

Olive oil increase catalase activity and glutathione peroxidase level in hyperglycemic rats



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ABSTRACT

Background: Diabetes mellitus, a prevalent endocrine disorder globally, leads to hyperglycemia, which in turn triggers oxidative stress, adversely affecting enzymatic antioxidants like glutathione peroxidase (GSH-Px) and catalase. These antioxidants are crucial in mitigating the oxidative damage associated with diabetic conditions.

Objectives: This study investigates the potential therapeutic effects of olive oil's antioxidants in increasing catalase and GSH-Px activities in hyperglycemic conditions induced by alloxan in rats.

Methods: The study employed a randomized design involving adult male Wistar rats divided into three groups (n=8 per group): an untreated and uninduced control group, an alloxan-induced untreated group (Alloxan), and an alloxan-induced treatment group (Treatment) receiving olive oil at a dosage of 25 mL/day for 14 days. Catalase activities were quantified using the spectrophotometry technique, while GSH-Px levels were measured via ELISA.

Results: In the treatment group, catalase activity significantly increased post-olive oil administration compared to alloxan-induced only. Similarly, glutathione peroxidase levels were elevated. The study identified significant differences in catalase activity between the alloxan-induced and treatment groups, alongside a positive correlation in glutathione peroxidase levels between these groups.

Conclusion: The antioxidants present in olive increase both catalase activity and glutathione peroxidase levels in rats subjected to alloxan-induced hyperglycemia. These findings suggest that olive oil may offer therapeutic potential in enhancing the body's antioxidative defense mechanisms against diabetes-induced oxidative stress.

Keywords: hyperglycemia, olive oil, glutathione peroxidase, catalase activity, oxidants

Introduction

Hyperglycemia, characterized by elevated blood glucose levels beyond normal limits, arises when the body either fails to produce insulin or when insulin does not function properly [1,2]. In diabetes mellitus, hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs, notably the eyes, kidneys, nerves, heart, and blood vessels [2,3]. Diabetes mellitus represents a complex disease, intricately linked with global patterns of oxidation and inflammation, and it ranks highly in prevalence and mortality rates worldwide [4].

The global diabetic population has been on the rise, with 463 million adults (8.8% of the global

population) diagnosed in 2019, and projections suggest this number could reach 700 million by 2045 [5]. Specifically, Indonesia reported 19.5 million adults with diabetes mellitus in 2021, ranking fifth among countries with the highest prevalence of diabetes. This figure is expected to increase to 28.6 million by 2045 [6]. According to the 2019 Health Data and Information Center report, Indonesia is among the ten countries with the highest diabetic population, with a prevalence rate of 10.7%. Notably, West Sumatra Province ranks fifth in the country with a prevalence rate of 1.6% [7].

Hyperglycemia in diabetes mellitus is known to induce oxidative stress [8]. Sensitive cells,

such as endothelial cells, under excessive glucose load, trigger the production of reactive oxygen species (ROS) in mitochondria, impairing their function [9,10]. Recent studies have highlighted that increased ROS formation augments the risk of diabetes and macrophage alterations due to shifts in glycolytic metabolism. Macrophages, crucial in diabetes development, promote inflammation by releasing pro-inflammatory cytokines and proteases. ROS serve as significant mediators in activating pro-inflammatory signaling pathways. Obesity and hyperglycemia-induced ROS production may induce pro-inflammatory macrophages, such as M1, during diabetes onset and development [11]. ROS can damage cellular components, including DNA, lipids, and proteins. Excessive ROS activate pro-inflammatory transcription factors, such as NF- κ B and activator protein-1 (AP-1), potentially increasing the expression of pro-inflammatory cytokines and adhesion molecules. Activated endothelial cells then attract monocytes, escalating inflammation and leading to macrovascular and microvascular injuries [10].

Glutathione peroxidase (GSH-Px) is an enzymatic antioxidant that detoxifies hydrogen peroxide and lipid hydroperoxides, converting or preventing the formation of free radicals into less reactive molecules. Its activation diminishes under diabetic conditions. Alloxan, a uric acid derivative, induces pancreatic beta cell necrosis through elevated oxidative stress, reducing insulin secretion and consequent hyperglycemia [12]. Catalase acts as a specific peroxidase enzyme in decomposing hydrogen peroxide into oxygen and water, forming a critical defensive mechanism against free radicals in the human body [13].

Dietary intake of foods rich in antioxidants and polyphenols enhances plasma antioxidant capacity and mitigates oxidative stress markers in individuals with diabetes, obesity, hypertension, and hypertriglyceridemia [8]. Olive oil, high in antioxidants and polyphenols, contains compounds that act as natural antioxidants [14]. It modulates genes related to insulin sensitivity and boosts the body's antioxidant defenses, including vitamins A, D, and E, along with nutrients like calcium,

iron, and sodium. Every 100 grams of olive oil provides 884 kcal of energy, 0.18 mg of calcium, 0.38 mg of iron, and 12.4 mg of vitamin E [15].

Olive oil's primary antioxidants are polyphenols, including oleuropein, tyrosol, and hydroxytyrosol. These components, particularly hydroxytyrosol and oleuropein, combat free radicals, reduce intracellular ROS levels, and prevent oxidative DNA damage in breast cancer cell lines [17]. Furthermore, they have been shown to enhance the expression of superoxide dismutase (SOD), catalase, and glutathione peroxidase [18], with catalase catalyzing the detoxification of hydrogen peroxide and preventing free radical formation [13]. Glutathione peroxidase serves as a mediator in DNA damage due to oxidation reactions. Glutathione, a key agent against xenobiotic poisons (e.g., drugs, pollutants, carcinogens), protects cells from the effects of excess oxidants. It is essential in regulating oxidation-reduction homeostasis, with its levels and redox status regulation closely associated with various diseases, including cardiovascular, neurodegenerative, cancer, aging, AIDS, cystic fibrosis, liver disorders, diabetes mellitus, and their complications [19].

Polyphenolic compounds from olive oil can capture free radicals and reduce oxidative stress, influencing MDA levels [20,21]. MDA, a marker of lipid peroxidation of membrane lipids, correlates directly with oxidative stress. The relationship between MDA and adenosine deaminase (ADA) levels in diabetes mellitus, based on HbA1C levels, indicates persistent production of MDA and ROS, leading to further glycation and lipoxidation end products [22]. Typically, the body employs systematic strategies, including superoxide dismutase and catalase enzymes, to combat free radical formation or accelerate their degradation. However, conditions like hypercholesterolemia and hyperglycemia can amplify ROS production, triggering lipid peroxidation, increasing MDA levels, and diminishing the capacity of intracellular antioxidant enzymes [23]. This study seeks to evaluate the impact of olive oil antioxidants on catalase and glutathione peroxidase activities in hyperglycemic rats, aiming to provide insights for further research on the efficacy of olive oil antioxidants.

Methods

Animals and hyperglycemic rat model

This study received ethical approval from the Faculty of Medicine Ethics Committee at Andalas University, Padang, with certificate number 1051/UN.16.2/KEP-FK/2022.

Twenty-four adult male Wistar rats, aged 2-3 months and weighing between 200-250 grams, were selected for this research. These rats, maintained in the animal house of Andalas University, were healthy and active during the acclimatization period. Exclusion criteria eliminated any rats previously subjected to treatment interventions, those displaying illness symptoms (e.g., hair loss, dullness, exudate discharge), or physical disabilities. Rats that died during the study were classified as dropouts.

The acclimatization period lasted one week, with rats housed in plastic cages (30 x 20 x 10 cm) topped with wire mesh. The cages were bedded with 0.5-1 cm thick rice husks and refreshed every three days. The facility maintained a controlled lighting environment of 12 hours of light (06:00 AM to 06:00 PM) and 12 hours of darkness (06:00 PM to 06:00 AM), with room temperature and humidity kept within natural ranges. Rats had ad libitum access to standard feed (B 551) and tap water.

Treatments

The study divided 24 adult male Wistar rats into three treatment groups of eight animals each. The control group received no alloxan induction or olive oil treatment, subsisting solely on ad libitum feeding. The alloxan group received a single intraperitoneal dose of alloxan (100 mg/kg body weight). In contrast, the treatment group received the same dose of alloxan followed by oral administration of olive oil (25 mL/day) for 14 days. Blood glucose levels in the latter two groups were monitored with a glucometer (Accu Check) between days 3 and 7 post-alloxan induction [24].

Measurement of catalase activity

Catalase activity was assessed via spectrophotometry, using hydrogen peroxide (H₂O₂),

catalase color (potassium dichromate in glacial acetic acid), and phosphate buffers (pH 7.0). The procedure involved homogenizing serum, plasma, or liver homogenate samples with H₂O₂ and phosphate buffer, followed by colorimetric analysis to measure the decomposed H₂O₂. Absorbance was measured at a wavelength of 570 nm, and catalase activity was quantified as the rate of H₂O₂ decomposition per minute per milligram of serum protein.

Measurements of GSH-Px levels

On the 15th day, blood plasma was collected from each rat to assess glutathione peroxidase (GSH-Px) activity using the ELISA technique.

Data analysis

Data were analyzed using statistical software and presented as mean ± standard deviation. The Shapiro-Wilk test assessed data normality, while the Levene test checked for homogeneity. Given the non-normal and heterogeneous distribution, non-parametric statistical analysis was employed, specifically the Kruskal-Wallis test, followed by post hoc analysis with the Mann-Whitney test to ascertain differences between control and treatment groups at a 95% confidence level.

Results

The experimental results delineated the effects of alloxan induction and olive oil treatment on catalase and glutathione peroxidase activities in rats. For catalase activity, the control group, which did not receive alloxan induction or olive oil treatment, exhibited the highest activity at 6.07 units/mg of protein. In contrast, the alloxan group, which underwent alloxan induction without receiving olive oil, displayed significantly lower catalase activity. Notably, the treatment group, which received both alloxan induction and olive oil, demonstrated intermediate catalase activity levels (Figure 1). Statistical analysis confirmed that the differences in catalase activity levels among the groups were significant, with the alloxan group showing a statistically significant

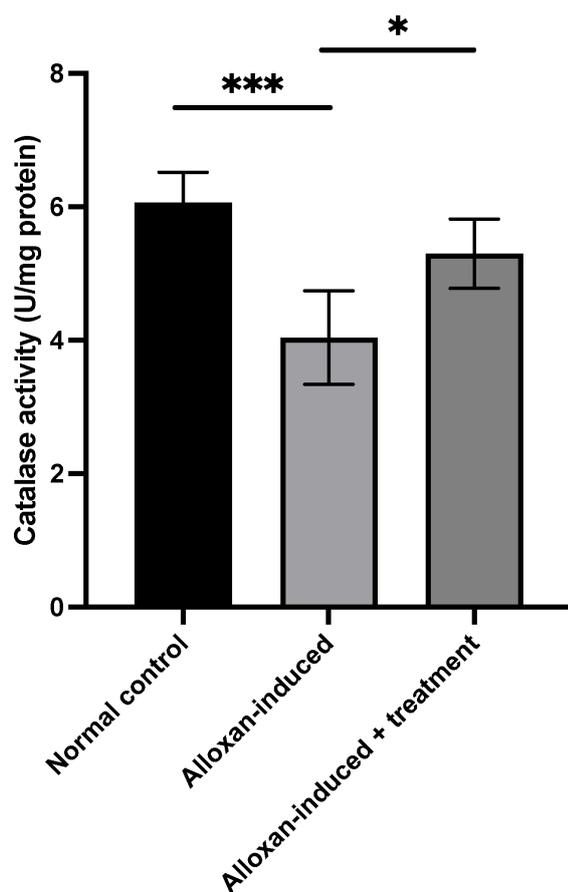


Figure 1. Catalase activity among groups. Control: without induction and treatment, Alloxan induction (100 mg/kg BW), and Treatment received olive oil 25 mL/day. * $p < 0.05$, *** $p < 0.001$

reduction in activity compared to the control group ($p < 0.05$).

Regarding glutathione peroxidase activity, the control group exhibited the highest level. The alloxan-only group presented with a reduced level of glutathione peroxidase level. Conversely, rats in the treatment group, administered olive oil following alloxan induction, showed nearly restored levels of glutathione peroxidase (Figure 2). This near restoration approached the baseline levels observed in the control group. Statistical analyses revealed homogeneity in the data, with significant different in glutathione peroxidase levels among the groups indicated by a p-value of 0.032 ($p < 0.05$). Specifically, the treatment group exhibited a significant increase in glutathione peroxidase levels compared to the alloxan group ($p < 0.05$).

These findings suggest that while alloxan induction suppresses the activity of both catalase and

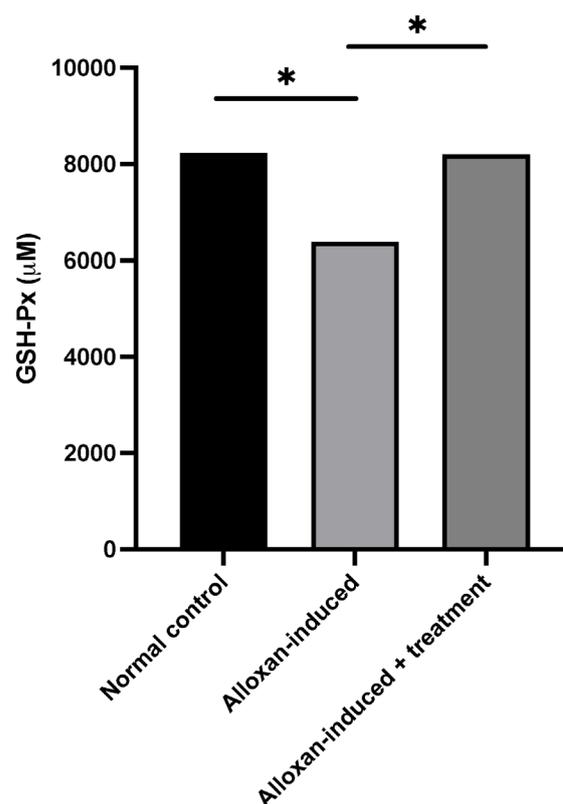


Figure 2. Glutathione peroxidase level among groups. Control: without induction and treatment, Alloxan induction (100 mg/kg BW), and Treatment received olive oil 25 mL/day. * $p < 0.05$

glutathione peroxidase, subsequent administration of olive oil can partially ameliorate these effects, as evidenced by increased enzyme activities in the treatment group compared to the alloxan-only group.

Discussion

This study delineates the impacts of alloxan induction and olive oil supplementation on catalase and glutathione peroxidase (GPx) activities in rats, elucidating the role of olive oil as a mitigator of oxidative stress in hyperglycemic conditions.

Catalase, an essential enzymatic antioxidant, mitigates oxidative stress, a common pathology in diabetic conditions [25]. Our findings reveal a decrement in catalase activity among hyperglycemic rats (alloxan group), in contrast to the elevated levels observed in the treatment group, which received olive oil supplementation. The control group exhibited the highest catalase activity, underscoring the detrimental effect

of hyperglycemia on catalase activity and the protective role of olive oil's antioxidant components. Previous studies corroborate these observations, noting decreased catalase activity in hyperglycemic conditions and the potential of antioxidants to restore catalase function, thereby reducing oxidative stress markers [26].

The study further revealed that olive oil supplementation in the treatment group increased catalase activity. This finding is attributed to the antioxidant constituents in olive oil, known for their capacity to modulate oxidative stress markers [27]. Hyperglycemia-induced free radical formation depletes pancreatic catalase, highlighting the vulnerability of β -cells, which possess lower levels of antioxidant enzymes than other tissues, thus heightening their risk of oxidative stress [28].

In a study involving streptozotocin-induced hyperglycemic rats treated for one month with the antioxidant SkQ1, an increase in catalase activity was observed in the treated group compared to the control group [29]. This finding highlights catalase's critical role as an effective hydrogen peroxide (H_2O_2) splitter within the enzymatic antioxidant defense system. For example, pathogenic bacteria with high catalase expression can inhibit the host's antibacterial defense. Catalase that occurs on the outer surface of cancer cells is also able to protect these cells from cell-to-cell apoptosis. Thus, catalase activity in normal cells can help reduce the formation of oxidative stress [30].

The significance of increasing catalase activity, particularly in hyperglycemia, lies in its potential to alleviate oxidative stress by converting hydrogen peroxide into water and oxygen. A deficiency or malfunction in catalase is implicated in the pathogenesis of several degenerative diseases, including diabetes mellitus [31]. Moreover, the antioxidative action of phenolic compounds in olive oil extends its therapeutic potential beyond systemic effects, inducing beneficial antioxidant actions within the digestive tract [18].

Glutathione peroxidase activity presented a similar trend, with the control group exhibiting

the highest levels and the alloxan group the lowest. Olive oil administration in hyperglycemic rats significantly increased GPx levels, suggesting olive oil's efficacy in enhancing cellular antioxidant defense mechanisms. The critical function of GPx in reducing lipid peroxides and hydrogen peroxide, thus preventing oxidative damage, underscores the enzyme's significance in mitigating oxidative stress [32]. The observed increase in GPx activity following olive oil supplementation aligns with previous findings, highlighting olive oil's potential to bolster antioxidant defenses against hyperglycemia-induced oxidative stress [36].

Oxidative stress, a deleterious consequence of hyperglycemia, results from the diminished activity of glutathione peroxidase (GPx), an essential intracellular antioxidant enzyme. Reactive oxygen species (ROS), including superoxide and hydrogen peroxide, are ubiquitously produced in cells by mitochondrial and enzymatic reactions. Without adequate regulation, these reactive molecules inflict oxidative damage on DNA, proteins, and lipid membranes, compromising cellular integrity and function [33].

A reduction in GPx activity undermines the cell's antioxidant defenses, exacerbating oxidative damage, particularly affecting membrane fatty acids and functional proteins [32]. Hyperglycemia exacerbates oxidative stress, challenging cells to activate their complex antioxidant defense mechanisms to restore redox balance. Among these defenses, GPx plays a pivotal role by catalyzing the conversion of hydrogen peroxide into water and oxygen, thereby mitigating oxidative damage [34].

In this study, rats subjected to alloxan-induced hyperglycemia displayed significantly lower GPx activity than those treated with olive oil, which is rich in polyphenolic antioxidants. This suggests that the polyphenols in olive oil enhance GPx activity, offering protective benefits against oxidative damage. Furthermore, GPx is instrumental in safeguarding hemoglobin from oxidative stress, reinforcing the enzyme's broader protective roles within the organism [35].

Our findings resonate with other research demonstrating that dietary antioxidants, such as those present in olive oil or derived from cardamom leaf extract, can ameliorate glucose intolerance, inflammation, and oxidative stress. These natural antioxidants share a mechanism of action with olive oil, underscoring their potential therapeutic benefits in managing oxidative stress and its associated metabolic disturbances [36].

Conclusion

Administering olive oil at a dosage of 25 mL/day for 14 days notably increased both catalase and glutathione peroxidase activities in hyperglycemic rats. These findings underscore the detrimental effects of hyperglycemia on enzymatic antioxidant systems and highlight the therapeutic potential of olive oil's antioxidant components.

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Author contributions

AZO wrote original draft, resources and visualization; EY and R supervised the study and write the revision manuscript.

Declaration of interest

None.

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References

1. PERKENI. Pedoman Pengelolaan dan Pencegahan Diabetes Mellitus Tipe 2 Dewasa Di Indonesia 2021. Indonesia: PB PERKENI; 2021.
2. Ruderman N, Williamson J, Brownlee M. HyperGlycemia, Diabetes and Vascular Disease. Clinical P. New York: Springer New York; 2016.
3. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. *Avicenna J Med.* 2020;10: 174-188. https://doi.org/10.4103/ajm.ajm_53_20
4. Kahraman C, Yümün G, Kahraman NK, Namdar ND, Cosgun S. Neutrophil-to-lymphocyte ratio in diabetes mellitus patients with and without diabetic foot ulcer. *Eur J Med Sci.* 2014;1: 8-13. <https://doi.org/10.12973/ejms.2014.102p>
5. International Diabetes Federation. IDF Diabetes Atlas, 9th edn. 2019.
6. International Diabetes Federation. IDF Diabetes Atlas 10th Edition. 2021.
7. Pusdatin Kemenkes. Infodatin Kesehatan Gigi Nasional September 2019. Pusdatin Kemenkes RI. 2019; 1-6.
8. Ávila-Escalante ML, Coop-Gamas F, Cervantes-Rodríguez M, Méndez-Iturbide D, Aranda-González II. The effect of diet on oxidative stress and metabolic diseases-Clinically controlled trials. *J Food Biochem.* 2020;44: e13191. <https://doi.org/10.1111/jfbc.13191>
9. Giacco F, Brownlee M. Oxidative stress and diabetic complications. *Circ Res.* 2010;107: 1058-1070. <https://doi.org/10.1161/CIRCRESAHA.110.223545>
10. Pitocco D, Tesauro M, Alessandro R, Ghirlanda G, Cardillo C. Oxidative stress in diabetes: implications for vascular and other complications. *Int J Mol Sci.* 2013;14: 21525-21550. <https://doi.org/10.3390/ijms141121525>
11. Rendra E, Riabov V, Mossel DM, Sevastyanova T, Harmsen MC, Kzhyshkowska J. Reactive oxygen species (ROS) in macrophage activation and function in diabetes. *Immunobiology.* 2019;224: 242-253. <https://doi.org/10.1016/j.imbio.2018.11.010>
12. Riyanti H, Simanjutak SBI, Winarsi H. Aktivitas glutathione peroksidase dan kadar gula darah tikus diabetes yang diberi ekstrak daun kapulaga (*Amomum cardamomum*). *Scr Biol.* 2014;1: 153-156. <https://doi.org/10.20884/1.sb.2014.1.2.442>
13. Sunaryo H, Rahmania RA, Dwitiyanti, Siska. Aktivitas antioksidan kombinasi ekstrak Jahe Gajah (*Zingiber officinale* Rosc.) dan zink berdasarkan pengukuran MDA, SOD dan katalase pada mencit hiperkolesterolemia dan hiperglikemia dengan penginduksi streptozotisin. *J ilmu kefarmasian Indones.* 2017;13: 187-193.
14. Oliveras-López M-J, Molina JJM, Mir MV, Rey EF, Martín F, de la Serrana HL-G. Extra virgin olive oil (EVOO) consumption and antioxidant status in healthy institutionalized elderly humans. *Arch Gerontol Geriatr.* 2013;57: 234-242. <https://doi.org/10.1016/j.archger.2013.04.002>

15. Astawan M. Sehat Dengan Rempah dan Bumbu Dapur. Jakarta: PT.Kompas Media Nusantara; 2016.
16. Ghanbari R, Anwar F, Alkharfy KM, Gilani A-H, Saari N. Valuable nutrients and functional bioactives in different parts of olive (*Olea europaea* L.)-a review. *Int J Mol Sci.* 2012;13: 3291-3340. <https://doi.org/10.3390/ijms13033291>
17. Imran M, Nadeem M, Gilani SA, Khan S, Sajid MW, Amir RM. Antitumor perspectives of oleuropein and its metabolite hydroxytyrosol: Recent updates. *J Food Sci.* 2018;83: 1781-1791. <https://doi.org/10.1111/1750-3841.14198>
18. Bilal RM, Liu C, Zhao H, Wang Y, Farag MR, Alagawany M, et al. Olive Oil: Nutritional Applications, Beneficial Health Aspects and its Prospective Application in Poultry Production. *Front Pharmacol.* 2021;12: 1-12. doi:10.3389/fphar.2021.723040 <https://doi.org/10.3389/fphar.2021.723040>
19. Yuniastuti A. Dasar Molekuler Glutathione dan Perannya Sebagai Antioksidan. Semarang: FMIPA Unnes; 2016.
20. Firdaus KL. Pengaruh Pemberian Minyak ZAITUN Terhadap Kadar MDA Plasma Darah pada Tikus Putih Strain Wistar dengan Induksi Aloksan. 2017.
21. Meilina. Extra Virgin Olive Oil Menurunkan Kadar MDA pada Tikus Jantan Galur Wistar yang dipapar Asap Rokok. *Fak Kedokt Univ Udayana.* 2017. doi:10.2307/j.ctv1k03g7r.9 <https://doi.org/10.2307/j.ctv1k03g7r.9>
22. Fajrin MS, Bamahry A, Karsa NS, Rijal S, Murfat Z. Pengaruh Minyak Zaitun (Extra Virgin Olive Oil) & Minyak Ikan (Omega-3) Terhadap Kadar Malondialdehyde Pada Tikus Putih Galur Wistar Hiperglikemik. *Fakumi Med J J Mhs Kedokt.* 2022;2: 42-50.
23. Kurniawati M, Jufriadi A, Subandi, Rumhayati B. Potensi Xanton Sebagai Anti Radikal Oxygen Species (ROS) pada Diabetes Mellitus. 2016.
24. Oladayo MI. Nigerian propolis improves blood glucose, glycated hemoglobin A1c, very low-density lipoprotein, and highdensity lipoprotein levels in rat models of diabetes. *J Intercult Ethnopharmacol.* 2016;5: 233-238. doi:10.5455/jice.20160502065029 <https://doi.org/10.5455/jice.20160502065029>
25. Hadwan MH. Simple spectrophotometric assay for measuring catalase activity in biological tissues. *BMC Biochem.* 2018;19: 1-8. <https://doi.org/10.1186/s12858-018-0097-5>
26. Amin EF, Rifaai RA, Abdel-latif RG. Empagliflozin attenuates transient cerebral ischemia/reperfusion injury in hyperglycemic rats via repressing oxidative-inflammatory-apoptotic pathway. *Fundam Clin Pharmacol.* 2020;34: 548-558. <https://doi.org/10.1111/fcp.12548>
27. Rowiński R, Kozakiewicz M, Kędziora-Kornatowska K, Hübner-Woźniak E, Kędziora J. Markers of oxidative stress and erythrocyte antioxidant enzyme activity in older men and women with differing physical activity. *Exp Gerontol.* 2013;48: 1141-1146. <https://doi.org/10.1016/j.exger.2013.07.010>
28. Suarsana N, Utama IH, Kardena IM. Immunohistochemical expression of insulin and glucagon, superoxide dismutase and catalase activity in pancreas in hyperglycaemia condition. *Asian J Biochem.* 2016;11: 177-185. <https://doi.org/10.3923/ajb.2016.177.185>
29. Agarkov AA, Popova TN, Boltysheva YG. Influence of 10-(6-plastoquinonyl) decyltriphenylphosphonium on free-radical homeostasis in the heart and blood serum of rats with streptozotocin-induced hyperglycemia. *World J Diabetes.* 2019;10: 546. <https://doi.org/10.4239/wjd.v10.i12.546>
30. Gebicka L, Krych-Madej J. The role of catalases in the prevention/promotion of oxidative stress. *J Inorg Biochem.* 2019;197: 110699. <https://doi.org/10.1016/j.jinorgbio.2019.110699>
31. Nandi A, Yan L-J, Jana CK, Das N. Role of catalase in oxidative stress-and age-associated degenerative diseases. *Oxid Med Cell Longev.* 2019;2019. <https://doi.org/10.1155/2019/9613090>
32. Ighodaro OM, Akinloye OA. First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid. *Alexandria J Med.* 2018;54: 287-293. <https://doi.org/10.1016/j.ajme.2017.09.001>
33. Lubos E, Loscalzo J, Handy DE. Glutathione peroxidase-1 in health and disease: from molecular mechanisms to therapeutic opportunities. 2011. <https://doi.org/10.1089/ars.2010.3586>
34. Sultan CS, Saackel A, Stank A, Fleming T, Fedorova M, Hoffmann R, et al. Impact of carbonylation on glutathione peroxidase-1 activity in human hyperglycemic endothelial cells. *Redox Biol.* 2018;16: 113-122. <https://doi.org/10.1016/j.redox.2018.02.018>
35. Brigelius-Flohé R, Flohé L. Regulatory phenomena in the glutathione peroxidase superfamily. *Antioxid Redox Signal.* 2020;33: 498-516. <https://doi.org/10.1089/ars.2019.7905>
36. Conde C, Escribano BM, Luque E, Aguilar-Luque M, Feijóo M, Ochoa JJ, et al. The protective effect of extra-virgin olive oil in the experimental model of multiple sclerosis in the rat. *Nutr Neurosci.* 2020;23: 37-48. <https://doi.org/10.1080/1028415X.2018.1469281>