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Regulating Endocrine Disrupting Compounds: A brief insight on Cross-Species Approach and One Health.

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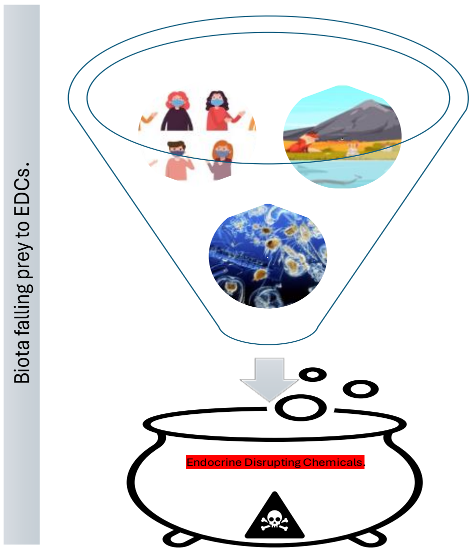
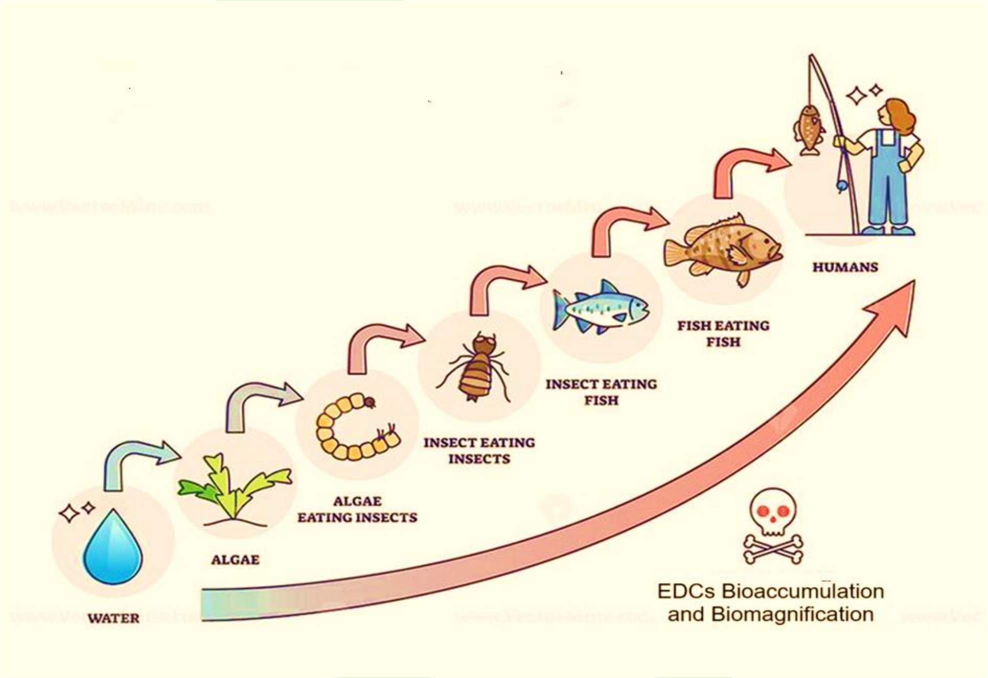
Introduction

Endocrine disrupting compounds (EDCs) are exogenous substances or mixtures that interfere with endocrine system functions, causing adverse health effects at multiple levels—from individual organisms to entire biota of an ecosystem. These compounds encompass a broad range of substances, including natural molecules (e.g., phytoestrogens), synthetic agrochemicals (e.g., DDT, atrazine), industrial compounds (e.g., bisphenol-A), pharmaceuticals (e.g., ethinylestradiol, ibuprofen), and heavy metals (e.g., lead, cadmium). Once introduced into the environment, these contaminants often end up in water bodies, impacting aquatic ecosystems and bioaccumulating through food webs, potentially reaching apex consumers, including humans.



EDCs pose significant risks to aquatic ecosystems as they enter through various sources, such as agricultural runoff, industrial discharges, and untreated sewage. Once in these water systems, EDCs interact with a range of aquatic species, influencing health and reproductive outcomes. Aquatic environments become hotspots for EDC accumulation, largely because contaminants persist in water, accumulate in sediments, and are readily absorbed by aquatic organisms.

As EDCs are absorbed by small organisms in the water, these chemicals move up through food chains—a process known as bioaccumulation and biomagnification. For example, phytoplankton or small invertebrates absorb EDCs from water, and these contaminants increase in concentration as they are consumed by fish, amphibians, and other predators (Chaturvedi et al., 2023). This has critical implications for both fish and their predators, as higher trophic levels (like humans, large fish, or birds) face more severe risks.



Cross-Species Extrapolation in Regulatory Toxicology: Toward Broader Assessments

This pervasive presence of EDCs in aquatic systems underscores the need for regulatory toxicology to protect both ecological and human health. However, assessing these risks is complicated by the fact that EDCs typically exist in complex mixtures—often referred to as "cocktails"—which pose unique challenges for toxicity assessment. These mixtures can produce aggregate and cumulative risks, with interactions among chemicals potentially resulting in synergistic or antagonistic effects beyond the sum of individual risks (Xiao et al.,

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2023). To effectively manage these risks, toxicology needs test methods and models that accurately reflect real-world environmental scenarios.

In regulatory toxicology, cross-species extrapolation is essential for creating relevant, efficient chemical safety assessments in different organisms (Margiotta-Casaluci et al., 2024). This approach allows researchers to extend findings from model species to other taxa, enhancing our ability to predict chemical impacts across diverse species and reducing the need for extensive animal testing. Here are key methods and approaches that enhance cross-species data integration:

- **Adverse Outcome Pathways (AOPs)**: AOPs offer a framework for linking molecular events to adverse outcomes across species, enabling extrapolation from model organisms to others (Tollefsen et al., 2022 and Wiklund et al., 2024).
- **Omics Technologies**: Genomics, proteomics, and metabolomics reveal molecular responses that may be conserved across species, aiding in the identification of shared mechanisms of toxicity (Maitre, et al., 2023).
- **In Vitro Assays**: Laboratory cell cultures and organ-on-a-chip models can mimic biological pathways relevant across species without involving live animals (Marlatt et al., 2022).
- **Toxicokinetic and Toxicodynamic Modelling**: These models map how chemicals are processed and affect cells, adapting to different species' biology to predict varied responses (Xie et al., 2024).
- **Machine Learning and AI**: These technologies process complex datasets to identify patterns and predict cross-species toxicity, increasing efficiency and accuracy in risk assessments (Fen et al., 2021).
- **Systematic Literature Review and Text Mining**: These techniques synthesize toxicological data from existing research, identifying knowledge gaps and informing extrapolation methods.

By employing these approaches, researchers and regulatory agencies can produce more accurate, ecologically relevant toxicity assessments, ultimately fostering a more holistic understanding of EDC impacts.

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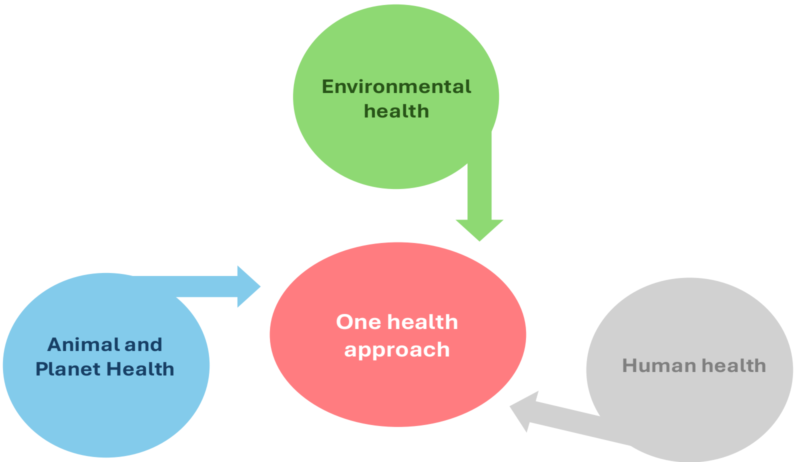
One Health: A Framework for Cross-Species and Environmental Integration

The One Health approach broadens our perspective, recognizing the interconnectedness of human health, animal health, and ecosystem health. As pollutants accumulate in aquatic ecosystems, they disrupt the balance of food webs, affecting fish species and, consequently, human populations dependent on these ecosystems for food and economic activities (Aguirre et al., 2016, Thuróczy et al., 2023). Through a One Health lens, we can better understand how pollutants impact fish and the humans who consume them, emphasizing the need for coordinated, cross-disciplinary efforts to address chemical risks comprehensively.



Incorporating One Health principles into toxicology assessments encourages pollution prevention at its source, rather than reactive responses to its effects. This proactive approach involves interdisciplinary collaboration among scientists, regulatory agencies, and public health officials, supporting the development of strategies that protect animal populations, human communities, and environmental integrity.

Conclusion

Ultimately, embracing a cross-species approach within a One Health framework strengthens our ability to regulate EDCs effectively. By aligning regulatory toxicology with cutting-edge science and interdisciplinary research, we not only enhance the consistency and reliability of safety assessments but also ensure a future where both ecosystems and human health are safeguarded.

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