta cells through the glucose transporters (GLUT-4) and induces to DND alkylation. DNA damage activates the poly ADP- ribosylation. The poly ADP- ribosylation process stimulates the reduction in ATP and NAD^+ at the cellules. Intensification of the ATP Dephosphorization after completion of Streptozotocin application provides substrate for Xanthine oxidase enzyme which creates super-oxide radicals. Hydroxyl and Hydrogen peroxide are generated following the mentioned reactions. In addition, Streptozotocin releases some toxic NO compound which retrains the Acunitase activity results in DNA damage. So, Beta cells destruction is indispensable through the Necrosis [36]. In a research conducted by Danowski, it was concluded that samples that

were at the intermediate level between the fully healthy, non-diabetic and fully diabetic groups were at the risk of diabetes under stressful conditions [37]. In other words, stress destruct the Carbohydrates metabolism in some of non-diabetic people in a short period of time and can theoretically induce to diabetes in people without diabetes background [37]. Hence, it can be expressed that the chronic stress is capable of alternating the glucose serum level under any circumstances, though the total glucose serum level at the diabetic samples under noise exposure were more than the non-diabetic samples under noise exposure. The ratio of glucose serum level variation was similar for both groups after noise exposure. So, it can be concluded that exposure to the high intensity noise may intensify diabetes and accelerate its symptoms outbreak. Sorensen et al reported that the risk of diabetes was high for people living near the roads with dense traffic [38, 39]. Results obtained from the study conducted by Fezil and Benson indicated that the chronic exposure to noise with intensity above 80dB increased blood sugar and Cortisol hormone level [18].

In the present study, Cortisol serum level at the diabetic mice under noise exposure was more than the non-diabetic mice under the same noise exposure. This increase in Cortisol level for the diabetic samples may be justified with the stress of having diabetes in comparison to the non-diabetic samples [40]. In a research conducted by Monsefi et.al on the rats that were under noise exposure with intensity above 100dB during 30 days, Cortisol level increase and Adrenal gland volume difference were observed at blood serum of the noise exposure groups with exposure time of 8h/day and 12h/day [17]. Ising and Ising in their study concluded that the chronic exposure to noise with intensity above 90dB increased Adrenalin and Noradrenaline hormones secretion through stimulation of sympathetic neural system [41]. Furthermore, exposure to noise with intensity above 120dB caused an increase at the Cortisol level for both human and animal samples [41]. Study of the literature indicates that chronic exposure to noise increases the heart beat rate, Cortisol level and Adrenaline secretion [42-44]. Stress can lead to the weight loss due to its effects

on the amount of hormones secretion (and probably the growth hormone) [30]. On the other hand, growth hormone (versus Cortisol) has higher sensitivity to the psychological stress where its response to stress is more noticeable at nervous people [45]. Results of present study indicated that the weight loss caused by diabetes had higher intensity in comparison to the psychological stress. This variation revealed the cumulative effect of stress and diabetes on the weight loss. Diabetes on one hand and stress on the other, induce to the hormone change and metabolic variations that result in the weight loss. Also, it was concluded that the noise with intensity above 90dB at frequency range of 700-5700Hz applied on mice during 30 days could induce to significant increase on the Cortisol hormone and blood sugar levels at Syrian male mice fed through diet containing 1% of garlic in comparison with the control group. This variation indicated that diet with 1% of garlic has not affected the Cortisol hormone and blood sugar levels during the exposure period; however, it has caused the mice body weight loss at the mentioned period. Hence, no significant relationship existed between the weights of the control group and group under noise exposure with high intensity fed by garlic additives. The results of the researches have indicated that oral long-term garlic consumption (3-5 months) and its extracted compounds have anti-diabetes effects [46]. It has been reported that garlic oil cures Hypoglycemia at the diabetic patients. Also, several researches represented that garlic has reductive effect on the blood sugar level on rats, pet mice and rabbits [47-49]. The mechanism in which garlic reduces blood sugar is not completely determined; however, garlic's Hypoglycemia activity can be related to the increase at insulin secretion from the beta Pancreas cells, enhancement of insulin, insulin receivers or sensitivity to insulin.

CONCLUSIONS

Results of the present study indicated that exposure to noise with intensity of 90dB in frequency range of 700-5700Hz can amplify the increase at Cortisol hormone and blood sugar levels. So, it is predicted that the noise presence at

the working environments (where workers are exposed to high intensity noises) can increase Cortisol hormone and blood sugar levels.

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