INTERNATIONAL JOURNAL OF
MEDICAL BIOCHEMISTRY

DOI: 10.14744/ijmb.2021.53825
Int J Med Biochem 2021;4(3):185-91

Research Article

Examination of fasting and postprandial dynamic thiol disulfide homeostasis and oxidative stress

Ahmet Rifat Balik[1], Betul Ozbek Iptec[2], Reyhan Ersoy[3], Gulsen Yilmaz[2], Ozcan Erel[2], Cemile Bicer[2]

[1]Department of Medical Biochemistry, Health Sciences University Gulhane Training and Research Hospital, Ankara, Turkey
[2]Department of Medical Biochemistry, Ankara Yildirim Beyazit University, Faculty of Medicine, Ankara, Turkey
[3]Department of Endocrinology, Ankara Yildirim Beyazit University, Faculty of Medicine, Ankara, Turkey

Abstract

Objectives: Oxidative stress has a central role in metabolic disorders associated with high-carbohydrate, animal-based-protein diets, and excessive fat consumption. However, the molecular mechanisms of nutrition-mediated oxidative stress are complex and not fully understood. Dynamic thiol-disulfide homeostasis (DTDH) is the regulation of a balance between thiols and their oxidized forms, and includes the reversal of thiol oxidation in proteins. This study was an evaluation of DTDH and postprandial oxidative stress.

Methods: A total of 86 participants (43 males and 43 females), were included in the study. Fasting and non-fasting blood samples were collected and the native thiol, total thiol, and disulfide parameters were analyzed. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

Results: The findings indicated that while the native thiol values were significantly lower in the postprandial samples, the disulfide values were significantly higher. There was no significant difference in the total thiol values.

Conclusion: Examination of the DTDH revealed that the oxidative stress level increased following food intake. Protein thiols involved in antioxidant defense were oxidized and transformed into disulfides.

Keywords: Fasting, non-fasting, postprandial oxidative stress, thiol-disulfide

Oxidative stress has an important role in metabolic disorders associated with high- carbohydrate, animal-based-protein diets, and excessive fat consumption. Obesity has become an epidemic and is considered a major risk factor for many chronic diseases, including diabetes, cardiovascular disease, and cancer [1]. The effects of oxidative stress are related to the type of macronutrients consumed and their absolute quantity [2]. Both of these properties contribute to oxidative stress and may lead to the development of obesity-related disease [3]. However, the molecular mechanisms of nutrition-mediated oxidative stress are complex and not yet fully understood.

Human life is sustained by oxygen and aerobic processes. Reactive oxygen species (ROS) are harmful by-products of human organism metabolism; however, the oxidative effects of ROS can be neutralized by the antioxidant capacity of the cells in order to maintain homeostasis [4]. The most common forms of ROS are superoxide anions, hypochlorous acid, hydrogen peroxide, singlet oxygen, hypochlorite, hydroxyl radicals, and lipid peroxides, which play a role in the development, growth, death, and differentiation of cells [5]. ROS are produced as a byproduct in normal aerobic metabolism, but when levels rise under stress, it can lead to health problems [6].

Mitochondria are the predominant source of ROS production. These cell organelles produce adenosine triphosphate through a series of oxidative phosphorylation processes. Oxidative damage can occur when single or 2-electron reduction of oxygen takes place, rather than 4-electron reduction. This leads to the formation of H_2O_2 or O_2- [7]. Redox control, particularly in the mitochondria, endoplasmic reticulum, and

Address for correspondence: Ahmet Rifat Balik, MD. Department of Medical Biochemistry, Ankara Yildirim Beyazit University, Faculty of Medicine, Ankara, Turkey
Phone: +90 532 367 24 55 **E-mail:** rifatbalik@hotmail.com **ORCID:** 0000-0002-3893-9721

Submitted Date: May 25, 2021 **Accepted Date:** June 28, 2021 **Available Online Date:** September 10, 2021

nuclei, is important. Extracellular compartments also provide defense barriers against external oxidants. Cysteine (Cys) and the disulfide form, cystine (CySS), generate the majority of low molecular weight thiol/disulfide in human plasma. The Cys/CySS pool is the central redox control point in biological signaling [8].

Organic compounds containing sulfhydryl groups are called thiols (-SH), and are composed of sulfur and hydrogen atoms. Thiols have a high sensitivity to oxidation. Disulfides (-S-S-) are the most important class of dynamic, redox-sensitive covalent bonds formed between 2 thiol groups. Dynamic thiol-disulfide homeostasis (DTDH) is the maintenance of balance between thiols and their oxidized forms, and includes the reversal of thiol oxidation in proteins. It is an important parameter associated with various biochemical processes, including the regulation of protein function, stabilization of protein structure, protection of proteins against irreversible oxidation of Cys residues, chaperone function, regulation of enzyme functions, and transcription [8]. In thiols, functional sulfhydryl groups (-SH) act as a substrate for antioxidant enzymes and as a free radical scavenger. While the majority of the plasma thiol pool consists of albumin and other plasma proteins, a small portion consists of low-molecular-weight thiols, such as Cys, cysteinyl glycine, glutathione, homocysteine, and g-glutamylcysteine. Under oxidative stress, thiol groups (SH) transform into a reversed form (-S-S-). These disulfide bonds can be reduced back to thiol groups, thus preserving thiol-disulfide homeostasis [9]. Therefore, the reduction of thiol groups to disulfides upon exposure to oxidation is recognized as an indirect indicator of oxidative stress. Erel and Neşelioğlu [10] demonstrated the oxidation-reduction potential in DTDH by measuring native thiol, disulfide, and the total thiol (SH + SS) parameters of DTDH with a novel assay. In other words, while measurement of the native thiol in human serum represents the defense power and capacity to reduce oxidative stress, measurement of disulfide levels provides information about the presence of oxidation. The authors reported that the decrease in native thiol groups and the increase in disulfide groups analyzed in human serum could be considered an indicator of exposure to oxidative stress.

To the best of our knowledge, postprandial oxidative stress has not been previously evaluated using DTDH. This study was designed to compare the oxidative stress levels of individuals in fasting and postprandial states, as well as the effect of fasting on DTDH.

Materials and Methods

Ethical considerations

The Ankara Yildirim Beyazit University Faculty of Medicine Clinical Research Ethics Committee granted approval for this study on October 7, 2020 (no: 87). A written, informed consent form was obtained from the patients who agreed to participate in the study.

Patient population

Fasting and postprandial serum samples of patients who presented at the Ankara City Hospital Endocrinology Outpatient Clinic were used in this study. In all, 86 participants, 43 male (mean age: 53.98±13.33 years) and 43 female (mean age: 53.95±9.74 years), were included. Patients whose complete blood count, biochemistry, and hormone test results were within the reference ranges and who had no previous chronic disease were enrolled. The participants had fasting and postprandial blood samples taken on the same day and care was taken to ensure that the samples were matched to the donor for accurate analysis of statistical differences. Fasting blood samples were obtained after 8-12 hours of fasting (n=86) and the postprandial samples were drawn 2 hours after a meal (n=86). The post-fasting meal was not standardized; the participants were free to eat whatever they wanted. All of the fasting blood samples were collected between 8:00 am and 11:00 am, and all of the postprandial samples between 10:00 am and 1:00 pm (n=86). Serum samples were kept in a -80°C freezer until the number of samples required for the research were obtained.

Sample analysis

On the day of analysis, all of the samples were thawed at room temperature for 20 minutes. Next, the samples were homogenized with an average of 1 minute of vortexing before the analysis. The total thiol, native thiol, and disulfide levels were measured according to the method described by Erel and Neşelioğlu [10]. Measurements were performed using an Advia 1800 autoanalyzer (Siemens Healthineers GmbH, Erlangen, Germany) at the Ankara City Hospital medical biochemistry laboratory. Index 1 (disulfide/native thiolx100), Index 2 (disulfide/total thiolx100) and Index 3 (native thiol/total thiolx100) data were calculated. Age, gender, and serum albumin values of the patients included in the study were obtained from the laboratory information system.

Statistical analysis

The results were analyzed using IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp., Armonk, NY, USA). The results were presented as mean and SD for the fasting and non-fasting groups. The distribution was evaluated using the Shapiro-Wilks test. The significant change in DTDH parameters in the fasting and non-fasting samples was determined using a paired-samples t-test. Values with a p value of <0.05 were considered statistically significant.

Results

While the albumin, native thiol, and Index 3 values were significantly lower in the non-fasting samples compared with fasting samples, the disulfide, Index 1, and Index 2 values were significantly higher ($p<0.001$) (Table 1). The non-fasting total thiol levels were lower, however, the difference was not sig-

Table 1. Changes of parameters according to fasting status

Parameters	Fasting (Mean±SD)	Non-fasting (Mean±SD)	p
Albumin (g/dL)	4.25±0.19	4.13±0.23	<0.001*
Native thiol (µmol/L)	407.90±47.99	393.81±47.89	<0.001*
Total thiol (µmol/L)	450.54±46.53	445.74±45.13	0.104
Disulfide (µmol/L)	21.32±6.37	25.97±6.78	<0.001*
Index 1	5.35±1.90	6.76±2.17	<0.001*
Index 2	4.78±1.53	5.89±1,68	<0.001*
Index 3	90.44±3.06	88.21±3.35	<0.001*

*Indicates a significant statistical difference: p<0.05. Index 1: Disulfide/native thiolx100; Index 2: Disulfide/total thiolx100; Index 3: Native thiol/total thiolx100.

nificant. The changes in the parameters between the 2 groups (fasting and non-fasting) are shown in Figure 1.

Discussion

Nutrient-specific consumption has been shown to lead to ROS production [11]. Oxidative stress is defined as an imbalance between ROS and antioxidants. Postprandial oxidative stress causes impaired redox signaling in favor of oxidants. Glucose, lipid, or protein intake has been demonstrated to induce ROS formation through mononuclear and polymorphonuclear leukocytes [12, 13]. Many studies have indicated that high macronutrient intake can increase oxidative stress. Oxidative stress is a significant element of a high-carbohydrate and animal-based protein diet and metabolic disturbances associated with excessive fat consumption [5]. Current research strongly supports the notion that a diet high in carbohydrates, animal proteins, and excessive fat produces ROS and leads to oxidative stress. With the production of ROS, activation of nuclear factor-kappa B (NF-kB) is triggered.

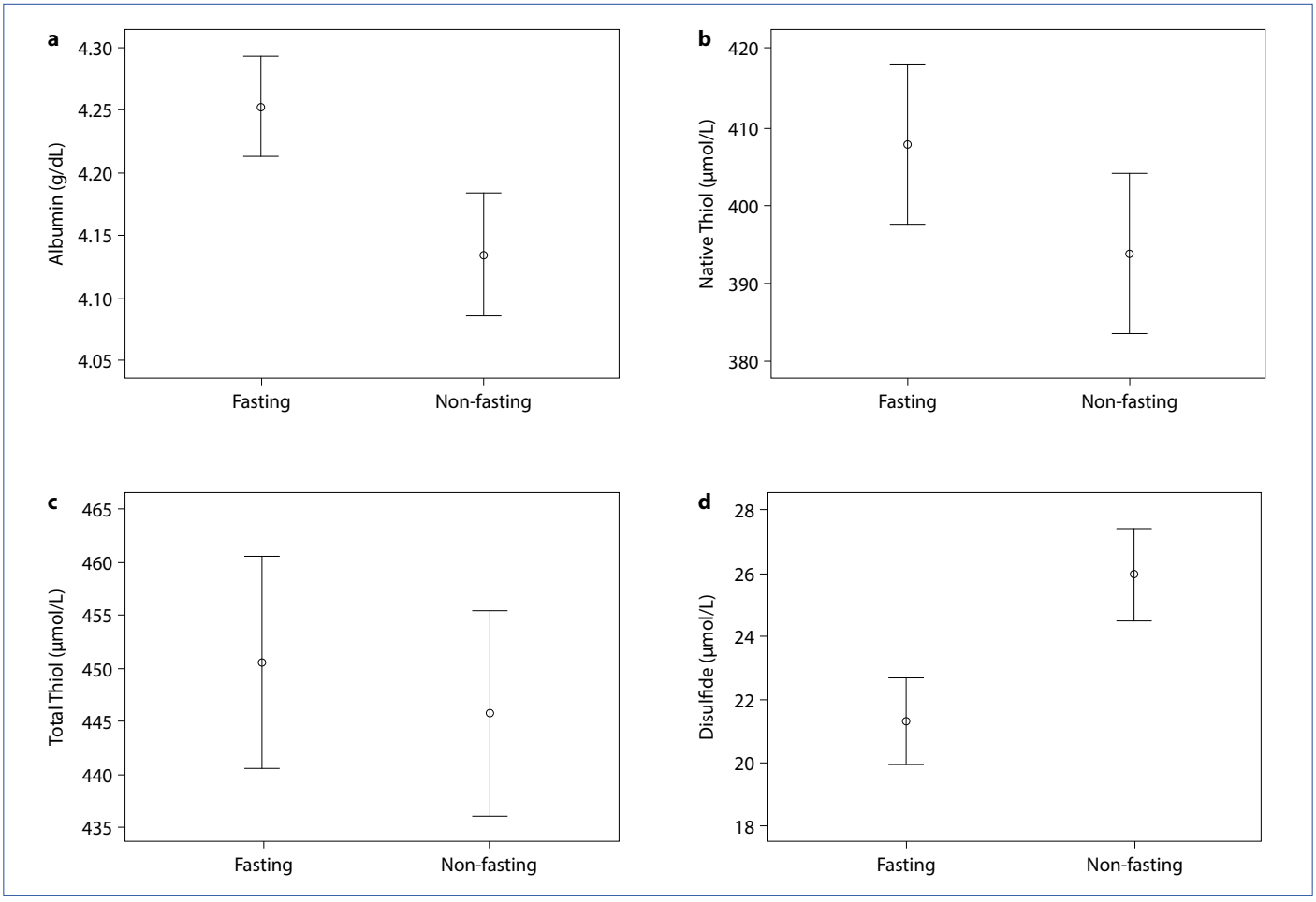

Figure 1. (a) Changes according to fasting status (a) albumin, (b) native thiol, (c) total thiol, (d) disulfide.

NF-kB activation plays an important role in the inflammatory process. Short-term calorie restriction plays a curative role in the inflammatory process by blocking NF-kB expression. [14]. Conversely, chronic overconsumption contributes to a persistent inflammatory state through the formation of white adipose tissue that secretes pro-inflammatory factors [15].

This study examined the presence of postprandial oxidative stress using DTDH analysis. It was observed that the albumin, native thiol, and Index 3 values were significantly lower in the non-fasting samples, while the values of disulfide, Index 1, and Index 2 were significantly higher ($p<0.001$) (Table 1). Albumin is the most abundant plasma thiol. The albumin values of the patients were also compared to examine potential deviations as a result of postprandial hemodilution. The level of albumin decreased 2.82% after a meal, and native thiol decreased 3.45%. However, a reduction in native thiol is insufficient to say that oxidative stress increases following caloric intake. There are structures other than albumin that transport the sulfhydryl group in the plasma thiol pool. Therefore, evaluation of the disulfide level is useful. A significant increase in the disulfide level in the non-fasting samples despite hemodilution indicates the presence of oxidative stress. Also, the Index 1 value increased significantly after food intake. While there was no significant change in the total thiol amount, the increase in disulfides led to a higher Index 2 value in the non-fasting samples. Furthermore, the fact that native thiols underwent oxidation and were lower in the non-fasting state than total thiol value resulted in a significant decrease in the Index 3 value.

A high-calorie diet rich in carbohydrates or fat causes more substrates to enter mitochondrial respiration [16]. Subsequently, the number of electrons passed to the electron transport chain may increase. Molecular oxygen is activated with the acceptance of extra electrons, forming a superoxide. [17] A hyperglycemia-induced overproduction of superoxide can result. Excessive quantities of carbohydrates can lead to decreased insulin binding and up-regulated transcription of insulin-receptor expression in skeletal muscle [18]. High insulin and glucose levels can reduce insulin-receptor binding in adipocytes [19]. A high insulin level may lead to ROS accumulation or decreased antioxidant capacity due to increased carbohydrate metabolism in target tissues. This can alter the phosphorylation of the signal pathways and subsequently cause deactivation. As a result, exposure to H_2O_2 promotes significant loss of the insulin signal and decreased glucose transport in muscles and adipocytes [20].

Most experimental studies have shown that oxidative stress is a key component of the harmful effects of fructose [21, 22]. Fructose-induced oxidative stress leads to impaired carbohydrate metabolism. Castro et al. [23] reported that fructose can modulate liver glucokinase activity through ROS production.

In many countries, meat typically constitutes an important part of the normal diet and may account for 15% of daily energy intake, 40% of daily protein, and 20% of daily fat [24]. Free Fe 2+ increases significantly during the process of cooking meat [25]. The application of heat during preparation also causes a decrease in antioxidant enzymes, such as glutathione peroxidase [26, 27]. Oxygen is produced from oxymyoglobin, which contributes to the production of H_2O_2 [28]. In addition, free Fe 2+ catalyzes the Fenton reaction when oxidative processes are initiated [29]. This reaction leads to the formation of ROS and oxidative damage, which have been implicated in many diseases.

Studies of animals fed a long-term high-fat diet have shown an increase in oxidative stress and dysfunctional mitochondria [30]. It has been found that a high-fat diet not only impairs the lipid profile, but also increases ROS accumulation and oxidative stress parameters in the blood, triggering mitochondrial damage. It has also been found that a high calorie intake or obesity was associated with increased mitochondrial superoxide production [31]. Valenzuela et al. [32] found that the antioxidant enzyme activities of superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase were significantly lower in mice given a high-fat diet [32]. In addition, it has been reported that an adipogenic diet and adipose tissue deposition can trigger oxidative stress in mammalian tissues, and obesity is associated with a significant increase in oxidative damage in all cellular macromolecules [33]. Fat accumulation is also linked to systemic oxidative stress in mice and humans through ROS accumulation accompanied by increased expression of nicotinamide adenine dinucleotide phosphate oxidase and decreased expression of antioxidative enzymes [34]. High consumption of a fat-rich diet promotes β-oxidation of fatty acids in the mitochondria, which then leads to excessive electron flow via cytochrome c oxidase and increased ROS accumulation. Mitochondria are a primary cellular source of ROS and lipid peroxidation by oxidizing unsaturated lipids of fat deposits. ROS and lipid peroxidation can consume vitamins and antioxidant enzymes [35]. Depletion of these antioxidants can inhibit ROS inactivation and increase ROS-mediated damage and lipid peroxidation [34].

The chronic consumption of high-carbohydrate foods can cause oxidative stress through the formation of free radicals that can destroy biological molecules and initiate abnormal cell growth through gene mutations [36]. In addition, ROS can cause oxidative stress by causing oxidation of proteins and lipids, and increase the risk of chronic disease [37]. The progression and development of disease can be prevented by changing dietary habits [38]. High-glucose and animal-based-protein diets and excessive fat consumption can increase oxidative stress [39]. Our results support previous studies, and using DTDH, demonstrated that 3 main food sources (carbohydrates, protein, and fat) increased ROS in the organism through various mechanisms, and as a result, reduced the antioxidant defense capacity and increased oxidative stress.

It has been observed that the postprandial plasma protein thiol concentration increased compared to a baseline mea-

surement with the consumption of bread containing wheat and rice flour. The chemical composition of bread was shown to be the reason; glutathione (GSH) and related thiol compounds, as well as Cys and cysteinyl-glycine, are naturally occurring substances in wheat and rice flour and appear to affect the change in post-meal protein thiol levels [40]. In another study, plasma antioxidant capacity and protein thiol levels were higher after consuming various yogurt mixes compared with fasting levels. This result was thought to be due to the milk proteins in yogurt and natural substances with antioxidant activity [41]. In other research analyzing the thiol concentration as a marker of protein oxidative damage and serum postprandial antioxidant capacity, higher thiol levels were found in people who had consumed almond flour compared with those who consumed bread, potatoes, or rice. This result was thought to be due to less post-meal protein damage following the consumption of almonds [42]. In another study evaluating the antioxidant activity in plasma by measuring thiol groups, it was observed that thiol levels were not affected after spicy meals [43]. Studies in this area are limited, and have examined only part of this homeostasis process, not the total DTDH (reductant [SH], oxidant [SS]). These studies, which have yielded varied results, focused on specific foods and the effects on only sulfhydryl groups. The nutritional habits of individuals and the presence of antioxidants in their meals can also affect postprandial oxidative stress and DTDH. Our findings indicated that 21 participants (24.42%) had an increase in their native thiol levels after a meal and 24 (27.9%) had a decrease in disulfide levels. However, when the general study population was evaluated, postprandial oxidative stress increased and this effect was reflected in the DTDH.

Oxidization of sulfhydryl groups is one mechanism of ROS damage to proteins. Disulfide bonds are formed in thiol-containing molecules, such as Cys, methionine, and glutathione, in both intracellular and plasma proteins. Therefore, a decrease in protein thiol concentrations can be used as a marker of oxidative stress. Protein thiols are an expendable source of plasma antioxidants. Studies have shown that thiols were lower in clinical conditions associated with increased oxidative stress, including autoimmune diseases, diabetes, and uremia [43]. Increased ROS production induces oxidation of sulfhydryl groups in thiol-containing molecules in addition to oxidative damage of proteins. Postprandial reduction in plasma protein thiols may be a sign of oxidative stress in the presence of free radicals [40].

To the best of our knowledge, the current research is the first study to investigate both aspects of the oxidative stress mechanism using DTDH. Our findings may be useful to more specific studies in this area in the future.

Conclusion

The data we obtained shows the following result; depending on the nutritional habits of individuals, postprandial oxidative stress increases. Postparandial oxidative stress causes a decrease in natural thiols and an increase in disulfides by affecting DTDH.

Acknowledgments: The authors would like to thank the technical staff of the Ankara City Hospital medical biochemistry laboratory.

Conflict of Interest: There is no conflict of interest.

Ethics Committee Approval: The Ankara Yildirim Beyazit University Faculty of Medicine Clinical Research Ethics Committee granted approval for this study on October 7, 2020 (no: 87).

Financial Disclosure: No financial support has been received for the research.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept – C.B.; Design – G.Y.; Supervision – O.E.; Funding – O.E.; Materials – R.E., O.E.; Data collection &/or processing – A.R.B.; Analysis and/or interpretation – B.O.I.; Literature search – A.R.B.; Writing – A.R.B.; Critical review – C.B.

References

1. Tan BL, Norhaizan ME, Liew WP. Nutrients and oxidative stress: friend or foe? Oxid Med Cell Longev 2018;2018:9719584.
2. Kitabchi AE, McDaniel KA, Wan JY, Tylavsky FA, Jacovino CA, Sands CW, et al. Effects of high-protein versus high-carbohydrate diets on markers of β-cell function, oxidative stress, lipid peroxidation, proinflammatory cytokines, and adipokines in obese, premenopausal women without diabetes: a randomized controlled trial. Diabetes Care 2013;36(7):1919–25. [CrossRef]
3. Yuzefovych LV, Musiyenko SI, Wilson GL, Rachek LI. Mitochondrial DNA damage and dysfunction, and oxidative stress are associated with endoplasmic reticulum stress, protein degradation and apoptosis in high fat diet-induced insulin resistance mice. PLoS One 2013;8(1):e54059. [CrossRef]
4. Yi MC, Khosla C. Thiol-disulfide exchange reactions in the mammalian extracellular environment. Annu Rev Chem Biomol Eng 2016;7:197–222. [CrossRef]
5. Rajendran P, Nandakumar N, Rengarajan T, Palaniswami R, Gnanadhas EN, Lakshminarasaiah U, et al. Antioxidants and human diseases. Clin Chim Acta 2014;436:332–47. [CrossRef]
6. Rahal A, Kumar A, Singh V, Yadav B, Tiwari R, Chakraborty S, et al. Oxidative stress, prooxidants, and antioxidants: the interplay. Biomed Res Int 2014;2014:761264. [CrossRef]
7. Inoue M, Sato EF, Nishikawa M, Park AM, Kira Y, Imada I, et al. Mitochondrial generation of reactiv e oxygen species and its role in aerobic life. Curr Med Chem 2003;10(23):2495–505.
8. Erel Ö, Erdoğan S. Thiol-disulfide homeostasis: an integrated approach with biochemical and clinical aspects. Turk J Med Sci 2020;50:1728–38. [CrossRef]
9. Eryilmaz MA, Kozanhan B, Solak I, Çetinkaya ÇD, Neselioglu S, Erel Ö. Thiol-disulfide homeostasis in breast cancer patients. J Cancer Res Ther 2019;15(5):1062–6. [CrossRef]
10. Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. Clin Biochem 2014;47(18):326–32.

11. Dhindsa S, Tripathy D, Mohanty P, Ghanim H, Syed T, Aljada A, et al. Differential effects of glucose and alcohol on reactive oxygen species generation and intranuclear nuclear factor-kappaB in mononuclear cells. Metabolism 2004;53(3):330–4. [CrossRef]
12. Mohanty P, Hamouda W, Garg R, Aljada A, Ghanim H, Dandona P. Glucose challenge stimulates reactive oxygen species (ROS) generation by leucocytes. J Clin Endocrinol Metab 2000;85(8):2970–3. [CrossRef]
13. Mohanty P, Ghanim H, Hamouda W, Aljada A, Garg R, Dandona P. Both lipid and protein intakes stimulate increased generation of reactive oxygen species by polymorphonuclear leukocytes and mononuclear cells. Am J Clin Nutr 2002;75(4):767–72. [CrossRef]
14. Jung KJ, Lee EK, Kim JY, Zou Y, Sung B, Heo HS, et al. Effect of short term calorie restriction on pro-inflammatory NF-kB and AP-1 in aged rat kidney. Inflamm Res 2009;58(3):143–50.
15. Fernández-Sánchez A, Madrigal-Santillán E, Bautista M, Esquivel-Soto J, Morales-González A, Esquivel-Chirino C, et al. Inflammation, oxidative stress, and obesity. Int J Mol Sci 2011;12(5):3117–32. [CrossRef]
16. Teodoro JS, Duarte FV, Gomes AP, Varela AT, Peixoto FM, Rolo AP, et al. Berberine reverts hepatic mitochondrial dysfunction in high-fat fed rats: a possible role for SirT3 activation. Mitochondrion 2013;13(6):637–46. [CrossRef]
17. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. Nature 2001;414(6865):813–20. [CrossRef]
18. Catena C, Cavarape A, Novello M, Giacchetti G, Sechi LA. Insulin receptors and renal sodium handling in hypertensive fructose-fed rats. Kidney Int 2003;64(6):2163–71. [CrossRef]
19. Burén J, Liu HX, Lauritz J, Eriksson JW. High glucose and insulin in combination cause insulin receptor substrate-1 and -2 depletion and protein kinase B desensitisation in primary cultured rat adipocytes: possible implications for insulin resistance in type 2 diabetes. Eur J Endocrinol 2003;148(1):157–67.
20. Henriksen EJ, Diamond-Stanic MK, Marchionne EM. Oxidative stress and the etiology of insulin resistance and type 2 diabetes. Free Radic Biol Med 2011;51(5):993–9. [CrossRef]
21. Castro MC, Massa ML, Arbeláez LG, Schinella G, Gagliardino JJ, Francini F. Fructose-induced inflammation, insulin resistance and oxidative stress: A liver pathological triad effectively disrupted by lipoic acid. Life Sci 2015;137:1–6. [CrossRef]
22. Castro MC, Francini F, Schinella G, Caldiz CI, Zubiría MG, Gagliardino JJ, et al. Apocynin administration prevents the changes induced by a fructose-rich diet on rat liver metabolism and the antioxidant system. Clin Sci (Lond) 2012;123(12):681–92. [CrossRef]
23. Castro MC, Francini F, Gagliardino JJ, Massa ML. Lipoic acid prevents fructose-induced changes in liver carbohydrate metabolism: role of oxidative stress. Biochim Biophys Acta 2014;1840(3):1145–51. [CrossRef]
24. Food and Agriculture Organization of the United Nations Statistics Division. Food Balance Sheets Millennium Issue 1999–2001 Special Charts. Rome: Food and Agriculture Organization of The United Nations; 2010.
25. Van Hecke T, Vossen E, Hemeryck LY, Vanden Bussche J, Vanhaecke L, De Smet S. Increased oxidative and nitrosative reactions during digestion could contribute to the association between well-done red meat consumption and colorectal cancer. Food Chem 2015;187:29–36. [CrossRef]
26. Serpen A, Gökmen V, Fogliano V. Total antioxidant capacities of raw and cooked meats. Meat Sci 2012;90(1):60–5. [CrossRef]
27. Hoar T, Daun C, Trafikowska U, Zackrisson J, Akesson B. Influence of heat treatment on lipid oxidation and glutathione peroxidase activity in chicken and duck meat. Innov Food Sci Emerg Tech 2006; 7(1-2):88–93. [CrossRef]
28. Ishikawa S, Tamaki S, Ohata M, Arihara K, Itoh M. Heme induces DNA damage and hyperproliferation of colonic epithelial cells via hydrogen peroxide produced by heme oxygenase: a possible mechanism of heme-induced colon cancer. Mol Nutr Food Res 2010;54(8):1182–91. [CrossRef]
29. Bokare AD, Choi W. Review of iron-free Fenton-like systems for activating H2O2 in advanced oxidation processes. J Hazard Mater 2014;275:121–35. [CrossRef]
30. Ballal K, Wilson CR, Harmancey R, Taegtmeyer H. Obesogenic high fat western diet induces oxidative stress and apoptosis in rat heart. Mol Cell Biochem 2010;344(1-2):221–30. [CrossRef]
31. Du Z, Yang Y, Hu Y, Sun Y, Zhang S, Peng W, et al. A long-term high-fat diet increases oxidative stress, mitochondrial damage and apoptosis in the inner ear of D-galactose-induced aging rats. Hear Res 2012;287(1-2):15–24. [CrossRef]
32. Valenzuela R, Echeverria F, Ortiz M, Rincón-Cervera MÁ, Espinosa A, Hernandez-Rodas MC, et al. Hydroxytyrosol prevents reduction in liver activity of Δ-5 and Δ-6 desaturases, oxidative stress, and depletion in long chain polyunsaturated fatty acid content in different tissues of high-fat diet fed mice. Lipids Health Dis 2017;16(1):64. [CrossRef]
33. Matsuda M, Shimomura I. Increased oxidative stress in obesity: implications for metabolic syndrome, diabetes, hypertension, dyslipidemia, atherosclerosis, and cancer. Obes Res Clin Pract 2013;7(5):e330–41. [CrossRef]
34. Le Lay S, Simard G, Martinez MC, Andriantsitohaina R. Oxidative stress and metabolic pathologies: from an adipocentric point of view. Oxid Med Cell Longev 2014;2014:908539. [CrossRef]
35. Jain SK, Micinski D. Vitamin D upregulates glutamate cysteine ligase and glutathione reductase, and GSH formation, and decreases ROS and MCP-1 and IL-8 secretion in high-glucose exposed U937 monocytes. Biochem Biophys Res Commun 2013;437(1):7–11. [CrossRef]
36. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. Diabetes 2005;54(6):1615-25. [CrossRef]
37. Carvalho AM, Miranda AM, Santos FA, Loureiro AP, Fisberg RM, Marchioni DM. High intake of heterocyclic amines from meat is associated with oxidative stress. Br J Nutr 2015;113(8):1301–7. [CrossRef]
38. Afshin A, Micha R, Khatibzadeh S, Fahimi S, Shi P, Powles J, et al; 2010 Global Burden of Diseases, Injuries, and Risk Factors Study: NUTRItrition and ChrOnic Diseases Expert Group (NUTRICODE), and Metabolic Risk Factors of ChrOnic Diseases Collaborating Group. The impact of di-

etary habits and metabolic risk factors on cardiovascular and diabetes mortality in countries of the Middle East and North Africa in 2010: a comparative risk assessment analysis. BMJ Open 2015;5(5):e006385. Erratum in: BMJ Open 2019;9(4):e006385corr1.
39. Guo R, Li W, Liu B, Li S, Zhang B, Xu Y. Resveratrol protects vascular smooth muscle cells against high glucose-induced oxidative stress and cell proliferation in vitro. Med Sci Monit Basic Res 2014;20:82–92. [CrossRef]
40. Chusak C, Pasukamonset P, Chantarasinlapin P, Adisakwattana S. Postprandial glycemia, ınsulinemia, and antioxidant status in healthy subjects after ıngestion of bread made from anthocyanin-rich riceberry rice. Nutrients 2020;12(3):782. [CrossRef]
41. Anuyahong T, Chusak C, Thilavech T, Adisakwattana S. Postprandial effect of yogurt enriched with anthocyanins from riceberry rice on glycemic response and antioxidant capacity in healthy adults. Nutrients 2020;12(10):2930. [CrossRef]
42. Jenkins DJ, Kendall CW, Josse AR, Salvatore S, Brighenti F, Augustin LS, et al. Almonds decrease postprandial glycemia, insulinemia, and oxidative damage in healthy individuals. J Nutr 2006;136(12):2987–92. [CrossRef]
43. Skulas-Ray AC, Kris-Etherton PM, Teeter DL, Chen CY, Vanden Heuvel JP, West SG. A high antioxidant spice blend attenuates postprandial insulin and triglyceride responses and increases some plasma measures of antioxidant activity in healthy, overweight men. J Nutr 2011;141(8):1451–7. [CrossRef]