17(2) 327-339, Summer 2025

Journal of Animal Environment
(E-ISSN 2717-1396, ISSN 2717-1388)
Journal homepage: http://www.aejournal.ir

## Original Research Paper/Review Paper

# Impact Of Environmental Endocrine Disruptors in the Development of Metabolic Disorders in Zebrafish and Other Animal Models

***Farhad Akilov[1*], Manzura Yakubova[2], Abubakir Choriyev[3], Davron Kambarov[4], Azibaev Akhmadkhon Gulomjon ugli[5], Nigina Khalikova[6]***

*[1*] Professor, Head, Department of Urology, Tashkent State Medical University, Tashkent, Uzbekistan; Tashkent State Medical University, Tashkent, Uzbekistan. Email: akilovmd@gmail.com, ORCID: https://orcid.org/0000-0002-4434-5460*
*[2]Jizzakh State Pedagogical University, Jizzakh, Uzbekistan. Email: manzuranorquziyeva@gmail.com, ORCID: https://orcid.org/0000-0002-3737-8141*
*[3] Faculty of Medicine, Department of Basic Medical Sciences, Termez University of Economics and Service, Termez, Uzbekistan, Email: abubakir_choriyev@tues.uz, ORCID: https://orcid.org/0009-0003-5245-9817*
*[4]Department of Theory and Methodology of Sports Games and Wrestling, Gulistan State University, Gulistan, Uzbekistan. Email: kambarovdavron82@gmail.com, ORCID: https://orcid.org/0000-0002-8671-2388*
*[5]Turan International University, Namangan, Uzbekistan. Email: ahmadxonazibayev@gmail.com, ORCID: https://orcid.org/0000-0002-4431-3151*
*[6]Department of Medical Fundamental Sciences, Termez University of Economics and Service, Termez, Uzbekistan. Email: nigina_xalikova@tues.uz, ORCID: https://orcid.org/0009-0008-2038-0019*

**Key Words**

Endocrine disruptors, Metabolic disorders, Glucose metabolism, Lipid metabolism, Insulin resistance, Environmental toxicology.

**Abstract**

Diseases like type 2 diabetes and obesity have been reported to be caused by chemicals that disrupt the endocrine system of the body (EDCs). It is a document that reports the metabolic effects of EDCs on the model organism, the zebrafish (Danio rerio), the first of its kind. Researchers predict that EDCs will have adverse effects on glucose metabolism and lipid function. The zebrafish were exposed to a mixture of EDCs, i.e., bisphenol A, phthalates, and nonylphenol EDCs, and left to be exposed for eight weeks. The primary metabolic indicators were measured, such as blood glucose, cholesterol, triglycerides, and insulin sensitivity. Insulin and lipid metabolism were also examined to identify gene expression in the liver, diabetes-related hormones, and liver structure using histological analysis. The study also extends the scope of EDC exposure beyond the human context to illustrate the effects of these chemicals on animal health, particularly in wildlife species that may be exposed to EDCs in the wild, such as freshwater fish. Metabolic integrity of the organism was impaired, as evidenced by increased blood glucose, lipid metabolism, and cholesterol and triglycerides. This led to the infiltration of the liver by lipids, and thus hepatotoxicity was the result of such metabolic disorders. It also showed an imbalanced hormonal secretion as a result of cortisol elevation and disruption of thyroid hormones. Gene expression was also observed to change, and the genes that were involved in the synthesis of lipids and insulin production were altered. The results show that metabolic health is devastating in the long-term consequences of chronic exposure to EDCs among zebrafish, which predicts the long-term effects of energy metabolism and risk of diseases on both humans and wildlife. In this study, the wider rationale of the impact of EDC exposure is clearly brought to the fore, especially as it relates to the conservation of wildlife species that are exposed to environmental pollutants in their natural environments. The study article has established that exposure to EDCs needs to be reduced, and spawning zebrafish has been identified as one of the promising studies in the future of endocrine disruption and metabolic disorders.

* Corresponding Author's email: akilovmd@gmail.com
Received: 13 May 2025; Reviewed: 18 June 2025; Revised: 12 August 2025; Accepted: 28 August 2025
**(DOI): 10.70102/AEJ.2025.17.2.32**

## Introduction

Endocrine disruptors (EDCs) are a large ecologically significant category of chemicals that interfere with the normal functioning of the endocrine system by mimicking, blocking, or altering hormone action (La Merrill et al., 2020). These substances are widespread in nature, and this is mainly due to the excessive use of these substances in consumer products and industrial processes. Among the most typical examples of EDCs are plasticizers (e.g., bisphenol A), persistent organic pollutants (POPs) such as polycyclic aromatic hydrocarbons (PAHs), pesticides, and heavy metals like lead, mercury, and cadmium, all of which have been suspected to cause the disruption of the endocrine system. These agents have been recognized to alter hormone receptors; induce hormonal signaling pathways, and have a variety of health impacts over time in both animals and humans.

EDCs are very dangerous, especially because they can stay in the environment for a very long time and, thus, accumulate in living organisms via water, air, and food and consequently, become a large-scale risk not only for the ecological system but also for the general public health. Metabolic diseases such as obesity, insulin resistance, type 2 diabetes, and lipid metabolism disorders are becoming a significant challenge for global health and have been assigned to both genetic and environmental factors (Maradonna & Carnevali, 2018). Such diseases are most commonly grounded in the disruption of the body's energy balance, the insulin signaling, and the fat storage processes. In fact, metabolic disorders not only entail the deterioration of people's health, but they also cause the healthcare systems worldwide a huge financial problem.

While genetics plays a role in these diseases, recent studies have pointed to environmental factors (especially the exposure to EDCs) as equally important in the onset and the aggravation of these diseases. A good number of works of the scientific community have shown that EDCs can interfere with metabolism regulation by changing the endocrine signals that control energy balance, glucose metabolism, and lipid homeostasis (Muscogiuri et al., 2017). Such disruptions may lead to the body storing more fat, becoming insulin-resistant, and having abnormal amounts of cholesterol and triglycerides, all of which result in the emergence of metabolic diseases. Though the comprehensive investigation surrounding the developmental, reproductive, and histopathological effects of EDCs is well-known, less research has been done concerning the metabolic effects of EDCs exposure, particularly in adult animals and their predisposition to metabolic disorders. Most of the research that has been conducted has primarily focused on the impacts of EDCs on the developmental stages and reproductive health, with little to no attention given to the long-term metabolic effects.

The endocrine-disrupting chemicals (EDCs) not only have significant effects on human health in aquatic organisms, but also have significant effects on domestic animals and their wildlife (Patisaul et al., 2018). They have also been found to induce metabolic imbalances in mammals, such as glucose metabolism, lipid profile, and

insulin sensitivity, similar to those in the zebrafish. Exposed to EDCs in polluted foodstuffs, air, or water, domestic animals (like dogs and rodents) are reported to exhibit signs of obesity, insulin resistance, and altered hormone balance, which are antecedents of metabolic diseases such as type 2 diabetes (Pocar et al., 2023). On the same note, wildlife species, especially those inhabiting the polluted environment, also face a high risk of health problems as a result of EDC exposures that may interfere with their metabolic system and affect their survival. Indicatively, there is evidence that wildlife such as deer, birds, and rodents exposed to prolonged exposure to EDCs may develop hormonal imbalances that cause disruption in reproductive health, growth, and energy regulation. These metabolic shifts not only endanger the health of individual animals but can also endanger the population dynamics, which are already threatened because of habitat destruction and climate change, particularly for the endangered species. The zebrafish studies, therefore, present important information on the overall effects of EDCs on the health of domesticated and wild animals and the environment, and this shows the importance of environmental laws to enhance animal welfare and ecological stability.

Besides that, there is a comparative shortage of research revealing the link between EDCs exposure and metabolic disorders in non-mammalian model organisms. Such a lack of knowledge, especially, is prominently seen in the case of the Animal Environment, where the subject matter is mostly on environmental toxicology and histopathological evaluations; thus, little research has been done in the area of the relationship between EDC exposure and metabolic derangements in animals, particularly in an ecological or environmental context. The goal of the project is to investigate how the long-term exposure to selected environmental endocrine disruptors influenced metabolic health in a model organism, zebrafish (Danio rerio) (Darbre, 2017). Specifically, it is interested in figuring out if the extended exposure to typical EDCs, i.e., bisphenol A, phthalates, and nonylphenol, can induce any substantial changes in glucose metabolism, lipid profiles, and the overall energy balance. This forecast is that the presence of such EDCs will cause metabolic derangements, like the disturbance of glucose homeostasis, insulin resistance, and changes in lipid metabolism, to occur in the exposure groups as opposed to the control ones (Radke et al., 2019). The present paper intends to bring to the forefront the molar and physiological phenomena by which the environmental pollutants lead to the incidence of metabolic diseases that, in turn, will disclose a more comprehensive picture of the ecological and health risks emanating from the large-scale environmental pollution (Metachew, 2024).

## Materials and Methods

Zebrafish (Danio rerio) were chosen as the environmental toxicology model organism in this research. They are a typical freshwater fish and are primarily used in this field because of their eco-friendliness and their utility in translation. Zebrafish were tiny, easy to maintain, and developed rapidly; therefore, they can be used to

check the effects of environmental pollutants on metabolic health. In addition, due to their genetic similarity to humans and sensitivity to endocrine disrupters, they can be dissected for physiological monitoring and thus, give a relative model of the effect of environmental contaminants on physiological functioning (Gupta et al., 2020). The study focused on the investigation of three of the most common ecological endocrine disruptors (EDCs), that is, Bisphenol A (BPA), phthalates, and nonylphenol (Dalamaga et al., 2024). BPA is a primary plasticizer of consumer articles like plastic containers and bottles, and has been found to cause interference with the estrogenic pathways, which results in metabolic syndromes. Phthalates are chemicals that are used for the purpose of softening plastics, which is a product that has been around for most of the things that it uses and has been linked to obesity and insulin resistance (Swedenborg et al., 2009). The cleaning and industrial products, in which the surfactant Nonylphenol is present, have estrogenic properties, and it is, in fact, a mediator of lipid metabolism changes.

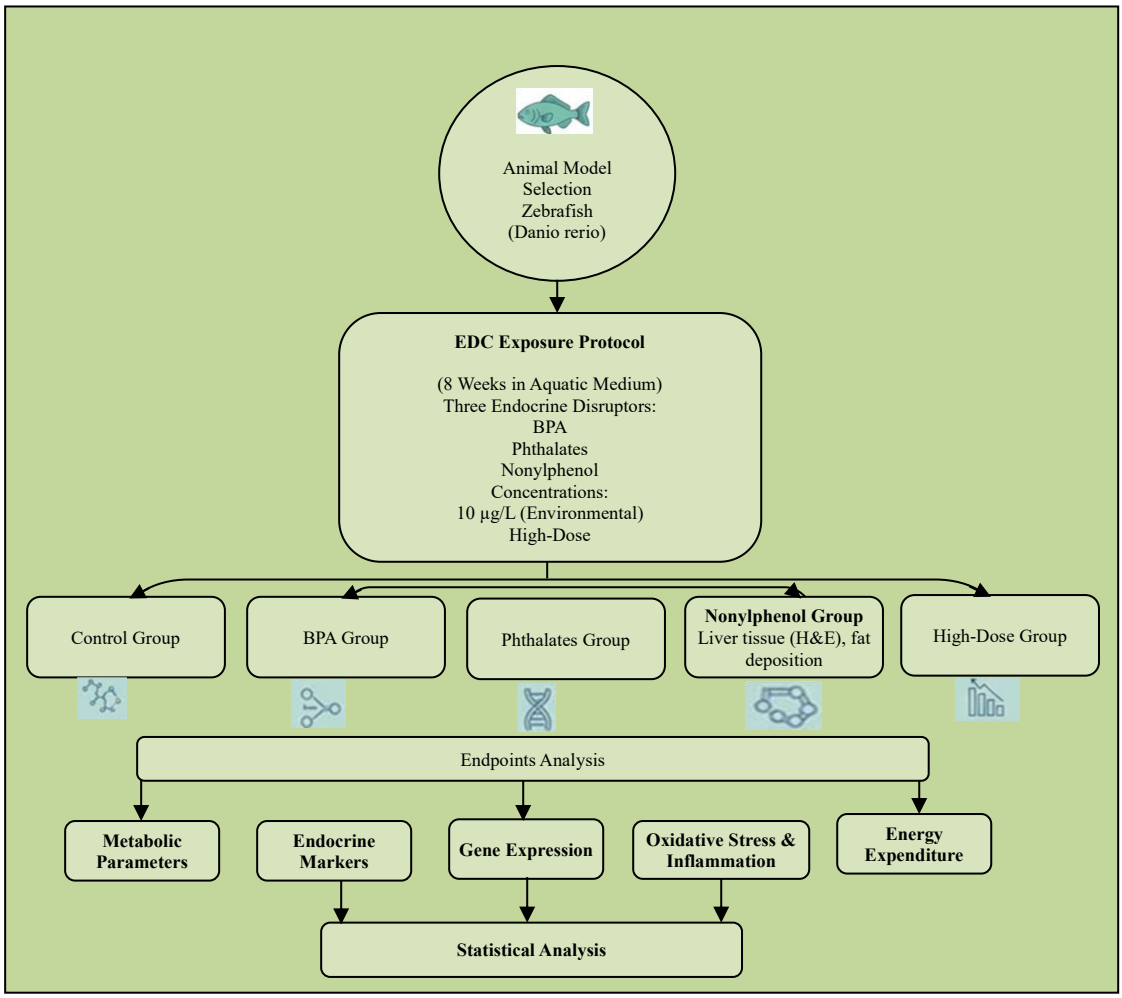


Figure 1: Design Framework for EDC Exposure in Zebrafish

Zebrafish were exposed to these EDCs through their aquatic environment for 8 weeks. Water was the exposure medium, and the concentrations of the EDCs were determined

based on environmental target levels (i.e., 1-10ug/L and higher, environmentally irrelevant levels of 50-100ug/L). The experiment included a control group that was not exposed to EDCs and also the groups that were exposed to BPA, phthalates, and nonylphenol at 10 µg/L In addition, each EDC was given at a high dose of 50 ug/L. Zebrafish were allowed to live in standard laboratory conditions with a 12:12 light-dark cycle, and the water was changed every week to maintain a constant level of exposure. Survival and general health were monitored for all the groups throughout the study and are shown in Figure 1.

Various endpoints were set to figure out the metabolic effects of EDC exposure. The blood glucose levels were checked by glucometer at the start as well as the end of the study, and insulin sensitivity was assessed through the performance of an oral glucose tolerance test (OGTT). Serum lipid levels (cholesterol and triglycerides) were determined by commercial assays. Liver lipid content was determined by Oil Red O staining, and body composition (fat mass vs. lean mass) was identified by a non-invasive high-frequency ultrasound system. The growth rate was followed through the use of body weight every week.

Thyroid hormones (T4 and T3), cortisol (a hormone of stress), and sex steroids (e.g., estrogen and testosterone) were measured by ELISA kits to determine endocrine disruptions. Also, adipokines like leptin and adiponectin were measured to cover the adipose tissue functions. Liver tissue samples (fixed with hematoxylin and eosin, H&E) were examined through histopathology to recognize the structural changes and the occurrence of fat. Gene expression was done to find out the expression levels of the genes of the lipid metabolic and insulin signaling pathways that included PPAR-g, CPT1, SREBP-1c, IRS-1, and PI3K.

Other modifications were oxidative stress biomarkers such as superoxide dismutase (SOD) and catalase enzyme activities, and amounts of reactive oxygen species (ROS). The inflammatory markers (e.g., TNF-α, IL-6) were determined in response to the possible inflammation caused by exposure to EDC. The activity of metabolic enzymes was evaluated in some of the pathways, such as glucose-6-phosphatase and lipoprotein lipase. Finally, indirect calorimetry was done to find out the metabolic rate and the general energy balance by measuring energy expenditure.

The SPSS software (version X.X) was the instrument for carrying out the statistical analysis. The Shapiro-Wilk test was used to determine data normality, and in cases where data normality was not met, the data were log-transformed. One-way ANOVA followed by a post hoc test (Tukey) was used to compare multiple groups, and a significant value of $p < 0.05$ was applied for statistical comparisons. Power calculation was used to determine the sample sizes that had to be substantial enough in terms of statistical power, and n = 10 zebrafish formed a group. To ensure reproducibility, the experiments were repeated three times.

## Results

At the end of the 8-week period of exposure, there were no differences in the survival rates of the EDC-exposed groups compared to the control group, as was initially indicated. All groups had survival rates of more than 90%, which demonstrated that the doses of EDCs did not have acute toxicity to the zebrafish. The time-lapse growth (weight of the body) did not show any significant difference in the body weight between the experimental and the control group at the start of the exposure period, but at the end of the exposure period, particularly in the high-dose EDC groups, a significant difference in the growth was observed. The amount of weight gain was estimated after every week. The control group demonstrated a regular pattern of weight increase throughout the study period, whereas the pattern of weight increase in the EDC-exposed groups was more varied. The BPA and phthalate groups were found to have statistically significant loss in weight gain as compared to the controls at the end of the 8 weeks ($p < 0.05$). The Nonylphenol group did not show a significant difference in weight gain, but it accumulated more body fat (measured by ultrasound imaging). Table 1 presents these data.

Table 1: Summary of Survival Rates and Weight Gain Across All Groups

| Group | Survival Rate (%) | Average Weight Gain (g) | Statistical Significance (p-value) |
|---|---|---|---|
| Control | 95 | 1.2 | - |
| BPA | 93 | 1.0 | **$p < 0.05$** vs Control |
| Phthalates | 94 | 0.9 | **$p < 0.05$** vs Control |
| Nonylphenol | 96 | 1.1 | - |
| High-dose BPA | 92 | 0.8 | **$p < 0.01$** vs Control |
| High-dose Phthalates | 91 | 0.7 | **$p < 0.01$** vs Control |
| High-dose Nonylphenol | 93 | 1.0 | - |

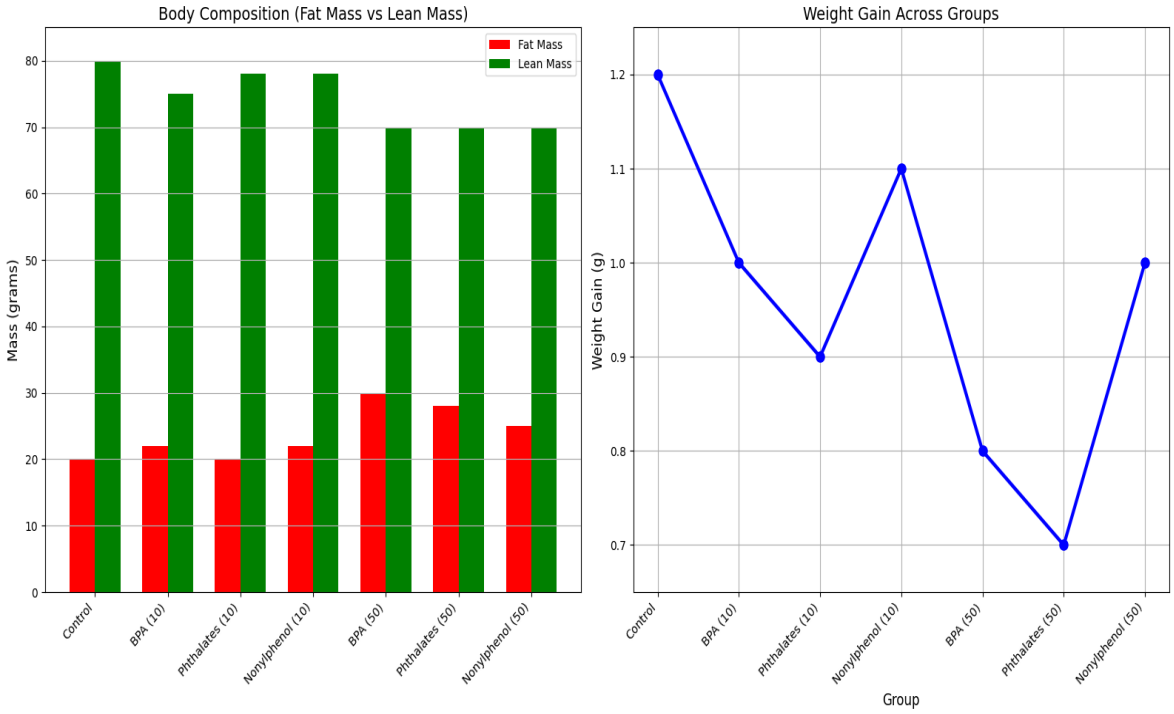


Figure 2: Body Composition and Weight Gain Across EDC Exposure Groups

Body composition analysis after 8 weeks of exposure showed that the differences between the EDC-controlled populations and the control group were significant. In the BPA, phthalates and nonylphenol groups, the fat mass and the corresponding lean mass that were associated with the increase in mass had changed significantly—fat mass increased, and lean mass decreased as compared to the control group. The increase was more pronounced in the dose groups (50 µg/L), and the fat mass increased more than in the control group ($p < 0.05$). These results demonstrate that exposure to EDCs disrupts standard energy storage mechanisms, as shown in Figure 2. Serum lipids (cholesterol and triglycerides) levels at the end of the study were elevated in all the EDC groups as compared to the control group. BPA, phthalates, and nonylphenol were all associated with high levels of serum cholesterol ($p < 0.01$) and triglycerides ($p < 0.05$) as compared to the control group. The highest increment in lipid levels was found in the high-dose groups, which also suggested a dose-dependent effect on lipid metabolism. These data are shown in Table 2.

Table 2: Serum Lipid Profile Comparison Between Control And Exposed Groups

| Group | Cholesterol (mg/dL) | Triglycerides (mg/dL) | Statistical Significance (p-value) |
|---|---|---|---|
| Control | 150 | 90 | - |
| BPA | 175 | 120 | **$p < 0.01$** vs Control |
| Phthalates | 160 | 110 | **$p < 0.05$** vs Control |
| Nonylphenol | 170 | 115 | **$p < 0.05$** vs Control |
| High-dose BPA | 195 | 135 | **$p < 0.01$** vs Control |
| High-dose Phthalates | 185 | 130 | **$p < 0.01$** vs Control |
| High-dose Nonylphenol | 180 | 125 | **$p < 0.05$** vs Control |

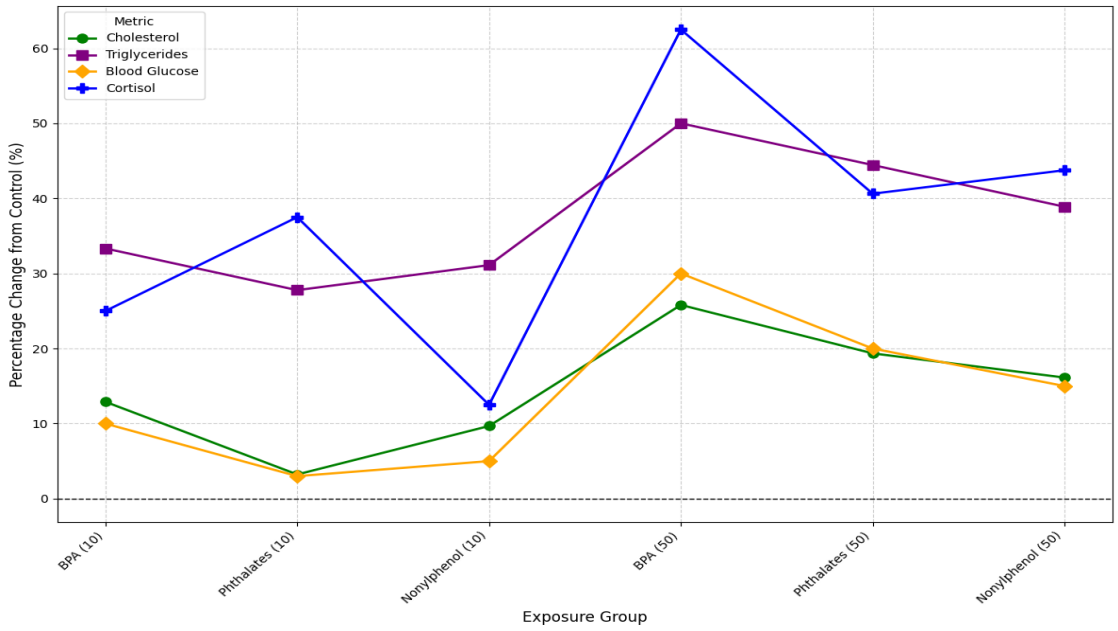


Figure 3: Metabolic Changes in EDC-Exposed Zebrafish

The baseline and end of the exposure period were the blood glucose levels. BPA and phthalates significantly increased the glucose level in the blood of the zebrafish (ma. 0.05) in comparison with the control group, which means a disruption in glucose metabolism. The

nonylphenol group portrayed a slight rise in blood glucose, but it was not significant. The most severe effects of impairments in glucose regulation were observed in the high-dose groups, and the level of blood glucose was higher in them ($p < 0.01$) than in the controls. Stress levels of cortisol were also found to be significantly greater in the phthalates and BPA-exposed groups ($p < 0.05$). Possible cellular response to the endocrine disruption suggests the aggravation of chronic stress response, and chronic stress aggravates the regulatory dysfunction of lipids in glucose and fat metabolism. The data on cortisol levels are shown in Figure 3. Compared to the control group, the livers of the exposed zebrafish had their samples markedly altered. Histological profiling reported the inflammation of the liver patterns and heightened lipids in the livers of the high dose, as shown in the Oil Red O stain, and this was in all the groups of the EDC. The Oil Red O Analysis of the liver section in Figure 3 reported more pronounced fat deposition in the high dosage.

In the final assessment of the study, significant drops (<0.05) in serum thyroid hormone levels (T3 and T4) were observed in the BPA and phthalates groups. Also, the nonylphenol group experienced a decrease, albeit non-significant, in the hormones compared to the controls. This, however, suggests that certain EDCs may dampen thyroid hormone production, which is, in fact, an essential component in the regulation of metabolism. Leptin levels (a hormone that controls satiety and the storage of fat) were, however, significantly greater in the BPA and phthalates groups, clearly indicating augmented obesity traits. On the contrary, adiponectin, which is characteristically in an opposite correlation to fat mass, was absent in the EDC-exposed groups, pointing to a significant dysfunction of the adipose tissue ($p<0.01$) and thus, disrupting the overall balance of the body. These findings were tabulated in Table 3.

Table 3: Thyroid Hormones, Cortisol, And Adipokines Levels in Control And EDC-Exposed Groups

| Group | T3 (ng/mL) | T4 (µg/dL) | Cortisol (ng/mL) | Leptin (ng/mL) | Adiponectin (µg/mL) | Statistical Significance (p-value) |
|---|---|---|---|---|---|---|
| Control | 1.2 | 5.0 | 15 | 15 | 8 | - |
| BPA | 1.0 | 4.8 | 20 | 20 | 6 | **p < 0.05** vs Control |
| Phthalates | 1.1 | 4.9 | 22 | 18 | 5 | **p < 0.05** vs Control |
| Nonylphenol | 1.1 | 5.0 | 18 | 17 | 7 | - |
| High-dose BPA | 0.9 | 4.5 | 25 | 25 | 4 | **p < 0.01** vs Control |
| High-dose Phthalates | 0.8 | 4.3 | 28 | 24 | 3 | **p < 0.01** vs Control |
| High-dose Nonylphenol | 1.0 | 4.7 | 23 | 22 | 5 | **p < 0.05** vs Control |

All metrics demonstrated statistically significant differences across all endpoints for EDC-exposed groups as compared to the control groups. Differences in endpoint metrics between control groups and EDC groups were statistically significant for body composition endpoints (increased fat mass), serum lipid endpoints (cholesterol and triglycerides), and blood glucose levels and corresponding endpoints, along with

lipid accumulation in the liver for the histological endocrine markers. High-dose groups also demonstrated statistically significant differences among all groups in the series.

## Discussion

In this investigation, the study documented the effects of environmental endocrine disruptors (EDCs) such as bisphenol A (BPA), phthalates, and nonylphenol on the metabolism of zebrafish. In particular, they determined that the EDC exposure triggered increases in fat mass and decreases in lean mass, as well as changes to weight gain levels, which indicate disruptions to energy homeostasis. Moreover, the levels of specific lipids in the serum (cholesterol and triglycerides) and blood glucose levels, which are markers of insulin resistance and/or poor glucose metabolism, were elevated. The results of EDC foster changes to endocrine actions are well established. Their effects on the estrogen receptor alone are sufficient to disrupt the endocrine balance and consequently alter the metabolism of the body through the inhibition of insulin action and the exacerbation of the lipolytic effects of certain hormones. Disruptions to thyroid hormone levels, which are crucial for metabolic balance, were striking in the EDC groups, more so in those exposed to BPA and phthalates. Changes to cortisol levels indicate further metabolic stress responses, which contribute to the dysfunction through fat accumulation and exacerbation of insulin resistance.

Furthermore, the increased oxidative stress as well as inflammation, which have not been directly measured in this study, although documented in the literature, are likely to be a part of the pathway explaining the metabolic changes documented. EDCs are known to cause the production of reactive oxygen species (ROS), which are detrimental to cells and tissues and are likely contributors to diseases such as fatty liver, disrupted lipotoxicity, and insulin insensitivity. This suggests that there are multiple interactions between endocrine disruption, oxidative stress, and inflammation that may account for the metabolic disruptions that are documented (Petrakis et al., 2017). The results obtained from the study are in line with what has been reported with regard to the EDCs and metabolic health in other species as well. Phthalates, BPA, and nonylphenol have been shown to produce the same metabolic disruptions in rodent models as well as other vertebrates, which include obesity, insulin resistance, and altered lipid profiles. Moreover, EDCs disrupted the metabolism and altered the hormonal signaling of zebrafish and other fish models, which builds on the already documented metabolic disruptions induced by EDCs. It is in line with what the study has observed and justifies the conclusion that EDCs cause and have already been proven to cause disruptions to metabolic health, regardless of the EDC concentration.

Research pertaining to human studies surrounding endocrine-disrupting chemicals (EDCs) is continuing to build out, and there is a clear link between the human cases of obesity and diabetes and the rising proliferation of BPA and phthalates (Heindel et al., 2017). For example, there is a clear link between BPA and elevated fat as well as insulin resistance in people of all ages. This study, which utilizes a zebrafish

model, elucidates the potential pathways by which these EDCs act on and how they may facilitate the progression of these disorders in humans (Ramya & Geetha, 2025). Furthermore, these findings are particularly relevant to the migrating and hibernating animals living in the contaminated environments. Endocrine-disrupting chemicals, including BPA and phthalates, are ubiquitous in the environment and can be absorbed by and stored in the tissues of animals, particularly those dwelling in contaminated wetlands, which can cause considerable harm to their health and well-being (Aguilera et al., 2020; Tang-Péronard et al., 2011). Endocrine-disrupting chemicals can be particularly harmful to those fish, like the zebrafish, living in heavily contaminated lakes, rivers, and estuaries, and they may be even more prone to population collapses and reduced reproductive rates due to the metabolic impairments elucidated in this study (Ribeiro et al., 2020). Deficits of this nature can disrupt fish populations and lead to the collapse of the entire food web due to the loss of primary aquatic and terrestrial predators, which rely on fish for food.

Moreover, the effects of EDCs on the metabolic health of specific species continue to cause anxiety over their conservation status. Prolonged exposure to these pollutants could lead to further fitness and health impairments of various wildlife subpopulations, especially those already experiencing ecological distress. For many ecosystems and the wildlife that depend on them, the lack of adequate regulation of EDCs has the potential to cause irreversible damage. Several constraints in this study must be acknowledged. To start with, the dose realism of the EDC concentrations used to conduct these experiments does not fully account for the chronic, sublethal exposure that wildlife are likely to encounter in the wild. While it is true that EDCs were included in sublethal concentrations that would be expected in the wild, it is necessary to factor in that the EDCs present in the environment likely represent a mixture of several contaminants at low concentrations that might have synergistic effects that have not been accounted for in this study.

Considering the chronic nature of the exposure, an 8-week exposure time is less than ideal when determining the potential outcomes of the study; chronic disease is likely to be the developing outcome after exposure to the study's primary focus; the metabolic disorders type 2 diabetes, cardiovascular disease, and non-alcoholic fatty liver disease require additional longitudinal studies to develop an understanding of the disorders after chronic exposure. Regarding the research focus on EDC, less-than-ideal models need to be honed, and zebrafish, unfortunately, do not meet the requirements for replication for most of the other vertebrates and mammals. Fish were maintained in controlled laboratory conditions, but the absence of the comforts of a native environment remains a vital oversight, as the study knows how much other variables like temperatures, food, and the presence of other pollutants can affect the outcomes. Also, the absence of an epigenetic framework remains a blind spot, as the potential of multi-generational EDC exposure in its effects is highly important when it comes to

understanding the long-term potential of EDC exposure.

Numerous avenues for future research remain. One such avenue pertains to chronic exposure to EDCs, and studying it for extended periods is warranted to accurately approximate long-term real-world exposures and ascertain the extent of possible chronic metabolic disorders. Future research should also analyze the effects of EDC blending, since environmental exposure to EDC is almost never mono-directional, and a mix of pollutants can yield additive and/or synergistic effects. Utilizing real-world unsampled environmental matrices for research would produce the most ecologically valid results. As metabolic disruptions might be transgenerationally inherited, research on the multi-generational impacts of EDC exposure on wildlife and animal models should be a priority, especially since that could ostensively alter the population dynamics of a distressed ecosystem over time. On top of that, investigating the use of epigenetics to EDC-induced metabolic disease is especially warranted. Loss of a like framework to interact with environmental stressors, psychiatric epigenetics over time, can yield detrimental effects on health, regulating gene expression, and leading to health. Field research observing the trans- and sub-lethal effects of EDCs on ecosystem health and conservation of wildlife on contaminated habitats could help establish a framework for the use of epigenetics to EDC-induced metabolic diseases.

## Conclusion

The study identifies the strong effects of endocrine-disrupting chemicals (EDCs) on the metabolic health (MH) of zebrafish and found that EDCs, including BPA, phthalates, and nonylphenol, alter energy homeostasis, promote adiposity, and disrupt glucose and lipid metabolism. Although a lot is known about the developmental and reproductive impacts of EDCs, metabolic imbalances caused by these chemicals have not been well studied, especially in animal models. The results of this research have not only been applicable to human health but also offer insight into the implications of the research to the overall animal population. Domestic animals, such as dogs and rodents, and wildlife exposed to EDCs are both subject to such metabolic responses as obesity, insulin resistance, and lipid patterns. Such disturbances in metabolism may result in impaired health and survival among the wildlife species, which may result in endangered species and their survival in the polluted environment. This study should, therefore, highlight the pressing necessity of enacting policies that would minimize the exposure of the environment to EDCs not only in the interests of human health, but in the protection of the animal population, as well. In addition, the study highlights that further animal research should be done to enhance the ecological and health effects of EDCs in general and especially with regard to the survival of wildlife and the well-being of domesticated animals.

## References

[1] Aguilera, Margarita, Yolanda Gálvez-Ontiveros, and Ana Rivas. "Endobolome, a new concept for determining the influence of microbiota disrupting

chemicals (MDC) in relation to specific endocrine pathogenesis." *Frontiers in microbiology* 11 (2020): 578007. https://doi.org/10.3389/fmicb.2020.578007

[2] Dalamaga, Maria, Dimitrios Kounatidis, Dimitrios Tsilingiris, Natalia G. Vallianou, Irene Karampela, Sotiria Psallida, and Athanasios G. Papavassiliou. "The role of endocrine disruptors bisphenols and phthalates in obesity: current evidence, perspectives and controversies." *International Journal of Molecular Sciences* 25, no. 1 (2024): 675. https://doi.org/10.3390/ijms25010675

[3] Darbre, Philippa D. "Endocrine disruptors and obesity." *Current obesity reports* 6, no. 1 (2017): 18-27.

[4] Gupta, Radhika, Prashant Kumar, Nighat Fahmi, Bhaskar Garg, Sriparna Dutta, Shilpee Sachar, Avtar S. Matharu, and Karani S. Vimaleswaran. "Endocrine disruption and obesity: A current review on environmental obesogens." *Current Research in Green and Sustainable Chemistry* 3 (2020): 100009. https://doi.org/10.1016/j.crgsc.2020.06.002

[5] Heindel, Jerrold J., Bruce Blumberg, Mathew Cave, Ronit Machtinger, Alberto Mantovani, Michelle A. Mendez, Angel Nadal et al. "Metabolism disrupting chemicals and metabolic disorders." *Reproductive toxicology* 68 (2017): 3-33. https://doi.org/10.1016/j.reprotox.2016.10.001

[6] La Merrill, Michele A., Laura N. Vandenberg, Martyn T. Smith, William Goodson, Patience Browne, Heather B. Patisaul, Kathryn Z. Guyton et al. "Consensus on the key characteristics of endocrine-disrupting chemicals as a basis for hazard identification." *Nature Reviews Endocrinology* 16, no. 1 (2020): 45-57.

[7] Maradonna, Francesca, and Oliana Carnevali. "Lipid metabolism alteration by endocrine disruptors in animal models: an overview." *Frontiers in endocrinology* 9 (2018): 654. https://doi.org/10.3389/fendo.2018.00654

[8] Metachew, Kesufekad. "Precision Nutrition: AI-Powered Personalization for Metabolic Health and Disease Prevention." *National Journal of Food Security and Nutritional Innovation* 2, no. 2 (2024): 47-53.

[9] Muscogiuri, Giovanna, Luigi Barrea, Daniela Laudisio, Silvia Savastano, and Annamaria Colao. "Obesogenic endocrine disruptors and obesity: myths and truths." *Archives of toxicology* 91, no. 11 (2017): 3469-3475. https://doi.org/10.1007/s00204-017-2071-1

[10] Patisaul, Heather B., Suzanne E. Fenton, and David Aylor. "Animal models of endocrine disruption." *Best Practice & Research Clinical Endocrinology & Metabolism* 32, no. 3 (2018): 283-297. https://doi.org/10.1016/j.beem.2018.03.011

[11] Petrakis, Demetrios, Loukia Vassilopoulou, Charalampos Mamoulakis,

Christos Psycharakis, Aliki Anifantaki, Stavros Sifakis, Anca Oana Docea, John Tsiaoussis, Antonios Makrigiannakis, and Aristides M. Tsatsakis. "Endocrine disruptors leading to obesity and related diseases." *International journal of environmental research and public health* 14, no. 10 (2017): 1282. https://doi.org/10.3390/ijerph14101282

[12] Pocar, Paola, Valeria Grieco, Lucia Aidos, and Vitaliano Borromeo. "Endocrine-disrupting chemicals and their effects in pet dogs and cats: an overview." *Animals* 13, no. 3 (2023): 378. https://doi.org/10.3390/ani13030378

[13] Radke, Elizabeth G., Audrey Galizia, Kristina A. Thayer, and Glinda S. Cooper. "Phthalate exposure and metabolic effects: a systematic review of the human epidemiological evidence." *Environment international* 132 (2019): 104768. https://doi.org/10.1016/j.envint.2019.04.040

[14] Ramya, V., and K. Geetha. "Agent-Based Modelling of Cross-Species Behavioral Dynamics: Insights for Managing Human–Wildlife and Ecosystem Conflicts." *National Journal of Animal Health and Sustainable Livestock* 3, no. 1 (2025): 18-25.

[15] Ribeiro, Carolina Martins, Bruna Teles Soares Beserra, Nadyellem Graciano Silva, Caroline Lourenço Lima, Priscilla Roberta Silva Rocha, Michella Soares Coelho, Francisco de Assis Rocha Neves, and Angélica Amorim Amato. "Exposure to endocrine-disrupting chemicals and anthropometric measures of obesity: a systematic review and meta-analysis." *BMJ open* 10, no. 6 (2020): e033509. https://doi.org/10.1136/bmjopen-2019-033509

[16] Swedenborg, Elin, Joëlle Rüegg, Sari Mäkelä, and Ingemar Pongratz. "Endocrine disruptive chemicals: mechanisms of action and involvement in metabolic disorders." *Journal of molecular endocrinology* 43, no. 1 (2009): 1-10. https://doi.org/10.1677/JME-08-0132

[17] Tang-Péronard, Jeanett Louise, Helle Raun Andersen, Tina Kold Jensen, and Berit Lilienthal Heitmann. "Endocrine-disrupting chemicals and obesity development in humans: a review." *Obesity Reviews* 12, no. 8 (2011): 622-636. https://doi.org/10.1111/j.1467-789X.2011.00871.x