Clinical and Experimental Health Sciences

A Natural Hope for Salivary Gland Health: Histological Evaluation of Cinnamic Acid in Diabetic Rats

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ABSTRACT

Objective: The aim of this study was to investigate the possible potential of cinnamic acid in preserving the structure and function of the parotid gland in diabetic rats.

Methods: The rats (n=32) were equally divided into four groups: Control (only physiological serum), Cinnamic acid (cinnamic acid 50 mg/kg/day), Streptozotocin-induced diabetes (experimentally-induced diabetes by intraperitoneal injection of streptozotocin 65 mg/kg), and Diabetes + cinnamic acid (cinnamic acid after diabetes induction). After the rats were sacrificed, tissue samples were obtained and processed for paraffin embedding. To visualize the histological structure, Hematoxylin&Eosin, Masson's Trichrome, and Periodic Acid-Schiff histochemical stains were applied, and images were captured.

Results: While normal serous acini, canal structures and normal connective tissue were observed in the control and cinnamic acid groups, deformation and atrophy were observed in some acinar cells in the diabetic group. In the treatment group, improvement in the shape of acinar cells and regular arrangement of parietal cells in glandular canals were noted compared to the diabetic group. The intense vacuolization observed in acinar cells in the diabetic group decreased in the treatment group. Periodic Acid-Schiff – positive reaction was determined in the basement membranes of acinar cells and parietal cells in glandular canals in all groups. No visible difference was obtained between the groups.

Conclusion: Diabetes affects the parotid gland, and cinnamic acid has been shown to prove a healing effect on deformed areas. Our study will guide further research in this area.

Keywords: Type 1 diabetes, cinnamic acid, parotid gland, histology

1. INTRODUCTION

Diabetes Mellitus (DM) is a common metabolic disease that occurs when the pancreas cannot produce insulin, called type 1 diabetes, or when body cells cannot use this insulin, called type 2 diabetes (1). Type 1 Diabetes is an autoimmune disease that occurs when the beta cells in the pancreas are destroyed by T cells, causing a disorder in their insulin production functions and the formation of autoantibodies at a rate of 70-90% (2). According to the World Health Organization's Diabetes Atlas, while the number of individuals with diabetes in the world is 537 million as of 2021, it is predicted that this number will increase by approximately 20% in 2030 to 643 million and by 46% (compared to 2021) to 783 million in 2045 (3). Type 1 diabetes is a disease characterized by chronic hyperglycemia, which often leads to diabetic complications and affects systems such as the cardiovascular system, nervous system, or organs such as the kidneys, eyes, and salivary glands. The increasing complications and severity of diabetes have caused serious morbidity and mortality, and have also affected the cost of healthcare (4-6).

Salivary glands play a major role in maintaining oral health. The saliva they secrete as exocrine glands contains mostly molecules such as water, mucus proteins, proteoglycans, salivary amylase, proline-rich proteins and salivary agglutinin. They have the ability to help with important functions such as moisturizing the epithelium, facilitating chewing, tasting, swallowing and speaking. They also promote mineralization with bicarbonate ions, which prevent tooth enamel from decalcifying thanks to their buffering systems (7).

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Recent studies have revealed a significant link between salivary gland disorders and DM. Saliva composition is affected by the metabolic, neurological, immunological, hormonal and nutritional conditions of the individual. Both the oral, dental and digestive functions of saliva depend primarily on the precise composition of organic substances in the secretory product. Accordingly, any change in the composition of saliva can lead to significant deterioration in salivary functions and trigger long-term complications in both the oral mucosa and the body system (6,8-11).

Cinnamic acid (CA)(3-phenylprop-2-enoic acid) is an organic acid that is commonly found in plants. Cinnamic acid also has antifungal, antimicrobial, antioxidant, antimutogenic, anticancer and anti-inflammatory effects (12-14). Cinnamic acid and its derivatives have been reported to have significant antidiabetic effects such as improving insulin secretion, accelerating glycolysis in the liver, increasing adiponectin secretion, increasing glucose uptake, improving pancreatic β-cell function, and reducing diabetes-induced protein glycation, and preventing diabetes complications (15-17).

Thus, it is revealed that cinnamic acid exhibits anti-diabetic effects by improving glucose tolerance and insulin secretion (18). These effects disrupt the balance of the body's defense system and trigger oxidative stress. In addition, dehydration and inadequate blood glucose control caused by diabetic effects negatively affect the function of the salivary glands and weaken their resistance to infections. This can lead to infections triggered by the microflora in the mouth and cause inflammation and cellular damage in the salivary glands (2).

As is the case with numerous pharmaceutical treatments, experiencing side effects in Type 1 diabetes is unavoidable. Therefore, medicinal plants and polyphenolic compounds obtained from them, which have been widely used in traditional medicine for centuries, have recently been used in the treatment and prevention of various metabolic diseases. No study has been found showing the effects of cinnamic acid on histopathological changes in salivary glands of diabetic rats. This study aimed to investigate the possible protective effects of cinnamic acid against changes in the histological structure of the parotid gland caused by streptozotocin (STZ) in a diabetic rat model.

2. METHODS

2.1. Experimental Animals and Ethical Declaration

The Local Ethics Committee approved this study for Animal Experiments of Burdur Mehmet Akif Ersoy University Presidency with decision number 1.288. 32 male Wistar albino rats weighing 200-280 grams and aged 8-12 weeks obtained from Burdur Mehmet Akif Ersoy University Experimental Animals Production and Experimental Research Center were used. The animals were placed in plastic cages with stainless steel grid tops and kept under a 12-h light/dark cycle with controlled temperature (23 ± 2°C) and humidity (50%). The animals were fed with standard laboratory feed and were allowed access to food and drinking water ad libitum. Blood sugar levels of animals were measured using the Accu-Check Performa Nano glucose meter (Roche, Germany) before the commencement of the study (13).

2.2. Experimental Design

Four groups were formed as control group (C) (n:8), streptozotocin-induced diabetes group (STZ-DM) (n:8), diabetes+cinnamic acid group (STZ-DM+CA) (n:8) and cinnamic acid (CA) (n:8) group. The CA group included animals that received an oral administration of 50 mg/kg CA in saline for 28 days after diabetes was induced. To induce type 1 diabetes in rats, 65 mg/kg dose of streptozotocin (19) freshly prepared in sodium citrate buffer (0.1 M, pH 4.5) (19) was administered intraperitoneally. After 72 h of diabetes induction, rats with fasted blood glucose level above 200 mg/dL were considered as diabetic. Following diabetic induction, only per os physiological serum was given to the control and diabetes groups for 28 days; 50 mg/kg dose of cinnamic acid prepared in DMSO was given orally to the cinnamic acid group and STZ-DM+CA group via gavage (13). In order to monitor whether the animals remained diabetic, weekly fasted blood glucose levels of animals (without feeding for 6 hours) were measured using the Accu-Chek Performa Nano glucose meter (Roche, Germany) throughout the study. At the end of this period, euthanasia was performed by cervical dislocation after anesthesia with ketamine/xylazine (90/10 mg/kg; Alfasan/Bayer) (20). The salivary gland material was then fixed in Bouin's solution and dehydrated in alcohol series of increasing concentrations. The samples were then passed through methyl benzoate and benzene series and embedded in paraffin.

2.3. Tissue Preparation for Histochemical Staining

Sections were taken, deparaffinized with xylol, and rehydrated in decreasing concentrations of alcohol (96%, 80%, 70%, 60%, 50% and then distilled water). The prepared preparations were stained with Hematoxylin and Eosin (H&E) for routine histological examination, Masson Trichrome (MT) for collagen fibers, and Periodic Acid Schiff (PAS) to show the polysaccharide concentration in the acinus and duct cells of the parotid gland (21). Then, the preparations were taken into distilled water and dehydrated, xylene and the samples were gradually rehydrated, and the slides closed with entellan. Figures were obtained using a light microscope (Zeiss, Germany) and photographed using DP72 digital camera (Olympus, Tokyo, Japan).

3. RESULTS

The examinations performed on tissue sections stained with H&E, MT, and PAS staining results of parotid gland were showed in Figure 1.

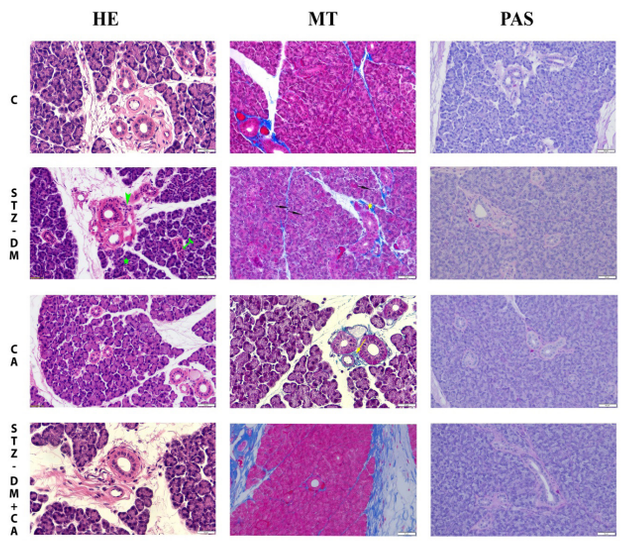

Figure 1. *Microscopic image of the parotid gland for all groups, green star; degenerative acinar cells, green arrowhead; inflammatory cell infiltration into the connective tissue, green arrow; degenerative striated duct, H&E staining. Yellow asterisk; collagen fibers surrounding ducts and blood vessels, black arrows; acinar cells containing lipid droplets, yellow arrow; decreased collagen fibers surrounding ducts and blood vessels, MT staining. PAS-positive reaction in the basement membranes of acinar cells in the glandular ducts and in parietal cells, PAS staining. Scala bar: 50 µm.*

3.1. H&E staining results

Normal serous acinus structures, duct structures, and normal connective tissue structures were observed in the parotid gland of control and CA groups. The lumen of the gland ducts was also clearly visible in the parotid parenchyma, which consisted of neatly packed pure serous acini. The intralobular ducts exhibited normal histological features, including intercalated ducts and poorly defined lobules of serous acini, lined by pyramidal basophilic cells and characterized by round nuclei, separated by thin septa. The striated ducts were easily recognized as they were lined by simple columnar cells with round nuclei and basal striations.

STZ-DM group showed a widening of the interlobular space, some acini were confluent and fused, while others were shrunken and atrophic. In addition, most acini showed darkly stained nuclei of varying size and shape. Some ducts were dilated and surrounded by inflammatory cell infiltration and fibrous tissue. The ducts showed structural changes; some showed disruption and disorganization of their epithelial lining, and some showed retention of secretions. The duct cells showed darkly stained nuclei flattened with cytoplasmic vacuolation.

STZ-DM+CA group, acinar cells showed improvement in their shape, prominent lumen in gland ducts and regular parietal cells were detected compared to the STZ-DM group

3.2. Masson's Trichrome results

Normal connective tissue was observed around intralobular ducts and blood vessels in the control group. In addition, a regular structure in acinar cells and regular arrangement of parietal cells in glandular ducts and their lumen were observed.

Masson's trichrome-stained slides of the parotid gland of the diabetic rat showed the presence of collagen fibers, especially surrounding the ducts and blood vessels. Vacuolization of acinar cells, glandular ducts with irregular parietal cells, and dilated glandular lumen were determined in the parotid gland.

Collagen deposition between lobules in parotid gland decreased significantly in the CA group compared to control and STZ groups. Whereas collagen decreased significantly in the STZ + CA group compared to STZ group (Figure 1)

The number of lipid droplet cells in the parotid gland was significantly reduced in the STZ-DM+CA group compared to the STZ-DM group.

3.3. PAS results

Samples from all groups were examined in the parotid gland and a positive reaction was determined in the basement membranes of acinar cells and parietal cells in glandular ducts. No visible difference was determined between the groups.

Mast cells with dark purple-stained granules were determined in the connective tissue between the lobes, especially around the vessels.

4. DISCUSSION

Salivary glands have an important role in maintaining oral health as they are exocrine glands that secrete saliva, an enriched medium consisting fundamentally of water, mucus proteins, proteoglycans, salivary amylase, proline-rich proteins and salivary agglutinin. They have important functions such as epithelial hydration, ease of chewing, taste, swallowing and speech. They also have a buffering effect with bicarbonate ions that prevent enamel decalcification and promote remineralization (22).

DM is a multifactorial disease triggered by a combination of epigenetic, genetic, and environmental factors. Increased life expectancy and unhealthy lifestyle habits, such as sedentary lifestyle and consumption of foods rich in saturated fats and added sugars, are risk factors for the development of obesity and associated comorbidities such as metabolic syndrome, also called insulin resistance syndrome (8,23).

DM progresses silently in the early stages (24,25), but in the long term, it damages many vital organs such as the kidneys, blood vessels, heart, and bones (2,26). The high prevalence of DM, its fatal complications, and the incomplete pathogenesis

of DM necessitate the use of preclinical models to better understand the disease.

Diabetes leads to changes in the oral cavity (23,27). Most of these changes are directly related to the reduction in salivary flow and changes in salivary composition, and abnormalities in collagen metabolism in the mucosa and the formation of glycated end products that negatively affect collagen stability and vascular integrity. Several studies have reported a negative impact on periodontal health (28). In one study, the decrease in PAS reaction in acinus and ductal cells in the diabetic group (29) was explained by the decrease in polysaccharide concentration in the acinus (10). However, Nicolau et al. (30) observed that enhanced glycogen synthase activity and decreased glycogen phosphorylase activity resulted in glycogen buildup in the salivary glands of diabetic rats. In this study, no significant difference was detected between the groups in terms of PAS-positive reaction in the basement membranes of acinar cells and gland parietal cells.

Cinnamic acid and its derivatives are reported to have important antidiabetic effects such as improving insulin secretion, accelerating glycolysis in the liver, increasing adiponectin secretion, increasing glucose uptake, improving pancreatic β-cell function and reducing diabetes-induced protein glycation, and prevent diabetes complications (15,17,31). The study showed that cinnamic acid improved memory by reducing oxidative stress and cholinergic dysfunction in the brain of diabetic mice (32). In cell culture and animal experiments, it has been reported that cinnamic acid derivatives have stimulating effects on insulin secretion, depending on the dose (33). These effects disrupt the balance of the body's defense system and trigger oxidative stress. In addition, dehydration and inadequate blood glucose control caused by diabetic effects negatively affect the function of the salivary glands and weaken their resistance to infections. This can lead to infections triggered by the microflora in the mouth and cause inflammation and cellular damage in the salivary glands (2).

Studies have reported that various damages such as cellular hypertrophy, atrophy, hyperplasia, and DNA damage occur with the development of diabetes in the major salivary glands (6,34). In studies conducted by Hasegawa et al. (35), it was stated that the parotid gland was damaged and its functions were impaired in animals with experimental diabetes and that this could be due to oral infections developing due to decreased salivary secretion. In addition, it has been stated that various secretory irregularities occur in the salivary glands of diabetic and menopausal rats, and that these irregularities may lead to damage in the acinus epithelium and trigger the migration of inflammatory cells with an increase in the protein ratio in the secretory composition and the accumulation of unsaturated fat droplets (36). In this study, morphological and structural abnormalities were observed, especially in the parotid gland of STZ-DM rats. In parallel with this study, Morsy et al. (6) reported that abundant collagen fibers were seen in the parotid gland of a diabetic rat, especially around the ducts and blood vessels. Anderson et al. (37) suggested that there were numerous lipid droplets, especially in the serous acini of the large salivary glands of diabetic rats, and that this could be due to excessive uptake into the cell to be used as an energy source or to decreased synthesis in secretory granules and plasma membrane material. Vacuolation was detected in parotid acinar cells in short-term DM, young and aging rats (8). In this study, the number of lipid droplet cells in the parotid gland was significantly reduced in the STZ-DM+CA group compared to the STZ-DM group.

Researchers who examined the effect of ascorbic acid on rats with a diabetes model reported that the STZ group showed normal glandular architecture with irregular acini, cytoplasmic vacuolization in glandular cells with apoptotic nuclei, thickened connective tissue septa with leukocyte infiltration, and congested vessels (10). Another study supported this with similar findings by (9,38), who reported severe acinar cell deformation and atrophy with reduced secretory granules, vacuolization, and leukocyte infiltration in the salivary glands of diabetic rats. In our study, it was determined that cinnamic acid improved the shape of acinar cells and had prominent lumens and regular parietal cells in the gland ducts in the salivary glands of diabetic rats compared to the DM group. The parotid glands showed a very similar picture to the control group in that the majority of acini and ducts had normal histological appearance.

One study showed that oral administration of CA could reduce body weight, FBG, and blood pressure in DIO mice and improve lipid profile (14). Moreover, CA derivatives have synergistic interactions with oral hypoglycemic drugs such as thiazolidinedione and metformin, which are useful in the treatment of diabetes (39), therefore, CA may offer preventive and therapeutic benefits in combating obesity and vascular dysfunction in diabetes.

5. CONCLUSION

Various mechanisms have been proposed by researchers to explain the effect of cinnamic acid and its derivatives on the management and prevention of diabetes and its complications. Although their potential benefits have been demonstrated in vitro and preclinical studies, there is insufficient clinical evidence to prove these beneficial effects. Therefore, more epidemiological studies are needed to evaluate the role of cinnamic acid on diabetes and its complications.

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Research idea: ST, DK

Design of the study: ST, DK, GBÖ

Acquisition of data for the study: ST, DK

Analysis of data for the study: ST, DK

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Revising it critically for important intellectual content: ST, DK, GBÖ, MÖ

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REFERENCES

[1] Sugandh FNU, Chandio M, Raveena FNU, Kumar L, Karishma FNU, Khuwaja S, Memon UA, Bai K, Kashif M, Varrassi G, Khatri M, Kumar S. Advances in the management of diabetes mellitus: A focus on personalized medicine. Cureus 2023;15(8):1-13. https://doi.org/10.7759/cureus.43697

[2] Martin-Carro B, Donate-Correa J, Fernández-Villabrille S, Martín-Vírgala J, Panizo S, Carrillo-López N, Martínez-Arias L, Navarro-González JF, Naves-Díaz M, Fernández-Martín JL, Alonso-Montes C, Cannata-Andia JB. Experimental models to study diabetes mellitus and its complications: limitations and new opportunities. International Journal of Molecular Sciences 2023;24:1-16. https://doi.org/10.3390/ijms241210309

[3] Başaralı MK, Sarışen Adıgüzel Ö, Atabey M. Türkiye Diyabet Programı 2023-2027. Ankara. Turkish.

[4] Moreira AR, Passos IA, Sampaio FC, Soares MS, Oliveira RJ. Flow rate, pH and calcium concentration of saliva of children and adolescents with type 1 diabetes mellitus. Brazilian Journal of Medical and Biological Research 2009;43(8):707–711. https://doi.org/10.1590/S0100-879X200.900.5000006

[5] Jiang H, Xia C, Lin J, Garalleh HA, Alalawi A, Pugazhendhi, A. Carbon nanomaterials: a growing tool for the diagnosis and treatment of diabetes mellitus. Environmental Research 2023;221:1-8. https://doi.org/10.1016/j.envres.2023.115250

[6] Morsy MM, Mostafa OAA, Ibrahim F, Hassan HA, Alabassery N. Histological and immunohistochemical study on the possible ameliorating effects of antox on the parotid gland of rats with streptozotocin-induced diabetes mellitus type 1. Egyptian Society of Clinical Toxicology Journal 2023;11(1);1-29. https://doi.org/10.21608/esctj.2022.179.739.1023

[7] Yasser S, Shon AA. Histomorphometric and immunohistochemical study comparing the effect of diabetes mellitus on the acini of the sublingual and submandibular salivary glands of albino rats. Macedonian Journal of Medical Sciences 2020;30(8):49-54. https://doi.org/10.3889/oamjms.2020.3722

[8] Monteiro MM, D'Epiro TT, Bernardi L, Fossati AC, Santos MF, Lamers ML. Long – and short-term diabetes mellitus type 1 modify young and elder rat salivary glands morphology. Archives of Oral Biology 2017;73:40-47. https://doi.org/10.1016/j.archoralbio.2016.08.028.

[9] Chen SY, Wang Y, Zhang CL, Yang ZM. Decreased basal and stimulated salivary parameters by histopathological lesions and secretory dysfunction of parotid and submandibular glands in rats with type 2 diabetes. Experimental and Therapeutic Medicine 2020;19(4):2707–2719. https://doi.org/10.3892/etm.2020.8505

[10] Rasheed RA, Embaby AS, Elkhamisy FAA, Mohamed MO, Abbasi AM, Ghaly WBA, Elshaer MMA, Almaary KS, Almoatasem MAM. Ascorbic acid alleviates oxidative stress and improves major salivary glands' structure and function in diabetic rats: A histological and immunohistochemical study. Journal of King Saud University Science 2022;34:1-10. https://doi.org/10.1016/j.jksus.2022.102273

[11] Park J, Yamamoto Y, Hidaka K, Wada-Takahashi S, Takahashi SS, Morozumi T, Kubota N, Saita M, Saruta J, Sakaguchi W, To M, Shimizu T, Mikuni-Takagaki Y, Tsukinoki K. Effects of diabetes and voluntary exercise on IgA concentration and polymeric immunoglobulin receptor expression in the submandibular gland of rats. Medicina 2023;18;59(4):1-13. https://doi.org/10.3390/medicina59040789

[12] Pontiki E, Hadjipavlou-Litina D. Multi-target cinnamic acids for oxidative stress and inflammation: design, synthesis, biological evaluation and modeling studies. Molecules 2018;24(1):1-13. https://doi.org/10.3390/molecules24010012

[13] Anlar HG, Bacanlı M, Çal T, Aydın S, Arı N, Ündeğer Bucurgat Ü, Başaran AA, Başaran AN. Effects of cinnamic acid on complications of diabetes. Turkish Journal of Medical Sciences 2018;48(1):168-177. https://doi.org/10.3906/sag-1708-8. (Turkish)

[14] Bai Y, Tan D, Deng Q, Miao L, Wang Y, Zhou Y, Yang Y, Wang S, Vong CT, Cheang WS. Cinnamic acid alleviates endothelial dysfunction and oxidative stress by targeting PPARδ in obesity and diabetes. Chinese Medicine 2025;20(1):1-12. https://doi.org/10.1186/s13020.025.01064-7

[15] Hafizur RM, Hameed A, Shukrana M, Raza SA, Chishti S, Kabir N, Siddiqui RA. Cinnamic acid exerts anti-diabetic activity by improving glucose tolerance in vivo and by stimulating insulin secretion in vitro. Phytomedicine 2015;22:297-300. https://doi.org/10.1016/j.phymed.2015.01.003. Turkish

[16] Taner G, Özkan Vardar D, Aydin S, Aytaç Z, Başaran A, Başaran N. Use of in vitro assays to assess the potential cytotoxic, genotoxic and antigenotoxic effects of vanillic and cinnamic acid. Drug and Chemical Toxicology 2017; 40: 183-190. https://doi.org/10.1080/01480.545.2016.1190740

[17] Onat KA, Kürkçü MS, Çöl B. Fenolik bileşiklerden sinnamik asit, kafeik asit ve p-kumarik asit'in bazı biyolojik aktiviteleri. Journal of the Institute of Science and Technology 2021;11(4):2587-2598. https://doi.org/10.21597/jist.885898. Turkish

[18] Adisakwattana S, Chantarasinlapin P, Thammarat H, Yibchok-Anun S. A series of cinnamic acid derivatives and their inhibitory activity on intestinal α-glucosidase. Journal of Enzyme Inhibition and Medicinal Chemistry 2009;24(5):1194-1200. https://doi.org/10.1080/147.563.60902779326

[19] Furman BL. Streptozotocin-ınduced diabetic models in mice and rats. Current Protocols 2021;1(4):1-21. https://doi.org/10.1002/cpz1.78

[20] Olson ME, McCabe K. Anesthesia in the Richardson's ground squirrel: comparison of ketamine, ketamine and xylazine, droperidol and fentanyl, and sodium pentobarbital. Journal of the American Veterinary Medical Association 1986; 189: 1035-1037

[21] Bancroft JD, Layton C. The hematoxylin and eosin, connective and mesenchymal tissues with their stains. In: Suvarna, S.K., Layton, C., Bancroft, J.D. (Eds.), Bancroft's Theory and Practice of Histological Techniques. 7th ed. Churchill Living one, Philadelphia, pp. 173–212; 2013.

[22] Barut Z. Tükürük biyokimyası. Oral biyokimya temel ve klinik kavramlar. İşbir T, Altay AN. (ed.). Türkiye Klinikleri. Ankara. S. 231-269; 2023.

[23] Negrato CA, Tarzia O. Buccal alterations in diabetes mellitus. Diabetol Metab Syndr 2010;15;2:3. https://doi.org/10.1186/1758-5996-2-3.

[24] Silva JAD, Souza ECF, Echazu Boschemeier AG, Costa C, Bezerra HS, Feitosa E. Diagnosis of diabetes mellitus and living with a chronic condition: Participatory study. BMC Public Health 2018;18:1-8. https://doi.org/10.1186/s12889.018.5637-9

[25] Von Birgelen C, Kok MM, Sattar N, Zocca P, Doelman C, Kant GD, Lowik MM, van der Heijden LC, Sen H, van Houwelingen KG, Stoel MG, Louwerenburg JW, Hartmann M, de Man HAF, Linssen CM, Doggen JM, Tandjung K. "Silent" diabetes and clinical outcome after treatment with contemporary drug-eluting stents: The BIO-RESORT silent diabetes study. Journals of the American College of Cardiology: Cardiovascular Interventions 2018;11:448–459. https://doi.org/10.1016/j.jcin.2017.10.038

[26] Stehouwer CDA. Microvascular dysfunction and hyperglycemia: a vicious cycle with widespread consequences. Diabetes 2018;67:1729–1741. https://doi.org/10.2337/dbi17-0044

[27] Dodds MW, Johnson DA, Yeh CK. Health benefits of saliva: A review. Journal of Dentistry 2005;33:223–233. https://doi.org/10.1016/j.jdent.2004.10.009

[28] Taylor GW, Borgnakke WS. Periodontal disease: associations with diabetes, glycemic control and complications. Oral Diseases 2008;14(3):191-203. https://doi.org/10.1111/j.1601-0825.2008.01442.x.

[29] El Sadik A, Mohamed E, El Zainy A. Postnatal changes in the development of rat submandibular glands in offspring of diabetic mothers: biochemical, histological and ultrastructural study. Plos One 2018;1-23. https://doi.org/0.1371/journal.pone.0205372

[30] Nicolau J, de Matos JA, de Souza DN, Neves LB, Lopes AC. Altered glycogen metabolism in the submandibular and parotid salivary glands of rats with streptozotocin-induced diabetes. Journal of Oral Science 2005;47(2):111–116. https://doi.org/10.2334/josnusd.47.111

[31] Yazdi M, Nafari A, Azadpour M, Alaee M, Hadipour Moradi F, Choghakhori R, Hormozi M, Ahmadvand H. Protective effects of cinnamic acid against hyperglycemia induced oxidative stress and inflammation in HepG2 cells. Reports of Biochemistry and Molecular Biology 2023;12(1):1-12. https://doi.org/10.52547/rbmb.12.1.1.

[32] Hemmati AA, Soheila A, Akram A. Effects of cinnamic acid on memory deficits and brain oxidative stress in streptozotocin-induced diabetic mice. KJPP 2018;22.3: 257.

[33] Adisakwattana S. Cinnamic acid and its derivatives: mechanisms for prevention and management of diabetes and its complications. Nutrients 2017;9(2):1-27. https://doi.org/10.3390/nu9020163

[34] Carda C, Carranza M, Arriaga A, Diaz A, Peydró A, Ferraris MEG. Structural differences between alcoholic and diabetic parotid sialosis. Medicina Oral Patologia Oral y Cirugia Bucal 2005;10(4):309-314.

[35] Hasegawa J, Hidaka H, Tateda M, Kudo T, Sagai S, Miyazaki M, Katagiri K, Nakanome A, Ishida E, Ozawa D. An analysis of clinical risk factors of deep neck infection. Auris Nasus Larynx 2011;38: 101-107.

[36] Parlak SN. Deneysel menopoz ve diyabetin sıçan parotis, submandibular ve sublingual bezinin üzerine olan etkilerinin incelenmesi: histopatolojik ve stereolojik çalışma. Atatürk Üniversitesi, Sağlık Bilimleri Enstitüsü, Histoloji ve Embriyoloji Anabilim Dalı, 116s, Erzurum;2014.

[37] Anderson LC, Garrett JR. Lipid accumulation in the major salivary glands of streptozotocin-diabetic rats. Archives of Oral Biology 1986;31: 469-75. https://doi.org/10.1016/0003-9969(86)90021-X

[38] Cui J, Yin S, Zhao C, Fan L, Hu H. Combining patulin with cadmium induces enhanced hepatotoxicity and nephrotoxicity in vitro and in vivo. Toxins 2021;13(3): 221. https://doi.org/10.3390/toxins13030221

[39] Prabhakar PK, Doble M. Interaction of cinnamic acid derivatives with commercial hypoglycemic drugs on 2-deoxyglucose uptake in 3T3-L1 adipocytes. Journal of Agricultural and Food Chemistry 2011;59(18):9835–9844. https://doi.org/10.1021/jf2015717