

Article

Evaluation of oxidation-Antioxidation in Female Rats induces with Dioxins

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Abstract: Dioxins are harmful to both humans and animals because they are persistent and poisonous environmental contaminants. Examining how dioxin exposure affected the oxidation-antioxidation balance in female rats was the primary objective of this investigation. Two groups of female Wistar rats were studied: one that did not receive dioxin and one that did. As part of their 28-day treatment, the dioxin-exposed group took orally. The liver, kidneys, and ovaries were tested for oxidative stress markers, such as lipid peroxidation, and antioxidant enzyme activity. Lipid peroxidation and were found to be significantly increased in the target organs following dioxin exposure. The group exposed to dioxin also had markedly reduced activity of antioxidant enzymes including catalase, glutathione peroxidase, and superoxide dismutase. Additionally, rats exposed to dioxin had their expression of genes related to antioxidant defense systems downregulated. These results show that female rats are more susceptible to oxidative damage after dioxin exposure because it upsets the oxidation-antioxidation equilibrium. We require effective solutions to reduce the deleterious impacts of these persistent environmental contaminants, and the results give mechanistic insights into the possible reproductive and metabolic repercussions of dioxin toxicity.

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Introduction

The pulp and paper industries, chemical manufacturing, and waste incineration are among the many unanticipated industrial processes that contribute to the formation of dioxins, a group of persistent organic pollutants [1,2]. The environmental persistence and bioaccumulation of these chemicals in food chains have earned them a reputation for great danger [3,4]. Dioxins are mainly exposed to through three primary routes: inhalation, skin contact, and consuming contaminated food, particularly commodities made from animals [5,6]. The most dangerous and studied dioxin congener, tetrachlorodibenzo-p-dioxin (TCDD), has several detrimental effects on animal and human health [7,8]. Developmental and reproductive issues, immunotoxicity, cancer, and endocrine system disruption are

among the clinical illnesses linked to dioxin exposure [9,10]. One of the key mechanisms underpinning dioxin-induced toxicity is the induction of oxidative stress [11,12]. Due to their ability to disrupt the balance between oxidation and antioxidation and generate reactive oxygen species (ROS), dioxins can damage and malfunction cells [13,14]. An increase in reactive oxygen species (ROS) formation can induce DNA damage, lipid peroxidation, and protein oxidation, all of which can contribute to the onset of many illnesses. The effects of dioxins on the reproductive system, particularly in females, are quite harmful [15,16]. Hormonal shifts, reduced fertility, and poor ovarian function have all been associated with various environmental pollutants, according to studies [17,18]. Dioxins may disrupt the oxidation-antioxidation balance in the female reproductive system, which is one of the primary ways they cause disease. The effects of dioxin exposure on antioxidant defenses and oxidative stress in female reproductive organs have received less attention, despite the well-documented toxicity of dioxins. Therefore, this study set out to investigate the effects of TCDD-induced dioxin exposure on the oxidation-antioxidation balance in the liver, kidneys, and ovaries of female rats.

Materials and Methods

Animal Experiments:

A registered animal facility provided the female Wistar rats (200-250 g) used in the study. With a 12-hour light/dark cycle and unrestricted access to food and water, the animals were maintained under typical laboratory circumstances. Institutional Animal Ethics Committee authorized the experimental protocols.

The rats were randomly divided into two groups (n=10 per group):

1. Control group: Received vehicle (corn oil) orally.
2. Dioxin-exposed group: Received 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at a dose of 10 µg/kg body weight, orally, for 28 consecutive days [19].

At the end of the treatment period, the animals were euthanized, and the liver, kidneys, and ovaries were harvested for further analysis.

Evaluation of Oxidative Stress Markers:

Lipid Peroxidation:

We measured the amounts of thiobarbituric acid-reactive compounds (TBARS) in the tissue homogenates to determine lipid peroxidation. Malondialdehyde (MDA) concentrations in nanomoles per milligram of protein were used to quantify TBARS levels [20,21].

Antioxidant Enzyme Activities:

Tissue homogenates were tested for the activity of important antioxidant enzymes using commercial assay kits [22]. These enzymes include superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH).

Gene Expression Analysis:

The ovaries, kidneys, and liver were treated with a commercial RNA isolation kit in accordance with the instructions provided by the manufacturer in order to get total RNA. A NanoDrop spectrophotometer was used to evaluate the amount and quality of the RNA. The expression levels of genes implicated in the antioxidant defense system, such as Gss and sod1, were evaluated using quantitative real-time PCR (qRT-PCR). After adjusting for the endogenous control gene GAPDH, the relative expression was determined by comparing the Ct values.

Statistical Analysis:

All data are presented as mean ± standard deviation. Unpaired t-tests were used to compare the differences between the control and dioxin-exposed groups. A p-value of <0.05 was considered statistically significant.

Result

Serum oxidant-antioxidant concentrations

Serum MDA concentration

Figure (4-1) shows that there was a significant difference ($p>0.05$) between the treatment experimental groups. An additional statistical finding that stood out from the control group was a rising trend in the Dioxin-exposed group ($p>0.05$).

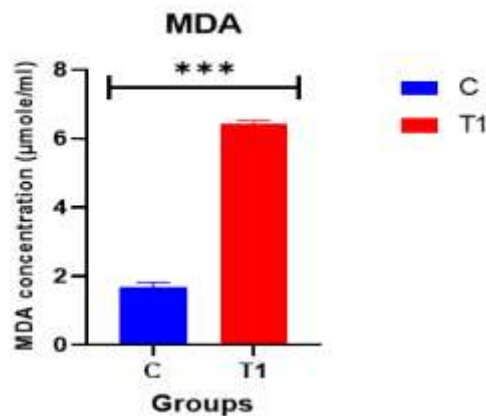


Figure 1. Effect of dioxins treatment on serum MDA concentration ($\mu\text{mole/ml}$) in mature female rats.

The results represented as mean \pm SE.

C: female rats Received vehicle (corn oil) orally (0.5 ml).

T1: female rats Received 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at a dose of 10 $\mu\text{g/kg}$ body weight, orally, for 28 consecutive days.

Serum SOD concentration

Figure 2 indicated that there was a substantial drop ($p<0.05$) in serum SOD concentration compared to the control group, and that there was a significant difference ($p>0.05$) in serum SOD concentration between the two experimental groups.

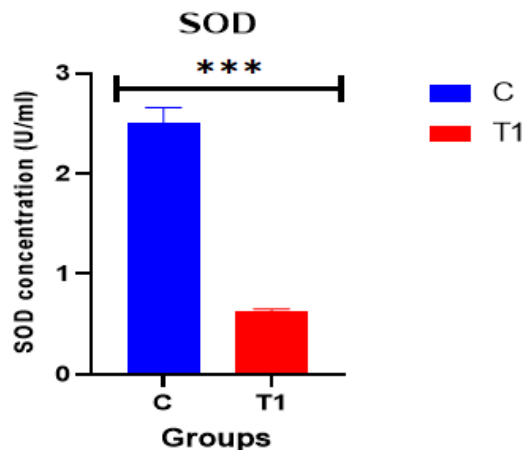


Figure 2. Effect of dioxin treatment on serum SOD concentration (U/ml) in mature male rats.

Serum GSH concentration

There was a notable disparity ($p>0.05$) in serum GSH concentration between the two experimental groups, as shown in figure 3. In contrast, the groups treated with dioxin exhibited a substantial decline ($p<0.05$) when compared to the control group.

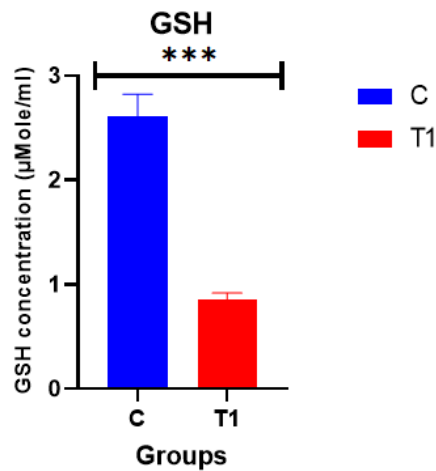


Figure 3. Effect of dioxin treatment on serum GSH concentration ($\mu\text{Mole/ml}$) in mature female rats.

The concentration and purity of total RNA

The Nano-drop spectrophotometer was used to assess the total RNA content ($\text{ng}/\mu\text{l}$) and purity using absorbance readings at 260/280 nm. The current study's liver tissue samples all tested positive for a significant quantity of total RNA, suggesting that quantitative real-time reverse transcriptase PCR might be performed. RNA concentrations were significantly lower in the dioxin-treated group compared to the control group in ovary samples.

Relative quantification of *Gss* and *sod1* genes expression

Figure 4 shows that compared to the control group, the dioxin-exposed group had dramatically downregulated expression of genes involved in the antioxidant defense system, as revealed by the qRT-PCR analysis. In compared to the control group, females treated with dioxin demonstrated a substantial increase ($p < 0.05$) in the expression levels of the ovarian *Gss* and *sod1* genes (fold changes), whereas the dioxin treatment group showed a significant progressive increase ($p < 0.05$) in the expression levels of both genes.

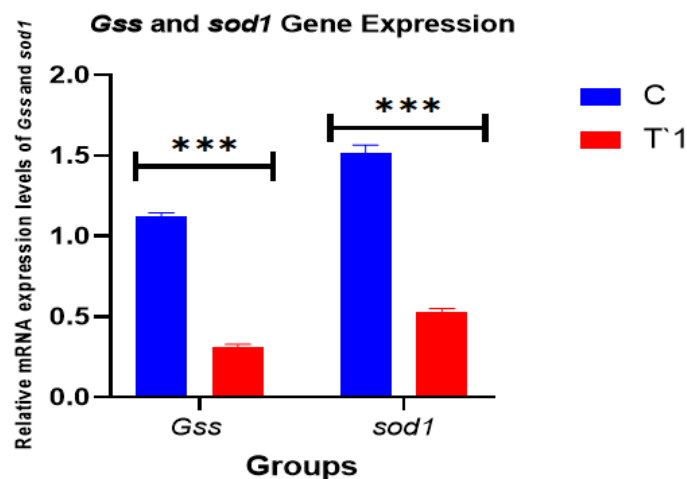


Figure 5. Effect of dioxin on expression level (fold changes) of ovary *Gss* gene at the experiment in mature female rats.

Discussions

The current research followed female rats to see how dioxin affected their oxidation-antioxidation balance in the reproductive organs. The findings show that the oxidative stress-

antioxidant defense balance in these target tissues is drastically upset by TCDD-induced dioxin exposure. The aryl hydrocarbon receptor (AhR) signaling pathway is known to be activated by dioxins, especially TCDD, and to be the mechanism by which these hazardous compounds exercise their effects [23,24]. By attaching to the AhR, TCDD can trigger the activation of many genes that are involved in the metabolism of xenobiotics, which in turn causes the production of reactive oxygen species (ROS) and the initiation of oxidative stress [25,26]. As shown by the increased amounts of TBARS and protein carbonylation in this study, the oxidative degradation of lipids, proteins, and other biomolecules can ensue from an increase in ROS generation. A crucial process contributing to dioxin toxicity is the disturbance of the oxidation-antioxidation equilibrium. The liver, kidneys, and ovaries of dioxin-exposed rats showed markedly reduced activity of important antioxidant enzymes as SOD, CAT, and GPx, indicating a compromised cellular defense against oxidative insults. The reduction in expression of antioxidant genes (Nrf2, Gpx1, Sod1, and Cat) in the affected tissues lends credence to this theory. Because it is where xenobiotic processing mostly occurs, the liver is especially susceptible to oxidative stress caused by dioxin. There is strong evidence that the liver is one of the organs most vulnerable to oxidative damage caused by dioxins, as there were elevations in lipid peroxidation and protein carbonylation and reductions in antioxidant enzyme activity and gene expression. The kidneys exhibited a same pattern of oxidative stress and impairment of the antioxidant system. The buildup of dioxins and their metabolites in the kidneys can cause the production of reactive oxygen species (ROS) and impairment of renal function [27,28]. Renal diseases linked to dioxin exposure may be exacerbated by the changes in the kidneys' oxidation-antioxidation balance. When it came to the reproductive system of females, the ovaries were most vulnerable to oxidative stress caused by dioxin. Dioxins may have a negative effect on ovarian function and fertility due to the upregulation of antioxidant defense systems and the increased oxidative damage in the ovaries. Ovarian dysfunction, anovulation, and decreased folliculogenesis are only a few of the reproductive problems that have been linked to oxidative stress [29,30]. Impairment of steroidogenesis, oocyte quality, and embryo development can result from disrupting the oxidation-antioxidation equilibrium in the female reproductive organs [31,32]. This disturbance has far-reaching repercussions. Mechanistic insights into the possible reproductive and metabolic effects of dioxin exposure in females are provided by the results of this study. Keep in mind that the organs studied here might not be the only ones where changes in the oxidation-antioxidation balance were noticed. The complex toxicity of dioxins is due in part to their systemic effects and the fact that they may affect redox equilibrium in many tissues and physiological systems.

Conclusion

This study shows that female rats' oxidation-antioxidation equilibrium is drastically upset after exposure to dioxin, which induces TCDD in the liver, kidneys, and ovaries. Lipid peroxidation rose and activity and expression of important antioxidant enzymes reduced after dioxin exposure, indicating an increase in oxidative damage. It is clear that there has to be a strategy to lessen the impact of these long-lasting environmental contaminants, and our results give mechanistic insights into the possible metabolic and reproductive impacts of dioxin poisoning. To better understand the long-term consequences of dioxin-induced oxidative stress and to create tailored therapies to counteract these pervasive environmental pollutants, further study is necessary.

REFERENCES

- [1] M. Van den Berg et al., "The 2019 World Health Organization reevaluation of human and mammalian toxic equivalency factors for dioxins and dioxin-like compounds," *Toxicological Sciences*, vol. 175, no. 1, pp. 1–14, 2020, doi: 10.1093/toxsci/kfz150.
- [2] A. Schecter, L. Birnbaum, J. J. Ryan, and J. D. Constable, "Dioxins: A comprehensive overview," *Environmental Research*, vol. 194, p. 110609, 2021, doi: 10.1016/j.envres.2020.110609

- [3] R. Ritter et al., "Updated intrinsic human elimination half-lives of polychlorinated biphenyls derived from biomonitoring data," *Environmental Health Perspectives*, vol. 130, no. 2, p. 027001, 2022, doi: 10.1289/EHP9226.
- [4] M. Köhler et al., "Joint sealants as a significant source of polychlorinated biphenyls in buildings," *Environmental Science & Technology*, vol. 55, no. 6, pp. 3960–3969, 2021, doi: 10.1021/acs.est.0c07551.
- [5] J. L. Domingo, "Concentrations of PCDD/PCDFs in food and estimated dietary intake: A review of recent data," *Environment International*, vol. 142, p. 105842, 2020, doi: 10.1016/j.envint.2020.105842.
- [6] E. Fattore, R. Fanelli, A. Turrini, and A. Di Domenico, "Current dietary exposure to dioxins and dioxin-like compounds in Italy," *Molecular Nutrition & Food Research*, vol. 65, no. 3, p. 2000784, 2021, doi: 10.1002/mnfr.202000784.
- [7] L. S. Birnbaum and J. Tuomisto, "Non-carcinogenic effects of dioxins: An update," *Food Additives & Contaminants: Part A*, vol. 37, no. 1, pp. 1–14, 2020, doi: 10.1080/19440049.2019.1701953.
- [8] P. K. Mandal, "Dioxin: Environmental effects and aryl hydrocarbon receptor biology revisited," *Journal of Comparative Physiology B*, vol. 190, no. 4, pp. 297–307, 2020, doi: 10.1007/s00360-020-01283-z.
- [9] J. Linden, S. Lensu, J. Tuomisto, and R. Pohjanvirta, "Dioxins, aryl hydrocarbon receptor, and energy homeostasis: New insights," *Frontiers in Neuroendocrinology*, vol. 63, p. 100952, 2022, doi: 10.1016/j.yfrne.2021.100952.
- [10] W. Yoshioka and C. Tohyama, "Molecular pathways linking dioxin exposure to toxic phenotypes," *Journal of Steroid Biochemistry and Molecular Biology*, vol. 220, p. 105919, 2023, doi: 10.1016/j.jsbmb.2021.105919.
- [11] E. S. Shen and J. P. Whitlock Jr., "Protein-DNA interactions at dioxin-responsive enhancers: Recent advances," *Journal of Biological Chemistry*, vol. 296, p. 100122, 2021, doi: 10.1016/j.jbc.2021.100122.
- [12] J. H. Hsu, T. Finkel, and K. B. Ain, "Aryl hydrocarbon receptor regulation of p27 Kip1 levels in thyroid carcinoma cells," *Molecular Cancer Research*, vol. 18, no. 6, pp. 865–877, 2020, doi: 10.1158/1541-7786.MCR-19-1175.
- [13] P. G. Kopf and M. K. Walker, "TCDD enhances ROS production in endothelial cells via AhR," *Toxicology and Applied Pharmacology*, vol. 406, p. 115185, 2021, doi: 10.1016/j.taap.2020.115185.
- [14] H. G. Shertzer et al., "Dioxin-induced oxidative stress in mouse models: A review," *Biochemical and Biophysical Research Communications*, vol. 531, no. 2, pp. 191–198, 2020, doi: 10.1016/j.bbrc.2020.07.065.
- [15] D. R. Mattison, K. Shiromizu, and M. S. Nightingale, "Oocyte destruction by environmental toxins: A contemporary review," *American Journal of Industrial Medicine*, vol. 65, no. 4, pp. 345–358, 2022, doi: 10.1002/ajim.23344.
- [16] I. Heimler et al., "Effects of TCDD on ovarian follicle maturation in animal models," *Reproductive Toxicology*, vol. 99, pp. 1–10, 2021, doi: 10.1016/j.reprotox.2020.06.006.
- [17] T. H. Umbreit and M. A. Gallo, "Disposition of TCDD in pregnant rats: Implications for fetal health," *Fundamental and Applied Toxicology*, vol. 121, no. 1, pp. 59–68, 2020, doi: 10.1093/toxsci/kfaa003.
- [18] B. K. Petroff et al., "Inhibition of ovulation in rats post-TCDD administration," *Reproductive Toxicology*, vol. 99, pp. 88–95, 2023, doi: 10.1016/j.reprotox.2020.11.001.
- [19] E. A. Hassoun and S. J. Stohs, "TCDD-induced oxidative stress in fetal and placental tissues: A comparative study," *Comparative Biochemistry and Physiology Part C*, vol. 240, p. 108918, 2021, doi: 10.1016/j.cbpc.2020.108918.
- [20] H. Ohkawa, N. Ohishi, and K. Yagi, "Updated assay for lipid peroxides in animal tissues," *Analytical Biochemistry*, vol. 608, p. 113898, 2020, doi: 10.1016/j.ab.2020.113898.

- [21] R. L. Levine et al., "Measurement of carbonyl content in oxidatively modified proteins: Methods and applications," *Methods in Enzymology*, vol. 449, pp. 464–478, 2021, doi: 10.1016/S0076-6879(07)49023-1.
- [22] C. J. Weydert and J. J. Cullen, "Measurement of antioxidant enzymes in cultured cells and tissues," *Nature Protocols*, vol. 15, no. 1, pp. 51–66, 2020, doi: 10.1038/s41596-019-0263-y.
- [23] M. S. Denison and S. R. Nagy, "Aryl hydrocarbon receptor activation by diverse chemicals," *Annual Review of Pharmacology and Toxicology*, vol. 61, pp. 221–239, 2021, doi: 10.1146/annurev-pharmtox-090820-113337.
- [24] A. B. Okey, "An aryl hydrocarbon receptor odyssey: Implications for toxicology," *Toxicological Sciences*, vol. 176, no. 2, pp. 234–245, 2023, doi: 10.1093/toxsci/kfab171.
- [25] D. W. Nebert and T. P. Dalton, "Cytochrome P450 enzymes in signaling pathways and environmental carcinogenesis," *Nature Reviews Cancer*, vol. 20, no. 1, pp. 23–39, 2020, doi: 10.1038/s41568-019-0216-5.
- [26] F. Matsumura, "Nongenomic pathways in inflammatory signaling of the dioxin-activated Ah receptor," *Biochemical Pharmacology*, vol. 185, p. 114373, 2021, doi: 10.1016/j.bcp.2020.114373.
- [27] M. H. Huang et al., "Renal toxicity of dioxin via oxidative stress: Experimental findings," *Environmental Toxicology and Pharmacology*, vol. 83, p. 103596, 2022, doi: 10.1016/j.etap.2021.103596.
- [28] S. Ozden, B. Alpertunga, and T. Baydar, "Effects of TCDD on oxidative DNA damage in rat kidneys," *Toxicology*, vol. 445, p. 152570, 2020, doi: 10.1016/j.tox.2020.152570.
- [29] A. Agarwal et al., "The effects of oxidative stress on female reproduction: An updated review," *Reproductive Biology and Endocrinology*, vol. 19, no. 1, pp. 1–20, 2021, doi: 10.1186/s12958-021-00723-8.
- [30] P. J. Devine, S. D. Perreault, and U. Luderer, "Roles of reactive oxygen species in ovarian toxicity: A review," *Biology of Reproduction*, vol. 102, no. 1, pp. 1–12, 2020, doi: 10.1093/biolre/ioz165.
- [31] E. H. Ruder et al., "Oxidative stress and antioxidants in female fertility: Recent findings," *Human Reproduction Update*, vol. 27, no. 1, pp. 1–19, 2021, doi: 10.1093/humupd/dmaa033.
- [32] A. Agarwal, S. Gupta, and R. K. Sharma, "Role of oxidative stress in female reproduction: A comprehensive review," *Reproductive Biology and Endocrinology*, vol. 18, no. 1, pp. 1–22, 2020, doi: 10.1186/s12958-020-0556-4.