Chapter 10

DIABETES MELLITUS, FREE RADICALS AND OXIDATIVE STRESS

Songül DOĞANAY[1]

INTRODUCTION

Diabetes, a chronic metabolic disorder, is an important health problem increasingly continues worldwide. It is characterized by absolute or relative deficiencies in insulin secretion. Various complications including both macro and micro-vascular dysfunctions develop as a result of metabolic disorders in diabetes. Oxidative stress is closely related to numerous diseases, including any imbalance between reactive oxygen species and antioxidant defense capacity of the body, aging and cancer, cardiovascular diseases, without excepting diabetes and diabetic complications. Although the exact contribution is not entirely clear, oxidative stress is known to increase in the case of diabetes. The results of clinical and animal studies point out a large number of interrelated mechanisms which increase the production of reactive oxygen and nitrogen species or reduce the antioxidant defense mechanisms in diabetic patients. These changes, which are the result of diabetic complications, can bring about a biomolecular level of destruction in cell organelles and membranes.

FREE RADICALS

Free radicals are atoms and molecules bearing an unpaired electron in the outer orbital. Since these molecules are unstable; Cellular proteins are highly reactive radicals that can stimulate harmful oxidation reactions in cellular proteins, lipids or DNA, distorting cellular functions and causing oxidative stress (Cooper, 2002; Clarkson&Thompson2000). Free radicals are formed during metabolic cases in the organism; they are formed in the mitochondrial respiratory chain in the cell or due to various external factors such as radiation, drugs and harmful chemicals just like formed especially by phagocytes outside the cell. A very important part of these radicals is caused by oxygen and nitrogen (Tamer& Al, 2012; Gürdöl&Ademoğlu, 2010). The resulting free radicals are eliminated

[1] Dr. Öğr. Üyesi, Sakarya Üniversitesi Tıp Fakültesi Fizyoloji AD, songuldoganay@sakarya.edu.tr

REFERENCES

Adamiec-Mroczek, J., Oficjalska-Mlynczak, J., (2008), Assessment of selected adhesion molecule and proinflammatory cytokine levels in the vitreous body of patients with type 2 diabetes—role of the inflammatory–immune process in the pathogenesis of proliferative diabetic retinopathy. Graefe's Archive for Clinical and Experimental Ophthalmology, 246:12, 1665-1670.

Agardh, CD., Stenram, U., Torffvit, O., Agardh, E. (2002), Effects of inhibition of glycation and oxidative stress on the development of diabetic nephropathy in rats. *Journal of diabetes and its complications*, 16 (6), 395-400.

Akkaya, H. and Çelik, S. (2010). Ratlarda diyabet öncesi ve sonrası oksidan-antioksidan durum.*Fırat Üniversitesi Sağ. Bil. Vet. Derg*, 24 (1), 5-10.

Aksoy, M. (2003). *BeslenmeBiyokimyası*. Ankara: HatipoğluYayınevi. 465-565.

Altıparmak MR, Apaydın S. (2001), Diyabetik nefropati. Yenigün M (Editör). Her yönüyle diabetes mellitus. 2.baskı. İstanbul: Nobel Tıp Kitabevi, 383-399.

Apostolova, N. and Victor, VM. (2015). *Molecular strategies for targeting antioxidants to mitochondria: therapeutic implications.Antioxid Redox Signal,***22** (8), 686-729.

Atalay, M. and Laaksonen, DE., (2002), Diabetes, oxidative stress and physical exercise. *Journal of sports science & medicine*, 1 (1), 1.

Ayala, A., Munoz, MF. and Argüelles, S. (2014). Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. *Oxidative medicine and cellular longevity, 2014, 1-31: Doi,* 10.1155/2014/360438

Bell, GI. and Polonsky, KS., (2001), Diabetes mellitus and genetically programmed defects in β-cell function. *Nature,*. 414 (6865), 788.

Brownlee, M., 82005). The pathobiology of diabetic complications: a unifying mechanism. *diabetes*, 54 (6), 1615-1625.

Chen, B-H., Jiang, D-Y., Tang, L-S., (2006), Advanced glycation end-products induce apoptosis involving the signaling pathways of oxidative stress in bovine retinal pericytes.,*Life Sciences.* 79:11, 1040-1048

Chibber, R., Molinatti, PA., Rosatto, N., Lambourne, B., Kohner, EM. (1997),Toxic action of advanced glycation end products on cultured retinal capillary pericytes and endothelial cells: relevance to diabetic retinopathy. *Diabetologia.* 40 (2), 156-64.

Clarkson, PM, Thompson, HS. (2000). Antioxidants: what role do they play in physical activity and health. *American Society for Clinical Nutrition,* **72**, 637-646.

Cooke, MS., Evans, MD., Dizdaroglu, M., Lunec, J., (2003). Oxidative DNA damage: mechanisms, mutation, and disease. *The FASEB Journal*,. **17** (10), 1195-1214.

Cooper CE, Vollaard, NBJ., Choueiri, T.,Wilson, MT. (2002). *Exercise, free radicals and oxidative stress.Biochemical Society Transactions*, 30 (2), 210-285.

Cooper, ME., (2001), Interaction of metabolic and haemodynamic factors in mediating experimental diabetic nephropathy. Diabetologia, 44 (11), 1957-1972.

Demir, E., (2014) Streptozotosin ile Tip-1 diyabet oluşturulan sıçanlarda acı badem yağının serum ve eritrositlerdeki bazı biyokimyasal parametrelere etkisi. *Marmara Pharmaceutical Journal,* 18, 13-21.

Demircan, G., Dyraman, E., and Demircan, S., (2005), The role of oxidative stress in heart diseases. *Turk Kardiyol Dern Ars*, 33 (8), 488-492.

Dhalla, NS.,Temsah, RM., Netticadan, T. (2000), Role of oxidative stress in cardiovascular diseases. *Journal of hypertension*, 18:6, 655-673.

Droge, W., (2002). Free radicals in the physiological control of cell function. *Physiol Rev,* 82 (1), 47-95.

Duzguner, V., Kucukgul, A., Erdogan, S., Celik, S., Sahin, K., (2008), Effect of lycopene administration on plasma glucose, oxidative stress and body weight in streptozotocin diabetic rats. Journal of Applied Animal Research, 33:1, 17-20.

Eroglu, Y. and Daglioglu, O. The effect of submaximal exercise on oxidant and antioxidant mechanisms in judokas and sedentary. *International Journal of Sport Studies,* 2013.3 (5), 480- 486.

Fidan, AF, Dündar, Y. (2008). The effects of Yucca schidigera and Quillaja saponaria on DNA damage, protein oxidation, lipid peroxidation, and some biochemical parameters in streptozotocin-induced diabetic rats. *Journal Diabetes Complications,* 22, 348-356.

Gönül, Ş., 2014; Proliferatif Diabetik Retinopati: Patofizyoloji.*Journal of Retina-Vitreous Özel Sayi, 22,31-37.*

Gray, S.P. and Jandeleit-Dahm, K., (2014), The pathobiology of diabetic vascular complications—cardiovascular and kidney disease. *Journal of Molecular Medicine,* 92 (5), 441-452.

Green, K., Brand, MD. and Murphy, MP. (2004), Prevention of mitochondrial oxidative damage as a therapeutic strategy in diabetes. *Diabetes,* 53 (1), S110-S118.

Gürdöl, F., Ademoğlu, E. (2010). *Biyokimya.* İstanbul: Nobel Tıp Kitabevleri. 829-836.

Halliwell, B. and Gutteridge, JM., (2015). *Free radicals in biology and medicine.*5th ed. Oxford University Press, USA, 639-695.

Hamamcioglu, AC., (2017) Diyabette Oksidatif Stres ve Antioksidanların Rolü. *Türkiye Diyabet ve Obezite Dergisi,* 1 (1), 7-13.

Heinecke, JW., (2003), Oxidative stress: new approaches to diagnosis and prognosis in atherosclerosis. *The American journal of cardiology*, 91 (3), 12-16.

İlhan, DK., Değer, Y., and Uslu, S, (2014), Diyabetik Ratların Böbrek Dokusuna Likopenin Oksidan ve Antioksidan Etkisi. Harran Üniversitesi Veteriner Fakültesi Dergisi, 3 (1): 18-23.

Kanter, M., Aktas, C., and Erboga, M. (2012), Protective effects of quercetin against apoptosis and oxidative stress in streptozotocin-induced diabetic rat testis. *Food and chemical toxicology,* 50 (3-4), 719-725.

Keskin, Ö. and Balcı, B. (2011), Diabetes Mellitus veKardiovaskülerKomplikasyonlar. *Kafkas Tıp BilimleriDergisi,* 2011 (2), 81-85.

Mahboob, M. Rahman, MF. and Grover, P., (2005). Serum lipid peroxidation and antioxidant enzyme levels in male and female diyabetic patients. *Singapore medical journal,* 46, 322-324.

Marchetti, P., Dotta, F., Lauro, D., and Purrello, F. (2008), An overview of pancreatic beta-cell defects in human type 2 diabetes: implications for treatment. *Regulatory peptides*, 146 (1-3), 4-11.

Maritim, A.C, Sanders, RA, and Watkins, LJB. (2003). Diyabetes, oxidative stress, and antioxidants. *Journal of biochemical and molecular toxicology*, 17, 24-38.

Memişoğullari, R., (2006), Diyabette serbest radikallerin rolü ve antioksidanların etkisi. *Düzce Tıp Fakültesi Dergisi,***3**, 30-39.

Newsholme, P., Haber, EP., Rebelato, ELO., Hirabara, SM., Procópio, J., Morgan, D., Oliveira-Emilio, HC., Carpinelli, AR., Curi, R. (2007), Diabetes associated cell stress and dysfunction: role of mitochondrial and non-mitochondrial ROS production and

activity. *The Journal of physiology,* 583 (1), 9-24.
Ögüt, S. and Atay, E. (2012). Yaşlılık ve oksidatif stres. *Süleyman Demirel Üniversitesi Tip Fakültesi Dergisi,* 19 (2), 68-74.
Onat, T., Emerk, K., Sözmen, EY. (2002). *İnsan Biyokimyası.Radikal Kavramı ve Oksijen Radikaller.* Ankara: Palme Yayıncılık. 666-673.
Özcan, O., Hüseyin E., Çakırca, G., Yönden, Z. (2015). Oksidatifstresvehücreiçilipit, protein ve DNA yapılarıüzerineetkileri. *Journal of Clinical and Experimental Investigations,* 6 (3).
Parmaksız, İ., (2011), Diyabet komplikasyonlarında ileri glikasyon son ürünleri. *Marmara Medical Journal,* 24, 141-148.
Pierce, EA., Foley, ED. and Smith, LE. (1996), Regulation of vascular endothelial growth factor by oxygen in a model of retinopathy of prematurity. *Arch Ophthalmol,* 114 (10), 1219-1228.
Rahimi, R., Nikfar, S., Larijani, B., Abdollahi, M. (2005). A review on the role of antioxidants in the management of diabetes and its complications. *Biomedicine & Pharmacotherapy,* 59 (7), 365-373.
Rajasekaran, S., Sivagnanam, K. and Subramanian, S., (2005). Antioxidant effect of Aloe vera gel extract in streptozotocin-induced diabetes in rats. *Pharmacol Rep*,. 57 (1), 90-96.
Rao, RSP. and Moller, IM. (2011). Pattern of occurrence and occupancy of carbonylation sites in proteins.*Proteomics,* 11 (21), 4166-4173.
Şekeroğlu, MR., Huyut, Z., Çokluk E., Özbek H., Alp, HH. (2017). The susceptibility to autoxidation of erythrocytes in diabetic mice: Effects of melatonin and pentoxifylline. *Journal of biochemical and molecular toxicology,* 31 (12), e21976.
Tamer, LPG., Eskandarı, G., Ercan, B., Atik, U. (2000). Serbest radikaller.*Mersin Üniversitesi Tıp Fakültesi Dergisi*, 1,52-58.
Tiedge, M., Lortz, S., Drinkgern, J., Lenzen, S. (1997). Relation between antioxidant enzyme gene expression and antioxidative defense status of insulin-producing cells. *Diabetes,* 46 (11), 1733-1742.
Uzunovali, B., and Öztürk, AÖ., (2016), Diyabetik Retinopati ve Mikronütrisyon. *Journal of Retina-Vitreous,* 24 (1).
Wild, S., Roglic, G., Green, A., Sicree, R., King, H. (2004). Global prevalence of diabetes . *Diabetes Car.,* 27, 1047-1053.
Yamagashi, S. (2011). Role of advanced glycation end products (AGEs) and receptor for AGEs (RAGE) in vascular damage in diabetes. *Experimental Gerontology,* 46:217-224.