Pharmaceutical waste and the risks for human health

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Introduction

Global pharmaceutical production exceeds **4 trillion doses annually**.

Incomplete metabolism and **inefficient wastewater treatment** → environmental release.

Presence of **pharmaceuticals in soil, surface water, and drinking water** documented globally.

Chronic low-dose exposure represents an **emerging public health challenge.**

Pharmaceuticals are biologically active by design. Their persistence in the environment introduces continuous low-level exposure that current risk assessments often underestimate due to complex mixtures and chronic bioactivity.

Sources of Pharmaceutical Waste

Manufacturing discharges – effluents from production facilities.

Hospital and clinical waste – cytostatics, antibiotics, contrast agents.

Household disposal – expired medications, improper flushing.

Agricultural use – veterinary drugs, aquaculture antibiotics, hormones.

Metabolic excretion – parent compounds and active metabolites in human/animal waste.

Each source contributes distinct chemical classes. For example, antibiotic residues from livestock operations are among the largest contributors to antimicrobial resistance propagation in environmental reservoirs.

Classification of Pharmaceutical Pollutants

Category	Representative Compounds	Environmental Relevance
Analgesics / NSAIDs	Ibuprofen, Diclofenac	Persistent, hepatotoxic to aquatic life
Antibiotics	Fluoroquinolones, β-lactams	AMR selection pressure
Antidepressants	SSRIs (Fluoxetine, Sertraline)	Neurobehavioral effects in fauna
Hormones	Ethinylestradiol, Progesterone	Endocrine disruption
Cytostatics	Cyclophosphamide	Genotoxic, carcinogenic
Antivirals	Acyclovir, Oseltamivir	Metabolic stability

Environmental Pathways and Fate

Aquatic route: wastewater → surface water → drinking water sources.

Soil route: sludge application → leaching → groundwater contamination.

Atmospheric route: volatilization and particulate sorption (rare).

Transformation: photolysis, hydrolysis, microbial degradation, sorption.

Persistent residues: carbamazepine, diclofenac, sulfamethoxazole.

Pharmaceuticals behave as pseudo-persistent contaminants. Even if individually degradable, continuous inputs maintain steady-state concentrations, creating chronic exposure scenarios for humans and ecosystems.

Analytical Detection and Monitoring

Techniques: LC–MS/MS, GC–MS, LC–HRMS for quantification at ng/L–µg/L levels.

Non-target screening: detection of transformation products.

Passive sampling (POCIS, SPMDs) for time-integrated exposure assessment.

Adductomics and biomarkers for biological exposure measurement.

High-resolution mass spectrometry and adductomics now reveal thousands of pharmaceutical residues and their metabolites in environmental and biological matrices, including human urine, plasma, and umbilical cord blood.

Persistence and Bioaccumulation

Physicochemical properties:

- High polarity → mobility in water.
- Lipophilicity (logKow > 3) → bioaccumulation in fatty tissues.

Bioconcentration factors (BCF): up to 5000 for synthetic estrogens.

Trophic transfer: biomagnification across aquatic food webs.

Mixture effects: non-linear dose–response at low concentrations.

The persistence and bioaccumulation of pharmaceuticals differ from industrial pollutants due to continuous introduction and complex degradation pathways, leading to long-term low-dose bioactivity in exposed populations.

Human Exposure Pathways

Drinking water: trace pharmaceuticals post-treatment.

Food chain: fish, dairy, crops irrigated with contaminated water.

Occupational: healthcare workers, pharmaceutical manufacturing.

Inhalation / dermal contact: limited but significant in hospital environments.

Vulnerable populations: infants, pregnant women, immunocompromised individuals.

Though concentrations are low, chronic exposure through multiple pathways leads to cumulative risk. Vulnerable populations exhibit higher sensitivity due to developing organs or compromised detoxification systems.

Pharmacokinetics in Environmental Toxicology

Environmental analog of ADME:

- **Absorption** (through ingestion, dermal, inhalation).
- **Distribution** (tissue-specific bioaccumulation).
- **Metabolism** (bioactivation or detoxification).
- **Excretion** (prolonged biological half-lives).

Example: Diclofenac bioactivation → reactive quinone imine → nephrotoxicity.

Pharmaceuticals in the environment retain their pharmacokinetic behavior in non-target organisms, often bioactivating to more toxic intermediates due to differing enzymatic pathways across species.

Human Health Effects: Overview

Acute toxicity: minimal under environmental concentrations.

Chronic effects:

Endocrine disruption.

Carcinogenesis (cytostatics, genotoxins).

Developmental and reproductive toxicity.

Neurobehavioral changes (psychoactives).

Indirect effects: antimicrobial resistance, microbiome dysbiosis.

The primary concern is not acute poisoning but chronic, subclinical physiological interference. Sub-therapeutic yet biologically active concentrations can subtly disrupt hormonal, immune, or neural systems.

Endocrine Disruption and Reproductive Effects

Synthetic estrogens (EE2): mimic endogenous hormones → receptor activation.

In humans: fertility reduction, altered puberty timing.

Animal models: intersex fish, feminization of aquatic fauna.

Mechanistic pathways: ERα/ERβ activation, SHBG modulation, gene transcription changes.

Endocrine disruptors act at picomolar concentrations, highlighting the sensitivity of hormonal networks. Epidemiological studies link estrogenic pollutants with altered sperm quality and reproductive anomalies.

Antimicrobial Resistance (AMR)

Antibiotic residues act as continuous selection agents in environment.

Promote proliferation of **resistance genes (ARGs)** in bacterial communities.

Horizontal gene transfer via **plasmids, transposons** in wastewater microbiota.

Human health outcome: resistant pathogens, reduced antibiotic efficacy.

Environmental antibiotic pollution creates a selective pressure that transforms aquatic and soil microbiomes into gene reservoirs of resistance, which ultimately cycle back into clinical pathogens through the food chain and water reuse.

Genotoxic and Carcinogenic Risks

Cytostatics and antiviral residues: alkylating agents → DNA crosslinking.

Mutagenic byproducts: N-nitrosamines, oxidative metabolites.

Genotoxic biomarkers: micronuclei, 8-OHdG, comet assay in exposed workers.

Long-term risk: increased cancer incidence in pharmaceutical effluent regions.

Cytostatics are designed to kill proliferating cells, yet their persistence in water systems poses genotoxic risks to both aquatic organisms and humans chronically exposed via low-level ingestion.

Microbiome and Immunotoxic Effects

Antibiotics, NSAIDs, and psychoactives alter gut microbial ecology.

Dysbiosis → impaired metabolism of xenobiotics, inflammation.

Disruption of microbial-derived metabolites (short-chain fatty acids).

Immune modulation: altered cytokine balance, autoimmunity risk.

The human microbiome is a key mediator of pharmaceutical toxicity. Chronic environmental exposure to antimicrobials and NSAIDs can perturb microbial homeostasis, compromising immune tolerance and metabolic health.

Risk Assessment and Modeling

Hazard Identification → Dose–Response → Exposure Assessment → Risk Characterization.

Predicted Environmental Concentration (PEC) vs **Predicted No-Effect Concentration (PNEC).**

Mixture toxicity models: concentration addition, independent action.

Cumulative risk index for multi-compound scenarios.

Traditional single-compound risk assessments fail to capture mixture effects. New computational models employ probabilistic and systems-level approaches to estimate cumulative risk under chronic exposure.

Wastewater Treatment and Limitations

- **Conventional processes (activated sludge):** 20–60% removal.
- **Advanced oxidation (ozonation, UV/H_2O_2):** improves degradation but forms toxic byproducts.
- **Membrane bioreactors, constructed wetlands:** emerging sustainable alternatives.
- **Pharmaceutical industry effluent:** often poorly regulated.
- No current treatment technology completely removes pharmaceuticals. Advanced processes must balance removal efficiency against formation of transformation products with unknown toxicities.

Environmental and Policy Framework

EU Water Framework Directive (2000/60/EC) – Watch List compounds.

US EPA Contaminant Candidate List (CCL 5).

WHO Guidelines for pharmaceutical residues in drinking water.

Green Pharmacy and **Extended Producer Responsibility (EPR)** initiatives.

Global disparity: minimal regulation in low-income countries.

While high-income countries have initiated regulatory responses, global harmonization remains limited. Pharmaceutical stewardship policies must extend responsibility beyond prescription to waste management.

Emerging Mitigation Strategies

Eco-pharmacovigilance: life-cycle monitoring of pharmaceuticals.

Green chemistry: biodegradable drug design.

Pharmaceutical take-back programs: reduce household disposal.

Microbial bioremediation and enzymatic degradation using engineered strains.

Digital surveillance: AI-driven wastewater monitoring networks.

The paradigm is shifting toward preventive design — drugs optimized for efficacy **and** environmental degradability. Combining biotechnology and informatics enables sustainable pharmaceutical stewardship.

Future Research Directions

- **Omics-based exposomics:** linking exposure to molecular biomarkers.
- **Transgenerational epigenetic studies** of low-dose exposure.
- **Nanopharmaceutical waste** as a new pollutant class.
- **Integrative One Health approach:** ecosystem–animal–human interface.
- **Policy-science integration** through global pharmaceutical footprint mapping.

Interdisciplinary research is critical — connecting molecular mechanisms with population health outcomes. The One Health model recognizes that human health cannot be disentangled from environmental integrity.

Conclusion

Pharmaceutical waste is a **persistent, bioactive environmental pollutant**.

Chronic exposure exerts **multifactorial risks**: endocrine, genotoxic, microbial, immunological.

Current wastewater treatment and policy frameworks are insufficient.

Sustainable solutions require **eco-pharmacology, global regulation, and systems toxicology integration.**

Pharmaceuticals, though life-saving, have unintended ecological and health consequences. Addressing this requires collaboration across pharmacology, environmental science, policy, and public health to ensure that human medicine does not become environmental poison.