ERCİYES ÜNİVERSİTESİ VETERİNER FAKÜLTESİ DERGİSİ
Journal of Faculty of Veterinary Medicine, Erciyes University
Research Article/Araştırma Makalesi
21(1), 65-71, 2024
DOI: 10.32707/ercivet.1455408

Histological and Immunohistochemical Examination in Testicular Tissue of Diabetic Rats Treated with Dandelion (*Taraxacum officinale*) Extract

Şükran YEDİEL ARAS[1,a]

[1]Kafkas University, Faculty of Health Sciences Department of Midwifery, Kars-TÜRKİYE
ORCID: [a]0000-0002-3267-5251

Corresponding author: Şükran YEDİEL ARAS; E-mail: s.yediel@hotmail.com
How to cite: Yediel Aras Ş. Histological and immunohistochemical examination in testicular tissue of diabetic rats treated with dandelion (*Taraxacum officinale*) extract. Erciyes Univ Vet Fak Derg 2024; 21(1):65-71

Abstract: The aim of this study was to evaluate the changes induced in testicular tissue by administration of dandelion (*Taraxacum officinale*) extract and its effects on the release of enzymatic antioxidants SOD-2 by immunohistochemical methods in rats with experimental diabetes. Degenerative changes in the seminiferous tubule structure were observed in the testicular sections of the diabetes group. Separations between the basement membrane and the seminiferous epithelium, disruptions in the structure and localization of spermatogenic cells toward the lumen of the seminiferous tubules, thickening of the basement membrane and tunica albuginea, changes in the shape of Sertoli cells, and shrinkage of the nucleus of Leydig cells were observed. While no immunopositivity was observed in spermatogonium and primary spermatocytes in the diabetes group, weak SOD-2 immunoreactivity was observed in other cells of the spermatogenic series and moderate SOD-2 immunoreactivity was observed in the diabetes+dandelion group. In conclusion, it was found that histopathological changes occurred in the testicular tissue and SOD-2 immunoreactivity decreased in diabetes, a chronic metabolic disease. It was concluded that dandelion administration may have beneficial effects on decreased SOD-2 immunoreactivity.
Keywords: Dandelion, diabetes, SOD-2, testicular

Karahindiba (*Taraxacum officinale*) Ekstraktı Uygulanan Diyabetik Ratların Testis Dokusunda Histolojik ve İmmunohistokimyasal İncelemeler

Öz: Bu çalışma deneysel diyabet oluşturulan ratlarda Karahindiba (*Taraxacum officinale*) ekstraktı uygulamasının testis dokusunda meydana getirdiği değişimleri ve enzimatik antioksidanlardan SOD-2 salınımı üzerindeki etkilerini immunohistokimyasal yöntemlerle ile değerlendirmek amacı ile yapıldı. Diyabet grubu testis kesitlerinde seminifer tübül yapısında yer yer dejeneratif değişiklikler izlendi. Bazal membran ile tübül epiteli arasında ayrışmalar, tübül lümenine doğru spermatogenik hücrelerin yapısında ve yerleşiminde bozulmalar, bazal membran ve tunika albugineada kalınlaşmalar, sertoli hücrelerinde şekil değişikliği ve leyding hücre çekirdeğinde küçülmeler olduğu belirlendi. Diyabet grubunda spermatogonyumlar ve primer spermatositlerde immun pozitiflik gözlenmezken, spermatogenik seriye ait diğer hücrelerde zayıf, diyabet+karahindiba gurubunda orta derecede SOD-2 immunoreaktivitesi gözlendi. Sonuç olarak kronik metabolik bir hastalık olan diyabet hastalığında testis dokusunda histopatolojik değişimlerin meydana geldiği ve SOD-2 immunoreaktivitesinin azaldığı belirlendi. Karahindiba uygulamasının azalmış olan SOD-2 immunoreaktivitesi üzerinde olumlu etkileri olabileceği kanısına varıldı.
Anahtar kelimeler: Diyabet, karahindiba, SOD-2, testis

Introduction

The testis are a pair of exocrine organs with an average weight of 12-15 g, secreting holocrine type secretion. It is generally reported that the right testicle is larger and heavier than the left testicle (Krause, 2005). There are approximately 20-1000 seminiferous tubules in each testicle. There are two types of cells in the structure of seminiferous tubules. These are spermatogenic (germ) cells and Sertoli (supporting) cells. Another type of cell found in the intestinal space (intestinal connective tissue) between the seminiferous tubules are Leydig cells. These cells are responsible for testosterone production and also support spermatogenesis. Leyding cells are round shaped cells with pale cytoplasm and euchromatic nuclei (Dongmei, 2011). Diabetes mellitus (DM), defined as a chronic disease, occurs when the pancreas is unable to produce insulin or the insulin produced cannot be used effectively. According to the 2019 data of the International Diabetes Federation (IDF), the number of adults with DM worldwide is reported to be 463 million. It is estimated that this number may increase and reach up to 700 million in the 2045s. Population growth, aging, change in lifestyle brought about by urbanization, increase in obesity and decrease in physical activity are among the main causes of diabetes (International Diabetes Federation, Diabetes atlas, 2019). Although it was

Geliş Tarihi/Submission Date : 20.11.2023
Kabul Tarihi/Accepted Date : 28.12.2023

thought that diabetes did not have a significant effect on the male reproductive system, this view has changed as a result of studies. It has been reported that testosterone level, sperm count and motility, and testicular weight are decreased in men with DM, histological changes in testicular tissue cells occur and there are findings of abnormal spermatogenesis (Yigitturk et al., 2017; Ersoy and Kizilay, 2018; Oroojan et al., 2021). In addition, it has been reported that apoptosis increases in diabetic testicular tissues and therefore impaired spermatogenesis occurs (Ersoy and Kizilay, 2018; Oroojan et al., 2021). While it has been suggested that the subfertility rate in diabetic men is 51% (La Vignera et al., 2009), it was reported that the infertility rate was 35% in a study conducted on 857 male individuals with type 2 diabetes (Bener et al., 2009).

The dandelion plant belongs to the genus *Taraxacum* and is a member of the *Asteraceae* family. In addition to being used by Arab doctors for liver and spleen disorders (Sarı et al., 2020), dandelion has also been used in Chinese medicine in the treatment of diseases such as upper respiratory tract infections, hepatitis, bronchitis and pneumonia by mixing with other herbs (Martinez et al., 2015). Molecules that prevent oxidation of other molecules in the tissue are called antioxidants (Sies, 1997). Antioxidants are divided into two as enzymatic and non-enzymatic (Sharma et al., 2012). Superoxide dismutase (SOD) is included in enzymatic antioxidants. SOD is an important enzyme for the antioxidant defense system and catalyzes the dismutation of superoxide radical and converts two superoxide anions into molecular oxygen and H_2O_2 (Fridovich, 1975). The aim of this study was to investigate the changes induced by dandelion (*Taraxacum Officinale*) administration in the testicular tissue of rats with experimental diabetes mellitus and its effects on the release of antioxidant enzymes SOD-2 by immunohistochemical methods.

Material and Methods

Material

Approval for the study was obtained from Kafkas University Animal Experiments Local Ethics Committee (Decision No: KAÜ HADYEK/2023-136). In the study, 28 3-month-old male *Spraque Dawley* rats were used. The rats were housed in standard cages at an ambient temperature of 22±2°C, 12 hours of light and 12 hours of darkness and fed ad-libitum.

Methods

In the study, 4 groups were formed from randomly selected rats with 7 rats in each group. Control Group: No application was made. Dandelion Group: Rats in this group were administered 2.4 g/kg dandelion extract by oral gavages for 14 days. Diabetes Group: Streptozotocin (STZ) (dissolved in 50 ml citric acid + 40 ml disodium hydrogen phosphate buffer solution and pH: 4.5) was administered 50 mg/kg i.p. as a single dose. Diabetes+Dandelion Group: Streptozotocin (STZ) (dissolved in 50 ml citric acid + 40 ml disodium hydrogen phosphate buffer solution and pH: 4.5) 50 mg/kg i.p. and after diabetes was induced, 2.4 g/kg dandelion extract was administered by oral gavages for 14 days. Blood samples were taken from the tail vein of rats fasted for 8 hours before the start of the study to determine fasting blood glucose levels using a glucometer (Yasee, GLM-76, Taiwan). Blood glucose levels of rats fasted for 8 hours 72 hours after STZ administration were measured and those with glucose levels of 200 mg/dL were included in the study. At the end of the study, testicular tissues were removed and fixed in 10% formol solution for histological and immunohistochemical examinations. They were then subjected to routine histological tissue follow-up procedures and blocked in paraffin. Hematoxylin-eosin and PAS stains were applied to 5 µm sections taken from parfin blocks to examine the general structure of the testicular tissue.

Immunohistochemical investigations

After routine deparaffinization and rehydration, the sections were rinsed in PBS (0.1 M, pH: 7.2) and incubated in 3% H_2O_2 prepared in 0.1 M PBS for 15 min. They were then boiled in citrate buffer solution (pH: 6.0)for 10 min in a microwave oven at 800 watts. Incubated with Large Volume Ultra V Block solution (Large Volüme Anti-polyvalent, HRP (RTU)- Thermo Scientific) for 10 min. SOD-2 (SANTA CRUZ BIOTECHNOLOGY, INC. SOD-2 (B-1): sc-133254) primary antibody (1/500 dilution) was added to the sections and kept for 1 hour at room temperature in a humid environment. The sections were washed with PBS and incubated with Biotinylated Goat Anti B Polyvalent and Streptavidin Peroxidase solutions (Large Volüme Anti-polyvalent, HRP (RTU)- Thermo Scientific) for 15 min each. DAB-H_2O_2 (Diaminobenzidine hydrogen peroxide) (Large Volüme DAB Substrate System (RTU)- Thermo Scientific) Substrate Solution was added for chromogen application and modified Gill III hematoxylin solution was used for counterstaining. The preparations were examined under a research microscope and photographed. Immunohistochemical evaluation was performed by looking at the staining characteristics of the target cells and the staining intensity of the stained target cells. Evaluation was performed by two independent observers by assigning values from 0 to 3 according to the characteristics of no staining (0), weak staining (1), moderate staining (2), strong staining (3). SOD-2 immunoreactivity positive cells were counted and seminiferous tubule measurements were made using image-j software program. Cell counting was performed by randomly selecting 5 slides from each group, from 4 areas on each slide, i.e. 20 areas in total, and compared between the groups. Seminiferous tubule di-

ameter measurements were made from a total of 24 tubules by randomly selecting 5 slides from each group and compared between the groups.

Statistical investigations

SPSS Statistic 22 package program was used for statistical analyzes. One-way analysis of variance was used to compare seminiferous tubule diameter measurements between groups and Kruskall Wallis H test was used to compare the number of cells positive for SOD-2 immunoreactivity between groups. In order to determine the source of the difference as a result of Kruskall Wallis H test, correction was made on the p value and comparison was made between paired groups.

Results

Statistical results

Table 1 shows the comparison results of seminiferous tubule diameter measurements between the groups. According to the results of the analysis, there was no significant difference between the groups in tubule diameter measurements (F=1.592, P>0.05).Table 2 shows the results of the Kruskall Wallis H test performed to compare the number of cells positive for SOD-2 immunoreactivity between the groups. As a result of the analysis, it was determined that there was a statistically significant difference in the comparison of immunopositive cell numbers between the groups (x^2=16.279, P<0.01). To determine the source of the difference, P values were corrected and comparisons were made between paired groups. As a result, cell counts in the diabetes group were significantly lower than in the control and dandelion groups.

Histopathologic results

When the sections belonging to the control and dandelion groups were examined, seminiferous tubules, cells belonging to the spermatogenic series (spermatogonium, primary spermatocyte, secondary spermatocyte, spermatid and spermium), Sertoli cells and Leydig cells were observed in normal structure when the rat testicular tissues of the control group were examined (Figure 1).

In the testicular sections of the diabetes group, degenerative changes were observed in the seminiferous tubule structure. It was determined that there were separations between the basement membrane and tubule epithelium, disruptions in the structure and localization of spermatogenic cells towards the tubule lumen, thickening of the basement membrane and tunica albuginea, changes in the shape of Sertoli cells and shrinkage in the nucleus of leyding cells (Figure 1, Figure 2). It was noteworthy that the histologic structure in the diabetes+dandelion group was similar to the control group. The thickness of the basement membrane and tunica albuginea was close to the control group. The structure and localization of spermatogenic cells towards the tubule lumen were found to be at a low level (Figure 2).

Table 1. Comparison of seminiferous tubule diameter measurements between groups

Groups	n	Mean	SS	F	P
Control	24	668.219	90.85		
Dandelion	24	669.531	167.60	1.592	0.197
Diabetes	24	607.405	95.42		
Diabetes+dandelion	24	661.687	88.80		

There was no significant difference between the groups in tubule diameter measurements (P>0.05).

Table 2. Comparison of the number of SOD-2 immunoreactivity positive cells between groups.

Groups	n	Rank Mean	Mean	SS	χ2	P	pairwise comparision
Control (a)	20	16.30	182.800	20.58			
Dandelion (b)	20	14.70	181.400	26.55	16.279	0.001	c < a, b
Diabetes (c)	20	3.00	85.200	9.15			
Diabetes+dandelion (d)	20	8.00	124.200	9.28			

There is a statistically significant difference in the number of SOD-2 immunoreactivity positive cells between the groups (P<0.01).

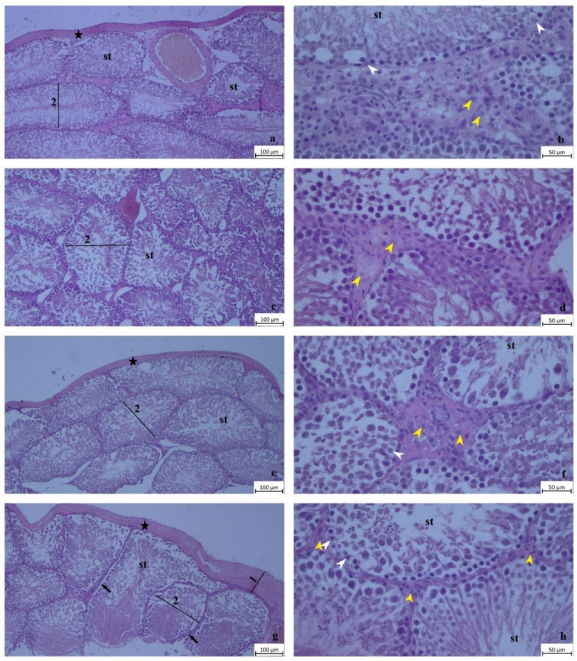

Figure 1. Rat testicular tissue. Control group (a, b), Dandelion group (c, d), Diabetes group (g, h), Diabetes+dandelion group (e, f). Seminiferous tubule (st), seminiferous tubule diameter (2), tunica albuginea (asterisk), tunica albuginea thickening (1), basement membrane thickening (black arrow), leyding cell (yellow arrow head), sertoli cell (white arrow head), H -E staining. Bar (a,c,e,g): 100 µm. Bar (b,d,f,h): 50 µm.

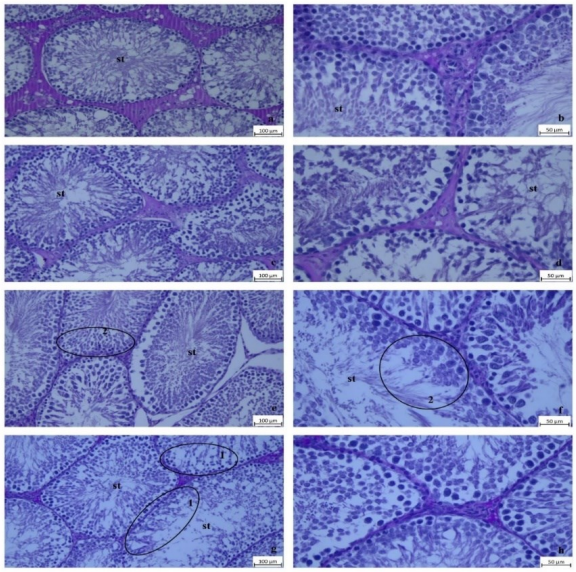

Figure 2. Rat testicular tissue. Control group (a, b), Dandelion group (c, d), Diabetes group (g, h), Diabetes+dandelion group (e, f). Seminiferous tubule (st), impaired structure and localization of spermatogenic cells in the diabetes group (1), near control appearance in the structure and localization of spermatogenic cells in the diabetes+dandelion group (2). PAS staining. Bar (a,c,e,g): 100 µm. Bar (b,d,f,h): 50 µm.

SOD-2 Immunoreactivity results

SOD-2 immunoreactivity was determined in seminiferous tubules and interstitial area in control and dandelion groups. Strong SOD-2 immunoreactivity was detected in all cells of the spermatogenic series from the basal lamina of the seminiferous tubules and moderate granular cytoplasmic SOD-2 immunoreactivity was detected in the interstitial area. While no immune positivity was observed in spermatogonia and primary spermatocytes in the diabetes group, weak SOD-2 immunoreactivity was detected in other cells of the spermatogenic series. While no immune positivity was observed in spermatogonia and primary spermatocytes in the diabetes+dandelion group, similar to the diabetes group, moderate SOD-2 immunoreactivity was observed in other cells of the spermatogenic series. It was noteworthy that there was no immunoreactivity in the interstitial area in diabetes and diabetes+dandelion groups (Figure 3).

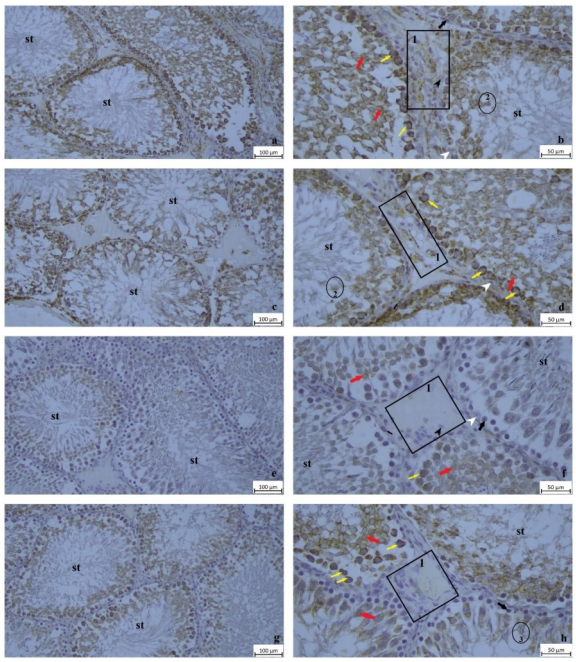

Figure 3. SOD-2 immunoreactivity in rat testicular tissue. Control group (a, b), Dandelion group (c, d), Diabetes group (e, f), Diabetes+dandelion group (g, h). Seminiferous tubule (st), interstitial space (1), leyding cell (black arrowhead), sertoli cell (white arrowhead), spermatogonium (black arrow), primary spermatocyte (yellow arrow), secondary spermatocyte (red arrow), spermatid (2), spermatozooon (3). Bar (a,c,e,g): 100 µm. Bar (b,d,f,h): 50 µm.

Discussion and Conclusion

It is suggested that diabetes is effective on male infertility due to its effects on molecular mechanisms. Since the drug treatments of diabetes and diabetes-related complications constitute a heavy burden for national economies, interest in the use of natural products with high antioxidant content that stabilize blood glucose in the treatment of diabetes has gradually increased (Lee et al., 2016). It is suggested that lipid peroxidation and free radical formation increase with blood glucose levels in diabetes, insufficiency occurs in the antioxidant defense system, and many complications may occur due to increased oxidative stress (Guneli et al., 2008; Sebai et al., 2015). In studies, it has been reported that due to the increase in oxidative stress, disorganization in spermatogenic series cells, cellular vacuolization, cells shedding into the seminiferous tubule lumen before completing their development, multinucleated giant cells in some seminiferous tubules and thickening of the basement membranes of tubules occur in diabetic testicular tissues (Öztürk et al., 2002; Sadik et al., 2011; Donmez et al., 2014). In addition, it has been reported that some of the spermatogenic cells in the testicular tissue of rats with experimental diabetes caused degeneration, shrinkage in the nuclei and nucleus pyknosis in some cells, structural changes in Sertoli cells, dilatation and hemorrhage in the vessels between tubules (İrtegün and Deveci, 2016). In our study, testicular tissues in the control and dandelion groups had normal histological appearance, but in the testicular tissues of the diabetes group, degenerative changes in the seminiferous tubule structure, separation between the basement membrane and tubule epithelium, disruptions in the structure and localization of spermatogenic cells towards the tubule lumen, thickening of the basement membrane and tunica albuginea, shape changes in Sertoli cells and shrinkage of Leyding cell nuclei were observed. Our results suggest that diabetes may cause structural changes and functional disorders in the testicular tissue and therefore there may be an important relationship between infertility and diabetes.

Dandelion is a plant that can grow in many places such as meadows, lawns, roadsides, gardens, orchards and wasteland in difficult natural conditions (Moyer et al., 2009). It has been reported that dandelion has a diuretic effect, increases bile secretion, can be used as an appetizer and in the treatment of dyspepsia. In addition, this plant has been used in traditional medicine in the treatment of many skin diseases such as eczema. It is reported to have positive effects in the treatment of diabetes, eye infection, insomnia, sore throat, lung disorders, jaundice, gout, kidney stone complaints, digestive system diseases, rheumatism and urinary tract infections (Sarı et al., 2010; Kırpık et al., 2019). When the phytochemical properties of dandelion were examined, it was reported that it contains organic acids, flavonoids, coumarins, terpenoids, carotenoids, phytosterols, sesquiterpene lactones, lignans, phenolic acids, inulin, fructose, fatty acids, vitamins A, B, C, D, potassium and mucilage. Sesquiterpenes and bitter substances in its structure increase its therapeutic properties (Schütz et al., 2006). Possible hypolipidemic and antioxidative effects of dandelion root and leaf were investigated. Plasma antioxidant enzymes and lipid levels were evaluated after the treatment period. As a result, it was suggested that it showed a positive effect on plasma antioxidant enzyme activities and lipid levels and therefore may have potential hypolipidemic and antioxidant effects (Choi et al., 2010). Dandelion methanol extract has been reported to inhibit the production of nitric oxide (NO), pro-inflammatory cytokines and prostaglandin E2 (PGE2) induced by lipopolysaccharide (LPS) in a dose-dependent manner (Park et al., 2011).In hyperglycemia, the imbalance between oxidative and antioxidative mechanisms in cells and tissues increases, resulting in an increase in reactive carbonyls (RCS) and reactive oxygen species (ROS) (Tian and Zhen, 2019). Recent studies have shown that superoxide dismutase (SOD), cata-

lase (CAT) and glutathione peroxidase (GPx) activity decreased, while malondialdehyde (MDA) and nitric oxide (NO) increased significantly in various tissue damages (Sharma et al., 2020). SOD levels were reported to be significantly decreased in streptozotocin-induced diabetic rats (Sua et al., 2022). It has been suggested that antioxidants can be used for the treatment of diabetes in male rats (Al-Salmi and Hamza, 2022). In our study, it was determined that the histological structure in the diabetes + dandelion group was close to the control group. It was determined that there was weak SOD-2 immunoreactivity in the testicular tissues of diabetic rats and moderate SOD-2 immunoreactivity in the testicular tissues of rats treated with dandelion extract. Our results suggested that dandelion may provide protection against diabetes-induced testicular damage by showing antioxidant effect.

In conclusion, diabetes is a metabolic disease with complications on testicular tissue. The use of natural treatment methods for the treatment of the disease and its complications has recently gained popularity. In our study, it was determined that histopathological changes in the testicular tissue of diabetic rats treated with dandelion extract were minimal and SOD-2 immunoreactivity increased compared to the diabetes group. Our results suggested that dandelion may have a protective effect against diabetes-induced testicular damage by positively affecting antioxidant defense mechanisms.

References

Al-Salmi AF, Hamza RZ. Efficacy of vanadyl sulfate and selenium tetrachloride as anti-diabetic agents against hyperglycemia and oxidative stress induced by diabetes mellitus in male rats. Curr Issues Mol Biol 2022; 44 (1): 94-104.

Bener A, Al-Ansari AA, Zirie M, Al-Hamaq AO. Is male fertility associated with type 2 diabetes mellitus? Int Urol Nephrol 2009; 41(4): 777-84.

Choi UK, Lee OH, Yim JH, Cho CW, Rhee YK, Lim SI, Kim YC. Hypolipidemic and antioxidant effects of dandelion (taraxacum officinale) root and leaf on cholesterol-fed rabbits. Int J Mol Sci 2010; 11(1): 67-78.

Dongmei C. Atlas of Histology with Functional and Clinical Correlations. First Edition. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2011; p.344-68.

Donmez YB, Kizilay G, Topcu-Tarladacalisir Y. MAPK immunoreactivity in streptozotocin-induced diabetic rat testis. Acta Cir Bras 2014; 29(10): 644-50.

Ersoy O, Kizilay G. Effects of fucoidan on diabetic rat testicular tissue. Biotech Histochem 2018; 93(4): 277-85.

Fridovich I. Superoxide dismutases. Annu Rev Biochem 1975; 44: 147-59.

Guneli E, Tugyan K, Ozturk H, Gumustekin M, Cilaker S, Uysal N. Effect of melatonin on testicular damage in streptozotocin-induced diabetes rats. Eur Surg Res 2008; 40(4): 354-60.

International Diabetes Federation, Diabetes atlas 9th edition. https://www.diabetesatlas.org/en/sections/worldwide-toll-of-diabetes.html. 2019. Access: 24.03.2020.

İrtegün S, Deveci E. Diyabetik sıçanların testis dokusunda VEGF ve Bcl-2 ekspresyon düzeylerinin immünohistokimya ve western blot yöntemleri ile incelenmesi. Dicle Tıp Dergisi 2016; 43(4) : 527-33.

Kırpık MA, Altunoğlu MK, Yıldız Asker Y, Altunkalem S. Evelik Bitkisi (*Rumex patientia L.*) ve Karahindiba (*Taraxacum officinale L.*) kullanılarak doğal yolla baklagil yaprak biti (*Aphis fabae Scop.*)'nin hedef konukçusunun değiştirilmesi. KAUFBED 2019; 12 (1): 1-8.

Krause William J. Krause's Essential Human Hıstology for Medical Students. Third Edition. Boca Raton: Universal Publishers, 2005; pp. 224-36.

La Vignera S, Calogero AE, Condorelli R, Lanzafame F, Giammusso B, Vicari E. Andrological characterization of the patient with diabetes mellitus. Minerva Endocrinol 2009; 34(1): 1-9.

Lee MW, Kwon JE, Lee YJ, Jeong YJ, Kim I, Cho YM, Kim YM, Kang SC. Prunus mume leaf extract lowers blood glucose level in diabetic mice. Pharm Biol 2016; 54(10): 2135-40.

Martinez M, Poirrier P, Chamy R, Prüfer D, Schulze-Gronover C, Jorquera L, Ruiz G. *Taraxacum officinale* and related species-An ethnopharmacological review and its potential as a commercial medicinal plant. J Ethnopharmacol 2015; 169(1): 244-62.

Moyer JR, Boswall AL, Kawchuk LM, Entz T, Tovell B, Lee B. Characterization of dandelion (*Taraxacum officinale* Weber in FH Wigg.) biotype morphology, chemical composition and response to glyphosate. Can J Plant Sci 2009; 89(2): 369-78.

Oroojan AA, Ahangarpour A, Paknejad B, Zareian P, Hami Z, Abtahi SR. Effects of myricitrin and solid lipid nanoparticle containing myricitrin on reproductive system disorders ınduced by diabetes in male mouse. World J Mens Health 2021; 39(1): 147-57.

Öztürk F, Gül M, Ağkadir M, Yağmurca M. Deneysel

diyabetin sıçan testislerinde meydana getirdiği histolojik değişiklikler. Turk Klinikleri J Med Sci 2002; 22(2): 173-8.

Park CM, Park JY, Noh KH, Shin JH, Song YS. Taraxacum officinale Weber extracts inhibit LPS-induced oxidative stress and nitric oxide production via the NF-κB modulation in RAW 264.7 cells. J Ethnopharmacol 2011; 33(2): 834-42.

Sadik NA, El-Seweidy MM, Shaker OG. The antiapoptotic effects of sulphurous mineral water and sodium hydrosulphide on diabetic rat testes. Cell Physiol Biochem 2011; 28(5): 887-98.

Sarı A, Özsoy N, Karahüseyin S. *Taraxacum farinosum* Hausskn. & Bornm. bitkisinin antioksidan aktivite yönünden incelenmesi. SABİAD 2020; 3(1): 13-9.

Sarı AO, Bilgin O, Bilgiç A, Nedret T, Güvensen A, Şenol SG. Ege ve Güney Marmara bölgelerinde halk ilacı olarak kullanılan bitkiler. Anadolu ETAE dergisi 2010; 20(2): 1-21.

Schütz K, Carle R, Schieber A. Taraxacum-a review on its phytochemical and pharmacological profile. J Ethnopharmacol 2006; 107(3): 313-23.

Sebai H, Selmi S, Rtibi K, Gharbi N, Sakly M. Protective effect of *Lavandula stoechas* and *Rosmarinus officinalis* essential oils against reproductive damage and oxidative stress in alloxan-induced diabetic rats. J Med Food 2015; 18(2): 241-9.

Sharma P, Jha AB, Dubey RS, Pessarakli M. Reactive oxygen species, oxidative damage, and antioxidative defense mechanism in plants under stressful conditions. J of Bot 2012; 217037.

Sharma R, Satyanarayana P, Anand P, Kumari GA. Adiponectin level association with MDA in the patients with type 2 diabetes mellitus. Biomed Pharmacol J 2020; 13: 1-9

Sies H. Oxidative stress: Oxidants and antioxidants. Exp Physiol 1997; 82: 291-5.

Sua H, Tianb CJ, Wangb Y, Shib J, Chenb X, Zhena Z, Baia Y, Denga L, Fenga C, Mab Z, Liua J. Ginsenoside Rb1 reduces oxidative/carbonyl stress damage and ameliorates inflammation in the lung of streptozotocin-induced diabetic rats. Pharm Biol 2022; 60(1): 2229-36.

Tian CJ, Zhen Z. 2019. Reactive carbonyl species: diabetic complication in the heart and lungs. Trends Endocrinol Metab 2019; 30(8): 546-56.

Yigitturk G, Acara AC, Erbas O, Oltulu F, Yavasoglu NUK, Uysal A, Yavasoglu A. The antioxidant role of agomelatine and gallic acid on oxidative stress in STZ induced type I diabetic rat testes. Biomed Pharmacother 2017; 87: 240-6.