TecnoLógicas

Editorial

Eco-Pharmacovigilance at the Water–Health Interface: Mechanistic Ecotoxicology for One Health in the Age of Mixtures

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Medicines are designed to be biologically active in low doses, and their biological “afterlife” often continues beyond the patient and beyond the clinic. Pharmacovigilance was created to detect, assess, understand, and prevent adverse effects and other medicine-related problems in patients [1]. Ecopharmacovigilance extends that vigilance to environmental compartments, where pharmaceuticals and their residues enter ecosystems through excretion, disposal, and effluent pathways [2], [3]. Looking through the lens of One Health, this is not a peripheral issue: the health of people, animals, and ecosystems is coupled through shared water, food, and environments [4].

The pressing challenge is not only the “presence,” but prioritization under mixture complexity. Integrative ecotoxicology emphasizes that real waters contain co-occurring stressors (pharmaceuticals, metals, plastics, and transformation products) and that multilevel responses—from transcriptional shifts to behavior—can be missed by single-compound, single-endpoint assays [5]. Eco-pharmacovigilance therefore needs mechanistic evidence that is exposure-realistic and decision-ready: evidence that supports risk triage and prevention.

Recent work in aquatic vertebrates makes this point concrete. Caffeine is frequently used as a marker of anthropogenic input but is neuroactive. In common juvenile carp exposed to caffeine (500–2500 ng/L), an integrative assessment combined biomarker of oxidative damage, antioxidant defenses, acetylcholinesterase activity, histology, behavior (Novel Tank and Dark–Light tests), and targeted gene expression related to neurophysiology and calcium signaling [6]. The value of this design is internal coherence: chemical exposure, plausible molecular pathways, and organism-level phenotypes are evaluated in the same study.

Antidepressants reinforce a second lesson: time matters. In adult zebrafish, short-term exposure (96 h) to venlafaxine at environmental concentrations of ng/L was evaluated through behavioral tests alongside acetylcholinesterase, oxidative stress, gene expression, and brain histopathology, showing adverse outcomes in multiple layers over a small-time window [7]. The prolonged exposure work then framed venlafaxine neurotoxicity as a multilevel process (behavioral impairment coupled to biomolecular dysregulation and brain tissue damage) underscoring why the hazard cannot be reliably inferred from a single endpoint or a single snapshot [8].

High-value medicines with specialized clinical roles also have a scope because they can enter wastewater through hospital use. Cisplatin was evaluated at realistic µg/L levels, with tissue-specific oxidative stress responses and gene expression changes reported in all organs, including liver, brain, gut, and gills [9]. Neurobehavioral endpoints provide an additional lens: locomotor activity assays were used to investigate cisplatin-associated neurobehavioral toxicity and to explore the mechanisms behind behavioral disturbance [10].

Similarly, imatinib (an essential tyrosine kinase inhibitor) was shown to cause anxiety-like behavior in adult zebrafish alongside oxidative stress, disruption of acetylcholinesterase, and transcriptional signals consistent with impaired regulation of redox and energy [11].

Mixtures are where ecopharmacovigilance becomes truly operational. Fluoxetine and microplastics coexist in aquatic matrices and their combination can change the dynamics of exposure. Microplastics associated with zebrafish chorion were observed, and exposures to fluoxetine, microplastics, and their mixtures altered embryonic development and increased malformations, including endpoints related to skeletal and pigmentation [12]. The implication is not only additive risk, but risk modulation: particulate co-stressors can change where chemicals go and what biological pathways are engaged.

Transformation products add another layer of uncertainty. Advanced oxidation processes are increasingly proposed to reduce pharmaceutical residues, yet degradation can yield by-products with different toxicological profiles. Photo-Fenton treatment of COVID-19 era drug mixtures (dexamethasone, metformin, paracetamol) was explicitly investigated because degradation by-products may display higher toxicity than parent compounds, so treatment efficacy must be paired with organism-level safety evaluation [13].

Eco-pharmacovigilance must also be geographically and socially grounded. In the Tepetitlán reservoir, contamination from multiple sources motivated the characterization of metals and pharmaceuticals and direct testing of reservoir water in the early stages of life of zebrafish, documenting altered development and malformations 12 to 96 h after fertilization [14]. In the context of Madín Dam, a pilot human health risk assessment linked long-term exposure to drinking water metals with oxidative damage, genotoxic indicators, and epigenetic signals, and highlighted increased risk among populations relying on the reservoir for water and fish consumption [15]. These studies illustrate a One Health logic in practice: contaminants in the environment are connected to biological effects in aquatic models and measurable risks to human communities [4].

Finally, eco-pharmacovigilance benefits from widening the lens to other persistent emerging contaminants that behave “pharmaceutical-like” in terms of bioactivity. Sucralose was investigated as a persistent artificial sweetener that can bioaccumulate; exposures were associated with oxidative protein damage and deterioration of the functional properties of fish muscle, connecting contamination to food-quality endpoints relevant to fisheries and food security [16]. At the terrestrial interface, work on lead stress in maize and mitigation with TiO_2 and MgO nanoparticles highlights how heavy-metal exposure and human health risk indices can be integrated with mechanistic plant responses, strengthening the continuum between ecosystem and human health risk assessment [17].

A prevention-oriented eco-pharmacovigilance agenda can be built around three linked commitments. First, mechanistic harmonization: effect-based monitoring should prioritize interpretable endpoint batteries (behavior, oxidative damage, histopathology, targeted transcription) that can be cross-validated and assigned to plausible adverse outcome pathways [5], [6], [10]-[15]. Second, exposure realism: mixture designs should be routine rather than exceptional, explicitly considering plastics, metals, and transformation products, where relevant [7], [12]. Third, upstream prevention: because disposal and everyday practices shape emissions, education and risk communication become part of the intervention toolkit. In this sense, the development of an environmental literacy tool that explicitly includes the disposal of medications along with other practices is more than pedagogy; it is a capacity-building of eco-pharmacovigilance [18].

Eco-pharmacovigilance is therefore not a niche extension of pharmacovigilance. It is a One Health practice: detect, explain, and prevent environmental harms of medicines and related contaminants, while protecting the integrity of water systems that sustain both aquatic biodiversity and human communities. Implementing this agenda will require partnerships between researchers, water utilities, health systems, and regulators. If we treat aquatic ecosystems as early-warning organs, eco-pharmacovigilance can move environmental management from reactive clean-up to preventive stewardship across sectors and disciplines.

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