Research Paper
Effect of Extracts of Cloves (Syzygium Aromaticum) on Hepatic Cell Damage and Oxidative Stress Caused by Diabetes in Adult Rats

Tala Pourlak*, Monireh Halimi1, Tannaz Pourlak2, Parham Maroufi3*, Saber Ghaderpour4, Arefeh Shokoohi5

1. Department of Pathology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Aging Research Institute, Tabriz University of Medical Sciences Tabriz, Iran.
3. Department of Orthopedics, Shohada Medical Research, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.
4. Department of Physiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.
5. Student Research Committee, North Khorasan University of Medical Sciences, Bojnord, Iran.

A B S T R A C T

Key words: Cloves, Oxidative stress, Diabetes, Insulin

Received: 17 May 2020
Accepted: 17 Aug 2020
Available Online: 01 Oct 2020

Aims: In this study, we investigated the effect of clove extract (Syzygium aromaticum) on liver cell damage and oxidative stress caused by diabetes in adult rats.

Methods & Material: For this study, 28 female rats were collected and divided into four groups: A: Control group; B: Diabetic Control group (DC) which received 20% glycerol dissolved in normal saline as carriers; C: Diabetic rats (DSA) treated with cloves hydroalcoholic extract (4 mg/kg); d) diabetic rats (DG) treated with glibenclamide (5 mg/kg) as a standard drug.

Findings: The fasting blood sugar and serum triglyceride levels in the DC group increased significantly compared to the control group (P<0.05). In DC, DG, and DSA groups, high-density lipoprotein, and serum insulin levels decreased significantly compared to the control group (P<0.05). Also, in DG and DSA groups, high-density lipoprotein and serum insulin levels increased significantly compared to the DC group.

Conclusion: Cloves can affect fasting blood sugar, serum insulin levels, serum fat profile levels, and prevent liver tissue damage in diabetic rats caused by streptozotocin.

English Version

I. Introduction

Diabetes Mellitus (DM) is a chronic metabolic disease characterized by high blood sugar, vascular problems, neurological problems [1], and high blood glucose levels due to decreased insulin excretion or insulin resistance or both [2, 3]. There are two types of diabetes: type 1 and type 2. In type 1 diabetes or insulin-dependent diabetes, pancreatic beta cells are destroyed and insulin secretion from these cells is impaired [4]. Typically, less than 10% of diabetic patients have type 1 diabetes [5]. The number of diabetics in 2003 reached 194 million between the ages of 20 and 79 years. An increase of up to 50% is expected in 2010, most of which are new patients found in Africa and Asia [6]. The prevalence of type 2 diabetes is also a public health concern and accounts for about 10 million chronic diseases and a significant percentage of deaths worldwide each year. It is estimated that about 5% to 8% of adults in the world have diabetes. The International Diabetes Association reported 285 million people with type 2 diabetes worldwide in 2010 and predicts that it will
reach 438 million by 2030 [7]. People with diabetes are at risk for advanced cardiovascular diseases because of high blood glucose levels [4]. Evidence suggests that oxidative stress plays a major role in the pathogenesis of both types of diabetes. An unusual increase of free radicals and a simultaneous decrease of antioxidant defense mechanisms can damage cellular organelles, increase lipid peroxidation, and develop insulin resistance [8, 9]. Chronic hyperglycemia can cause extensive and irreversible damage to the eyes, nerves, kidneys, heart, and blood vessels, and other parts of the body. Liver is one of the organs that is damaged in diabetes [10]. It is an effective organ in maintaining normal blood glucose levels, and hyperglycemia leads to an imbalance in oxidation-reduction (redox) reactions within hepatocytes. Thus, hyperglycemia causes the production of free radicals by increasing the production of advanced glycation end products by disrupting the production of superoxide scavengers such as reactive oxygen species (ROS), endogenous Superoxide Dismutase (SOD), and Catalase (CAT). Thus, it is clear that diabetic liver damage is caused by several factors and cannot be controlled only by inhibiting hyperglycemia [11].

In diabetic animals, the activities of SOD, CAT, and glutathione are reduced [9]. CAT and SOD are the most important known oxidative enzymes. SOD, which is present in most aerobic organisms and converts superoxide to hydrogen peroxide and oxygen in the cytoplasmic space, may protect DNA and intracellular organelles from damages caused by ROS [12]. Recent evidence suggests using traditional herbal remedies for diabetes. Herbs often contain significant amounts of antioxidants, including tocopherols (vitamin E), carotenoids, ascorbic acid (vitamin C), flavonoids, and tannins. It has been suggested that the antioxidant action of these plants may be an essential and important property of herbal medicines used to treat diabetes [4].

Clove (Syzygium aromaticum) is a fragrant sprout plant commonly used in Africa, Asia, and other parts of the world. Syzygium aromaticum (DSA) has several therapeutic effects, including antibacterial, antifungal, and kidney strengthening effects, and has traditionally been used as a preservative and antimicrobial in food [8, 13]. In a study, the effect of DSA on lowering glucose levels and increasing serum insulin, the levels of SOD and CAT enzymes were investigated [8]. Also, the antioxidant effects of DSA and its ability to reduce malondialdehyde (MDA) have been studied [14]. This study aimed to evaluate the effect of DSA on liver cell damage and oxidative stress caused by diabetes in adult rats.

2. Materials and Methods

For this study, 28 female mice weighing an average of 200-250 g were used. The animals were purchased from the Razi Institute of Mashhad, Mashhad city, Iran, and kept in standard conditions (temperature 25°C, and 12:12 hours of light:dark cycle). During the experiment, rats had free access to water and food. All research stages of this study were performed following the instructions related to the care and use of laboratory animals of Gonabad University of Medical Sciences.

Rats were randomly divided into one healthy control group (𝑛 = 7) and three experimental groups (𝑛 = 21). To induce diabetes in the experimental groups, a single intraperitoneal injection of 50 mg/kg streptozotocin (STZ) (Sigma) dissolved in 5 mm of 0.1 M citrate buffer (pH = 4.5) was performed [6]. In the control group (normal), the same amount of citrate buffer was injected as a single dose instead of STZ. About 72 hours after the injection, rat blood glucose was measured to confirm diabetes (blood glucose > 250 mg/dL was considered diabetic).

Diabetic rats were divided as follows: a) the healthy control group, b) the diabetic control group (DC) that received normal saline as a solvent, c) diabetic rats treated with 50 mg/kg of hydroalcoholic extract of DSA, d) diabetic rats (DG) treated with 5 mg/kg glibenclamide (GBC) as a standard drug. Treatment was performed once a day for 21 days for all groups by intraperitoneal injection. After a treatment period of 21 days, the rats were anesthetized and their blood samples were taken and their kidneys, pancreas, and liver were frozen at -70°C. Blood samples were used to test for glucose, insulin, lipid profiles, some oxidative stress markers, and antioxidant enzymes. Their serum samples were stored at -70°C.

To extract the hydroalcoholic extract of DSA, we first pulverized the dried clove buds that were prepared and mixed in absolute alcohol and distilled water at a rate of 50% and shaken by a shaker for 48 hours. It was then filtered and centrifuged at 1000 rpm. After evaporating water and alcohol, we dissolved the powder obtained as an extract in normal saline and used it at a dose of 4 mg/kg.

SOD activity was measured using the RANSOD (UK) kit method. MDA was measured by placing plasma in a test tube containing glacial acetic acid, to which 1% thiobarbituric acid in 2% NaOH was added. An equal volume (600 μL) of glacial acetic acid and thiobarbituric acid solutions was added to 40 μL of plasma. The test tube containing the mixture was then placed in boiling water for 15 minutes. After cooling, the adsorption was read at 532 nm. MDA
level was calculated using the MDA-TBA absorption coefficient ($\varepsilon = 1.56 \times 10^5 \text{ cm}^{-1} \text{ M}^{-1}$) [13, 15].

Serum glutathione peroxidase (GPx) level was measured using the Pars Test Kit (Iran) method. Finally, the data obtained from this experiment were analyzed by 1-way analysis of variance, and Tukey’s post hoc test was used to determine the groups with significant differences (P<0.05). In this study, the data were presented as Mean±SEM form.

3. Results

Fasting Blood Sugar (FBS)

Fasting Blood Sugar (FBS) level in the DC group increased significantly compared to the healthy control group (P<0.05). Also, FBS levels in DG and DSA groups showed a significant decrease compared to the DC group (P<0.05) (Figure 1).

Serum insulin levels

In the DC, DG, and DSA groups, serum insulin levels significantly decreased compared to the healthy control group (P<0.05). Also, in the DG and DSA groups, insulin levels increased compared to the DC group. This increase was significant in the DSA group (P<0.05) (Figure 2).

Serum levels of fat profile

Serum cholesterol level

The serum cholesterol level in the DC group was significantly higher than that in the healthy control group (P<0.05).

<table>
<thead>
<tr>
<th>Group</th>
<th>Low-density Lipoprotein Mean±SEM</th>
<th>High-density Lipoprotein Mean±SEM</th>
<th>Cholesterol Mean±SEM</th>
<th>Triglyceride Mean±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy control</td>
<td>19.4807±0.726*</td>
<td>34.8412±0.57*</td>
<td>64.0150±2.23*</td>
<td>38.5965±1.58*</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>25.2614±1.26</td>
<td>27.8700±1.13</td>
<td>8.1617±2.13</td>
<td>62.3748±3.58</td>
</tr>
<tr>
<td>Diabetic+DSA extract</td>
<td>13.8968±2.09*</td>
<td>43.6900±1.62*</td>
<td>59.0191±3.97*</td>
<td>44.6541±5.14*</td>
</tr>
<tr>
<td>Diabetic+GBC</td>
<td>8.6100±2.57*</td>
<td>30.9222±0.67*</td>
<td>72.9426±3.65*</td>
<td>40.6709±0.835*</td>
</tr>
</tbody>
</table>

Healthy control group: The healthy group treated with normal saline (for 20 days), diabetic control group: diabetic rats treated with normal saline (for 20 days), diabetic+DSA extract: diabetic group treatment with DSA extract at 4 mg/kg (for 20 days) Diabetic+GBC: Diabetic group treated with glibenclamide extract at 5 mg/kg (for 20 days). * Significantly different from the diabetic control group.

<table>
<thead>
<tr>
<th>Group</th>
<th>Superoxide dismutase Mean±SEM</th>
<th>Glutathione peroxidase Mean±SEM</th>
<th>Malondialdehyde Mean±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy control</td>
<td>2.407±0.11</td>
<td>321.35±1.57*</td>
<td>0.11±1.478</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>1.029±0.22</td>
<td>1.13±95.80</td>
<td>0.29±2.272</td>
</tr>
<tr>
<td>Diabetic+DSA extract</td>
<td>2.351±0.17*</td>
<td>2.56±226.10*</td>
<td>0.11±1.643*</td>
</tr>
<tr>
<td>Diabetic+GBC</td>
<td>2.179±0.21*</td>
<td>1.48±180.22*</td>
<td>0.20±1.859*</td>
</tr>
</tbody>
</table>

Healthy control group: The healthy group treated with normal saline (for 20 days), diabetic control group: the diabetic group treated with normal saline (for 20 days), diabetic+DSA extract: the diabetic group treated with 4 mg/kg DSA extract (for 20 days) Diabetic+GBC: Diabetic group treated with GBC extract 5 mg/kg (for 20 days). * Significantly different from the diabetic control group.
Figure 1. Chart of fasting serum glucose levels in study groups

Healthy control group: healthy group treated with normal saline (for 20 days), diabetic control group: diabetic group treated with normal saline (for 20 days), diabetic+DSA extract: diabetic group treated with 4mg/kg DSA extract (for 20 days) Diabetic+GBC: Diabetic group treated with GBC extract 5 mg/kg (for 20 days). * Significantly different from the diabetic control group.

Figure 2. Graph of serum insulin levels in study groups

Healthy control group: healthy group treated with normal saline (for 20 days), diabetic control group: diabetic group treated with normal saline (for 20 days), diabetic+DSA extract: diabetic group treated with 4mg/kg DSA extract (for 20 days) Diabetic+GBC: Diabetic group treated with GBC extract 5 mg/kg (for 20 days). * Significantly different from the diabetic control group.

Figure 3. Examination of liver histological results (magnification, ×100)

1: Tissue section image related to the healthy control group; 2: Tissue section image related to the diabetic control group; 3: Tissue section image related to the diabetic group treated with DSA extract; 4: Tissue section image related to the diabetic group receiving GBC. The black arrow indicates the areas of tissue bleeding. The red arrow indicates the dilated sinusoid. The orange arrow indicates the central vein.
Also, cholesterol levels in DG and DSA groups decreased significantly compared to the DC group (P<0.05) (Table 1).

Levels of low-density lipoprotein (LDL)

The serum level of Low-Density Lipoprotein (LDL) increased slightly in the DC group compared to the healthy control group (P<0.05). Also, the LDL level in the DG and DSA groups decreased significantly compared to those in the DC group (P<0.05).

Serum levels of high-density lipoprotein (HDL)

The serum level of High-Density Lipoprotein (HDL) in the DC group significantly decreased compared to the healthy control group (P<0.05). Also, HDL significantly increased in DG and DSA groups compared to the DC group (P<0.05). On the other hand, HDL levels in the DSA group were significantly higher than the healthy control group (P<0.05) (Table 1).

Serum triglyceride (TG) levels

The serum triglyceride (TG) level in the DC group significantly increased compared to that in the healthy control group (P<0.05). Besides, TG mean level in the DSA group significantly decreased compared to that in the DC group (P<0.05) (Table 1).

Oxidative stress markers

Table 2 presents serum levels of glutathione peroxidase GPx, SOD, and MDA. The activity of GPx and SOD enzymes in the diabetic control group was significantly lower than those in the healthy group (P<0.05); however, treatment with clove extract increased the serum activity of GPx and SOD in comparison with the control diabetic group (P<0.05). In the diabetic control group, serum MDA level increased significantly compared to that in the healthy group (P<0.05). On the other hand, in the groups treated with clove extract, MDA significantly reduced compared to that in the control diabetes group (P<0.05) (Table 2).

Histopathology of the Liver

The liver tissue obtained from the healthy group was histologically normal. Histological studies have shown that diabetes leads to degenerative changes such as edema, rupture, bleeding in the central arteries, dilation of the sinusoids, and pyknotic nuclei. However, the degenerative changes mentioned in the treatment groups decreased (Figure 3).

4. Discussion

Streptozotocin (STZ) is a compound commonly used to induce type 1 diabetes in rats [16]. STZ causes diabetes by rapidly decreasing pancreatic beta cells, which ultimately leads to decreased insulin secretion. Glibenclamide (GBC) has been shown to cause hypoglycemia by increasing insulin secretion from beta cells in the pancreas. The compound is active in moderate STZ-induced diabetes (some beta cells are still healthy), while in severe diabetes it inactivates STZ (which is lost in almost all beta cells) [17]. Our results showed that GBC reduced FBS levels in hyperglycemic animals, so the diabetic status of the animals was moderate. The hypoglycemic effects of plant extracts depend on the extent to which pancreatic beta cells are destroyed. Treatment of moderate diabetic rats with medicinal plant extract resulted in the activation of beta cells and increased insulin production [18]. The antihyperglycemic activity of DSA was associated with an increase in plasma insulin, indicating that the antihyperglycemic activity of DSA may be due to the insulin-producing activity of this extract. The increase in insulin levels observed in the present study showed that the extract of DSA can lead to insulin secretion from the remnants of beta cells or regenerated beta cells. Also, the results of this study showed that the extract of DSA significantly reduced FBS due to increased insulin secretion [19].

Diabetes affects several metabolic pathways, including lipid metabolism. Insulin deficiency (type 1 diabetes) or low insulin function (type 2 diabetes) leads to decreased glucose uptake by tissues that need insulin (such as the liver) as well as increased glucose production by increasing gluconeogenesis, which ultimately leads to a decrease in blood sugar level. Because of the increase in glucose and a decrease in insulin levels in the blood plasma, the hepatic regulation of lipid metabolism is greatly altered. Insulin is an important regulator of many enzymes involved in lipolysis and lipogenesis, so its deficiency causes major changes in the activity of these enzymes and thus affects the overall metabolism of fats and fat profiles in various tissues [20].

In STZ-induced diabetes, elevated blood sugar levels are usually associated with elevated plasma cholesterol, triglycerides, and LDL but decreased HDL [21]. The activation of hormone-sensitive lipase during insulin deficiency is associated with the release of free fatty acids (FFAs) from adipose tissue [22]. Thus, excess fatty acids produced by STZ-induced diabetes in plasma enhance the conversion of excess fatty acids to phospholipids and cholesterol in the liver. These two substances along with excess triglycerides formed in the liver may be excreted into the blood as lipoproteins [16].
Our observations showed that DSA extract alone and in combination with GBC significantly reduced plasma cholesterol, triglycerides, and LDL compared to the diabetic control group. Also, DSA extract increased HDL compared to the diabetic control group (Table 1). DSA extract may restore plasma lipid status to normal by controlling lipid metabolism. These results were in agreement with the results of previous studies [23, 24].

Our observations showed that carnation caused a significant increase in GPx and SOD compared to the healthy control group (Table 2). Glutathione (GSH) is one of the cytoplasmic scavengers of radicals that can reduce free radicals [25]. It is generally believed that the protective effect of GSH against the oxidative degradation of lipids is achieved through GPx by reducing the endogenously formed hydroperoxides of polyunsaturated fatty acids (PUFA) and converting them to hydroxyl derivatives [26]. GSH can inhibit the production of free radicals by temporarily forming metal catalysts, breaking chain reactions, reducing the concentration of Reactive Oxygen Species (ROS), and increasing the levels of enzymes involved in the antioxidant system (SOD, CAT, GPx, and GST) [27, 28].

Selenium is an important cofactor for the SOD enzyme [29] and the use of DSA extract in rats increases selenium, reduces oxidative stress, and liver damage. Similar results were observed in the study of Adefegha et al. [8], which showed that the Fenton reaction is a combination of H2O2 and Fe2+, which is frequently used to induce lipoxygenase (LPO) reactions [30]. LPO releases hydrogen, the most powerful oxidant in the biological system, from PUFA and hydroxyl radicals, and it can use hydrogen released from PUFA to increase oxidative stress [29].

The antioxidant activity of DSA may be due to phenolic compounds such as eugenol, eugenol acetate, and thymol [31]. DSA can prevent cell damage by scavenging free radicals, chelating temporary metal ions, inhibiting oxidant enzymes, or by repairing α-tocopherol from the α-tocophoxyl radical [32]. Also, flavonoids can scavenge O₂⁻, OH, and peroxy radicals and inhibit LPO activity [33]. DSA can increase SOD, GPx, and GSH and decrease MDA [34].

Hyperglycemia and hyperlipidemia in diabetic patients are associated with increased oxidative stress [35] and increased MDA levels in type 2 diabetic rats. This indicates that increased lipid peroxidation leads to tissue damage and the inability of antioxidant defense mechanisms to prevent the free radical attack, which may lead to leakage of enzymes and metabolites into the bloodstream [36]. Elevated levels of enzymes such as alanine transaminase (ALT), Aspartate Transaminase (AST), markers of liver damage, and evaluation of AST and ALT indicate liver status and necrotic cells, respectively [37]. Abnormal levels of alkaline phosphatase (ALP) in the blood can also indicate liver or bone problems [38]. In the present study, AST, ALT, and ALP levels were significantly higher in the diabetic group compared to the healthy control group. Also, in the group treated with DSA, a significant decrease in AST and ALT levels was observed compared to the diabetic group. In previous studies, an increase in ALT and AST enzymes was observed in diabetic patients [39, 40]. Nyblom et al. reported that in patients with progressive alcoholic liver disease, liver enzymes such as AST and ALT would increase [41]. DSA can reduce liver damage by increasing enzymes in the antioxidant system (SOD, CAT, and GPx) and reducing oxidative stress [42, 43]. Also, the results of liver histology in this study showed that DSA extract reduces liver tissue damage caused by diabetes.

5. Conclusion

The results of this study showed that DSA extract has beneficial effects in lowering blood sugar, oxidative stress, plasma cholesterol, triglycerides, and LDL level. DSA also increases blood insulin levels and improves liver tissue damage and has beneficial effects in reducing tissue damage caused by diabetes. Therefore, because of these beneficial effects of clove plant, it can be used as an effective herbal medicine in reducing and treating the complications of diabetes on liver tissue.

Ethical Considerations

Compliance with ethical guidelines

The ethical code of this research (IR.TBZMED.VCR.REC.2018.167) has been obtained from the Ethics Committee of Research Projects of Tabriz University of Medical Sciences.

Funding

This article is the result of a research project on diabetic rats approved by the Student Research Committee of Tabriz University of Medical Sciences. The project did not receive financial support.

Authors’ contributions

Study concept: Tala Pourlak and Monireh Halimi; Writing and final approval of the article: Tala Pourlak, Monireh Halimi, Parham Maroufi, Saber Ghaderpour, Arefeh Shokouhi; Data collection and interpretation: Tala Pourlak, Saber Ghaderpour, and Arefeh Shokouhi
Conflicts of interest

The authors declared no conflict of interest.

Acknowledgements

We would like to thank the Vice-Chancellor for Research and Technology of Tabriz University of Medical Sciences and the Student Research Committee of Tabriz University of Medical Sciences and all those who helped in this research.
اثر عصاره میخک بر سیستم تاثیرگذاری اکسیداتیوی ناشی از دیابت در موش های صحرایی بالغ

شماره طلا پورتلک ۳۳۵، سالن پورتلک ۳۳۵، قاب مروری ۰، صابر قادی‌پور، عارفه شکوهی \*، پرهام معروفی، صابر قادرپور، عارفه شکوهی

در این مطالعه اثر عصاره میخک صدپر بر آسیب سلول های کبدی و استرس اکسیداتیو ناشی از دیابت در موش های صحرایی بالغ بررسی گردید.

اوهای میخک صدپر ۴ میلی گرم بر کیلو گرم عصاره هیدروالکلی میخک و سالین به عنوان حلال دریافت کردند. برای این مطالعه موش های صحرایی به چهار گروه تقسیم شدند: 
الف) گروه کنترل;
ب) گروه کنترل دیابتی;
ج) گروه موش های صحرایی دیابتی درمان شده با ۳ میلی گرم بر کیلو گرم گلیبنکلامید به عنوان یک داروی استاندارد;
د) گروه موش های صحرایی که با عصاره میخک صدپر در مقایسه با گروه کنترل به طور معنی‌داری افزایش یافت.

در مقایسه با گروه دیابتی، میزان قند خون ناشتا و سطح سرمی انسولین و HDL در گروه DSA، و DSA و DCA در گروه DC و TDCA نسبت به گروه DCA و TDCA به طور معنی‌داری کاهش یافت. در همه گروه‌ها P > 0/05.

یافته‌ها میخک صدپر احتمالاً می تواند بر قند خون ناشتا، سطح سرمی انسولین، سطح سرمی پروفایل چربی مؤثر باشد و باعث نتیجه‌گیری شود.

کلیدواژه‌ها: میخک، استرس اکسیداتیو، دیابت، انسولین، کبد، موش صحرایی

مقدمه

1. دیابت مزمن بیماری است که با افزایش قند خون، مشکلات عروقی، مشکلات عصبی و غلظت بالای گلوکز خون به دلیل کاهش دفع انسولین یا مقاومت در برابر انسولین یا هر دو مشخص می‌شود. در دیابت نوع ۱ و ۲ دو نوع دیابت وجود دارد: نوع ۱ وابسته به انسولین، سلول‌های بتا لوزالمعده تخریب می‌شوند. به تریشح انسولین از این سلول‌ها دچار اختلال می‌شود.

2. درصد بیماران دیابتی، به دیابت نوع ۲ در طول زمان به دلیل مقاومت در برابر انسولین گروه دیابتیک دریافت کننده گلیبنکلامید.

3. شواهد نشان می‌دهد که استرس اکسیداتیو نقش اصلی در پاتوژنز دیابت نوع ۲ دارد. افزایش غیرمعنی‌دار رادیکال های آزاد و کاهش تعداد انتقال سلول‌ها می‌تواند منجر به آسیب دیدگی ارگانل‌های بدنی، افزایش پراکسیداسیون لیپیدها و پیشرفت مقاومت به انسولین شود.

4. گروه میخک مخصوصاً در کنترل گلیبنکلامید
Materials and Methods

The study was conducted on 30 male Wistar rats divided into six groups. Group 1 served as the control group and received saline solution. Groups 2 and 3 received streptozotocin (STZ) at 55 mg/kg and 250 mg/kg, respectively, intraperitoneally. Groups 4 and 5 received vitamin E (50 mg/kg) and vitamin E (100 mg/kg), respectively, intraperitoneally. Group 6 received vitamin E (100 mg/kg) and a combination of vitamin E and metformin (50 mg/kg) intraperitoneally.

Blood samples were collected from the tail vein of the rats daily for 14 days, and the blood glucose level, insulin, and blood lipid profile were measured.

Results

The blood glucose levels in the control group remained stable throughout the study period. In contrast, the blood glucose levels in the STZ-treated groups increased significantly compared to the control group. The blood glucose levels in groups 4 and 5, which received vitamin E alone or in combination with metformin, were significantly lower than those in groups 2 and 3.

The blood insulin levels in the control group remained stable throughout the study period. In contrast, the blood insulin levels in the STZ-treated groups decreased significantly compared to the control group. The blood insulin levels in groups 4 and 5, which received vitamin E alone or in combination with metformin, were significantly higher than those in groups 2 and 3.

The blood lipid profile showed a significant increase in the STZ-treated groups compared to the control group. The blood lipid profile in groups 4 and 5, which received vitamin E alone or in combination with metformin, returned to normal levels.
میزان عایق رادیکال (MDA) و کاهش یافته در DC دیابتی مقایسه با گروه کنترل سالم: گروه سالم که تحت درمان با نرمال سالین قرار گرفته اند (به مدت 30 روز)، دیابتی: گروه دیابتی برنامه شده با نرمال سالین، عصاره میخک، گروه کنترل دیابتی برنامه شده با نرمال سالین، دیابتی: گروه دیابتی برنامه شده با عصاره میخک.

نتایج پروفایل لیپیدی در سرم خون

11. Acetic Acid Glacial
گروه کنترل سالم: گروه سالم که تحت درمان با نرمال سالیون قرار گرفته بود (نمونه 40 روز) گروه کنترل دیابتی: گروه دیابتی که تحت مرسوم بالداران و داروسازان قرار گرفته بود (نمونه 40 روز) گروه دیابتی+گلیبنکلامید: گروه دیابتی که تحت درمان با گلیبنکلامید به میزان 5 میلی گرم بر کیلوگرم در مدت 20 روز (جدول شماره 14). مطالعات بافت شناسی نشان داد که دیابت منجر به تغییرات دژنراتیو مانند ادم، پارگی، خونریزی در رگ های بالینی خون و انسولین سرمی، در صورت عدم درمان بیماری، افزایش معنی داری داشته و باعث آسیب سلول های کبدی شده و افزایش معنی داری نشان می دهند.

نتایج مارکر های استرس اکسیداتیو در سرم خون

<table>
<thead>
<tr>
<th>مارکر</th>
<th>میانگین ± انحراف معیار</th>
<th>مقدار P</th>
<th>گروه</th>
<th>دیابتی+عصاره میخک</th>
<th>دیابتی+گلیبنکلامید</th>
<th>دیابتی کنترل</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA</td>
<td>2.478 ± 0.11</td>
<td>&lt; 0.05</td>
<td>کنترل سالم</td>
<td>2.472 ± 0.29</td>
<td>2.471 ± 0.28</td>
<td>2.478 ± 0.29</td>
</tr>
<tr>
<td>GPx</td>
<td>371.8/37.8/37</td>
<td>&lt; 0.05</td>
<td>کنترل سالم</td>
<td>371.8/37.8/37</td>
<td>371.8/37.8/37</td>
<td>371.8/37.8/37</td>
</tr>
<tr>
<td>SOD</td>
<td>2/407 ± 0.11</td>
<td>&lt; 0.05</td>
<td>کنترل سالم</td>
<td>2/407 ± 0.11</td>
<td>2/407 ± 0.11</td>
<td>2/407 ± 0.11</td>
</tr>
<tr>
<td>TG</td>
<td>140/120 ± 0.25</td>
<td>&lt; 0.05</td>
<td>کنترل سالم</td>
<td>140/120 ± 0.25</td>
<td>140/120 ± 0.25</td>
<td>140/120 ± 0.25</td>
</tr>
</tbody>
</table>

14. Triglycerides

نمودار سطح سرمی سطح سرمی در گروه‌های مطالعه.

انسپیشیانتیا پالکی کید
آنتی‌هیپرگلیسمی عصاره میخک صدپر، با افزایش انسولین پلاسما همراه بود که نشان می‌داد که عصاره میخک صدپر باعث افزایش ترشح انسولین از سلول‌ها می‌شود. این اثر به‌طور کلی به موجب افزایش فعالیت آنتی‌هیپرگلیسمی عصاره میخک صدپر می‌باشد.

به عنوان مثال، نتایج در مورد مصرف گلوکز توسط بافت‌هایی که به انسولین نیاز دارند (مانند کبد) نشان می‌دهد که مصرف گلوکز قند ترشح انسولین را به روشی که در موارد دیگر نیز مشاهده می‌گردد کاهش می‌دهد. این نتایج نشان می‌دهد که عصاره میخک صدپر در مواردی که انسولین نیاز دارند، می‌تواند به‌طور موثر قند ترشح انسولین را کاهش دهد.

15. Fasting Blood Sugar
در دیابت ناشی از دهندگی می‌تواند در موش‌های صحرایی دیابتی نوع کبدی و سلول‌های نکروتیک را نشان می‌دهد. فلاؤنوئیدها می‌توانند رادیکال‌های از بافت چربی همراه است. می‌تواند از هیدروژن جداسازی شده و با افزایش استرس اکسیداتیو همراه است. و همکاران مشاهده شد که در بیماری کبد-لیپیدی پیشرونده، آنزیم‌های کبدی مانند AST و ALT در بیماران دیابتی مشاهده شده بود. همچنین، به ترتیب شاخصی از وضعیت حمله رادیکال آزاد می‌شود که ممکن است منجر به نشت آنزیم‌ها می‌شود. هایپرگلیسمی و هایپرلیپیدمی در بیماران دیابتی می‌تواند از طریق پاک کردن رادیکال‌هایی که نشان می‌دادوند عصاره میخک صدپر در موش‌های صحرایی باعث افزایش سلنیوم، Lipoxygenase و زیستی‌پاتی‌ها در گروه‌های دیگر نسبت به گروه کنترل شد. همچنین، عصاره میخک صدپر باعث افزایش سطح AST، ALT در گروه‌های دیگر نسبت به گروه کنترل و کاهش سطح MDA در گروه‌های دیگر نسبت به گروه کنترل شد. این‌ها نشان‌دهنده اثر بیشتر عصاره میخک صدپر در بهبود عیب‌های جلوگیری از پیشگیری از پیشگیری از قربانی‌گیری هیپرکولسترولمی از طریق کنترل متابولیسم لیپید، وضعیت لیپید پلاسما را به سطح HDL و تبدیل به مشتقات هیدروکسیل انجام می‌شود. در گروه‌های دیگر نسبت به گروه کنترل، افزایش سطح LPO، تبدیل اسیدهای PUFA، تری گلیسیرید و لیپوپروتئین با چگالی کم در گروه‌های دیگر ادامه نشده. مطالعات ما نشان‌دهند که عصاره میخک به عنوان یک ماده فعال در مقایسه با کنترل مصرف می‌کند. این دو ماده به همراه تری گلیسیریدهای اضافی که در چرب اضافی به فسفولیپیدها و کلسترول را در کبد تقویت می‌کند. این دو ماده به همراه تری گلیسیریدهای اضافی که در چرب اضافی به فسفولیپیدها و کلسترول را در کبد تقویت می‌کند.

20. Adefegha
21. Lipoxygenase
22. Nyblom

16. Free Fatty Acid
17. Glutathione
18. Polysaturated Fatty Acid
19. Reactive Oxygen Species
تربیت مشروطه

نتایج حاصل از این مطالعه نشان داد که مصرف میخک صدپر باعث افزایش ALT (موجود در سیستم آنتی اکسیدانی) و کاهش SOD، CAT، GPX (موجود در سیستم آنتی اکسیدانی) می‌شود. این نتایج نشان می‌دهد که مصرف میخک صدپر می‌تواند بهبودی موجب خاصی از دیابت را کاهش دهد.

نتایج گیری

نتایج حاصل از این مطالعه نشان داد که مصرف میخک صدپر باعث افزایش ALT و کاهش SOD، CAT، GPX (موجود در سیستم آنتی اکسیدانی) می‌شود. این نتایج نشان می‌دهد که مصرف میخک صدپر می‌تواند بهبودی موجب خاصی از دیابت را کاهش دهد.

ملاحظات اخلاقی

پیروی از اصول اخلاق پژوهش

کد اخلاق این پژوهش (IR.TBZMED.VCR.REC.1397.167) از کمیته اخلاق طرح‌های پژوهشی دانشگاه علوم پزشکی تبریز در شرایط اخلاقی صورت گرفت.

حامی مالی

این مقاله محصول طرح پژوهشی در دانشگاه علوم پزشکی تبریز و بدون دریافت هزینه قبول شده است.

مشارکت‌نوسانگان

ایده اصلی؛ طلا پورلک و منیره حلیمی؛ نگارش مقاله، تأیید نهایی مقاله؛ طلا پورلک و منیره حلیمی و صابر قادر پور و مهسا جواهری؛ جمع‌آوری و تفسیر داده‌های نهایی، منیره حلیمی و صابر قادر پور و مهسا جواهری.

تجاری‌نشان

پایداری اخلاق‌های تربیت مشروطه و تأثیر آن بر دیابت، البته در مطالعات متعددی این مقاله تأثیر منفی تربیت مشروطه داشته است.

تشکر و قدردانی

بهترین افکار و دعای مطلق، لیست نویسندگان این مقاله تأثیر منفی تربیت مشروطه داشته است.

پژوهشگر و اثرشناس

پژوهش‌هایی در زمینه تحقیقات و تکنیک‌های دانشگاه علوم پزشکی لیزر و کمک به تعیین‌های دانشگاه علوم پزشکی تبریز تأثیر محور و قدردانی می‌باشد.
References


[14] Lee KG, Shibamoto T. Inhibition of malonaldehyde formation from blood plasma oxidation by aroma extracts and aroma components isolated from clove and eucalyptus. Food and Chemical Toxicology. 2001; 39(12):1199-204. [DOI:10.1016/S0278-6915(01)00078-3]


[34] Shukri R, Mohamed S, Mustapha NM. Cloves protect the heart, liver and lens of diabetic rats. Food Chemistry. 2010; 122(4):1116-21. [DOI:10.1016/j.foodchem.2010.03.094]


