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Ecopharmacovigilance: Concepts, Developments, and Implementation in Reducing the Environmental Impact of Phamaceuticals

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A B S T R A C T

The increasing use of pharmaceuticals has led to greater release of pharmaceutical residues into the environment, posing risks to aquatic organisms, promoting bioaccumulation, and contributing to antimicrobial resistance. This study reviewed the development, implementation, and challenges of ecopharmacovigilance (EPV) through a narrative review of 30 articles published between January 2021 and June 2026. The findings indicate that pharmaceutical residues originate from human and veterinary excretion, healthcare facility effluents, pharmaceutical manufacturing, and improper disposal of unused medicines. These residues contribute to environmental contamination, ecosystem disruption, and the emergence of antimicrobial resistance. The implementation of EPV is supported by Environmental Risk Assessment (ERA), environmental monitoring technologies, the One Health approach, and green pharmacy strategies. However, inadequate monitoring systems, fragmented regulatory frameworks remain.

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INTRODUCTION

The increasing consumption of pharmaceuticals over the past few decades has substantially improved the prevention and treatment of numerous diseases. However, it has also led to a growing release of pharmaceutical residues into the environment through human and animal excretion, hospital wastewater, pharmaceutical manufacturing effluents, and the improper disposal of unused or expired medicines (García et al., 2024; Khamkar et al., 2021a). Pharmaceutical residues have been detected in surface water, groundwater, sediments, soils, and even drinking water in many countries at varying concentrations (Inaudi et al., 2025; Khamkar et al., 2021a). Their widespread occurrence has become a global environmental concern because many pharmaceutical compounds are persistent, are not completely removed by conventional wastewater treatment processes, and have the potential to accumulate in ecosystems (Inaudi et al., 2025; Khamkar et al., 2021).

Long-term exposure to pharmaceutical residues may cause a wide range of ecological consequences, including physiological disturbances in aquatic organisms, disruption of reproductive and endocrine systems, bioaccumulation, and the emergence of antimicrobial resistance resulting from exposure to subtherapeutic concentrations of antibiotics (Dikshit, 2024; Khamkar et al., 2021a). These findings indicate that pharmaceutical pollution is not merely an environmental issue but also poses significant risks to human and animal health, highlighting the need for a multidisciplinary approach based on the One Health concept (Dikshit, 2024; García et al., 2024).

In response to these concerns, the concept of ecopharmacovigilance (EPV) has emerged as the science and practice of detecting, assessing, understanding, and preventing the adverse environmental effects of pharmaceuticals after they have been marketed (García et al., 2024; Khamkar et al., 2021b). Unlike conventional pharmacovigilance, which primarily focuses on drug safety in patients, EPV broadens its scope to include the impacts of pharmaceuticals on humans, animals, plants, and ecosystems as a whole (García et al., 2024; Inaudi et al., 2025; Khamkar et al., 2021a). The implementation of EPV includes environmental monitoring of pharmaceutical residues, Environmental Risk Assessment (ERA), the development of environmentally sustainable pharmaceuticals through green pharmacy, sustainable pharmaceutical waste management, and collaborative efforts involving regulatory authorities, the pharmaceutical industry, healthcare professionals, academic institutions, and the public (García et al., 2024; Khamkar et al., 2021a).

Despite the growing recognition of ecopharmacovigilance in recent years, its implementation continues to face several challenges, including the lack of harmonized international regulations, limitations in environmental monitoring systems, and insufficient integration between pharmacovigilance and environmental surveillance frameworks (García et al., 2024; Khamkar et al., 2021a). Therefore, this narrative review aims to examine the fundamental concepts, recent developments, implementation strategies, and challenges of ecopharmacovigilance as an approach to reducing the environmental impacts of pharmaceuticals while supporting sustainable healthcare systems under the One

Health framework (Dikshit, 2024; García et al., 2024; Inaudi et al., 2025; Khamkar et al., 2021a).

THEORETICAL REVIEW

The increasing consumption of pharmaceuticals over the past few decades has substantially improved the prevention and treatment of numerous diseases. However, it has also led to a growing release of pharmaceutical residues into the environment through human and animal excretion, hospital wastewater, pharmaceutical manufacturing effluents, and the improper disposal of unused or expired medicines (García et al., 2024; Khamkar et al., 2021b). Pharmaceutical residues have been detected in surface water, groundwater, sediments, soils, and even drinking water in many countries at varying concentrations (Inaudi et al., 2025; Khamkar et al., 2021b). Their widespread occurrence has become a global environmental concern because many pharmaceutical compounds are persistent, are not completely removed by conventional wastewater treatment processes, and have the potential to accumulate in ecosystems (Inaudi et al., 2025; Khamkar et al., 2021b).

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METHODOLOGY

This article was conducted as a narrative review to examine the development, implementation, and challenges of ecopharmacovigilance in mitigating the environmental impacts of pharmaceutical residues. The literature review process was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement to support the identification, screening, and selection of relevant studies (Page, Mckenzie, et al., 2021; Page, Moher, et al., 2021).

A comprehensive literature search was performed using PubMed, Scopus, Web of Science, ScienceDirect, SpringerLink, and Google Scholar for articles published between January 2021 and June 2026. The search strategy employed combinations of the following keywords: *ecopharmacovigilance*, *environmental pharmacovigilance*, *pharmaceutical residues*, *environmental risk assessment*, *green pharmacy*, *One Health*, and *antimicrobial resistance*, using the Boolean operators AND and OR (Greenhalgh et al., 2018).

The inclusion criteria comprised original research articles and review articles available in full text, published in either English or Indonesian, and relevant to the objectives of this review. Editorials, letters to the editor, conference abstracts, duplicate publications, and studies that were not aligned with the scope of the review were excluded from the selection process (Ferrari, 2015).

Data extracted from the selected studies included the authors, year of publication, study design, research objectives, and key findings. The extracted data were analyzed descriptively and synthesized narratively. The characteristics of the 30 eligible studies are presented in tabular form, while the findings are interpreted and discussed in the Discussion section(Snyder, 2019).

RESULTS

A total of **30 studies** published between **2021 and 2026** met the inclusion criteria and were included in this narrative review (Table 1). The selected publications comprised narrative reviews, systematic reviews, critical reviews, observational studies, meta-analyses, computational studies, and editorial reviews conducted across various countries, including India, Italy, the United Kingdom, Poland, the Netherlands, South Africa, China, Malaysia, Colombia, Ecuador, Mexico, Norway, and Georgia. Overall, the literature demonstrates the growing global interest in **ecopharmacovigilance (EPV)** as an emerging multidisciplinary field that integrates pharmaceutical sciences, environmental sciences, public health, and regulatory policy.

Table 1. Characteristics of the 30 studies included in this narrative review, including the authors, publication year, country, study design, research focus, principal findings, and contributions to the development and implementation of ecopharmacovigilance.

No.	Author (Year)	Country	Study Design	Research Focus	Main Findings	Contribution to Ecopharmacovigilance
1	(Khamkar et al., 2021b)	India	Narrative Review	Fundamental concepts of ecopharmacovigilance	Introduced the concept of EPV, its scope, relationship with pharmacovigilance, and pharmaceutical waste management.	Established the conceptual foundation for the development of EPV in pharmaceutical sciences.
2	(Dikshit, 2024)	India	Review	EPV and One Health	Described the relationship between EPV and human, animal, and environmental health, emphasizing the importance of the One Health approach.	Strengthened the integration of EPV into sustainable healthcare systems.
3	(Spilsbury et al., 2024)	United Kingdom	Observational Study (VigiBase Database Analysis)	Environmental impact reporting in VigiBase	Identified 713 reports related to environmental impacts, with an increasing reporting trend since 2001, although the number remains relatively low.	Demonstrated the need for environmental reporting within global pharmacovigilance systems.
4	(Inaudi et al., 2025)	Italy	Narrative Review	Analytical techniques for pharmaceutical residues	LC–MS/MS and UHPLC were identified as the primary analytical methods for detecting pharmaceutical residues in various environmental matrices.	Supported the development of laboratory-based environmental monitoring methods for EPV.
5	(Nana Shashiashvili, 2025).	Georgia	Review	Pharmacists' role in environmental risk management	Pharmacists play an important role in promoting rational medicine use,	Expanded the role of pharmacy professionals in EPV implementation.

					pharmaceutical waste management, and the implementation of green pharmacy.	
6	(Vitanza et al., 2025)	Italy	Narrative Review	Sustainability of healthcare systems	Reviewed the environmental impacts throughout the pharmaceutical life cycle and mitigation strategies based on the One Health concept.	Demonstrated the implementation of EPV within sustainable healthcare policies.
7	(Cristini et al., 2025)	Italy	Narrative Review	Environmental impacts of pharmaceuticals and regulation	Highlighted the importance of Environmental Risk Assessment (ERA), prescribing appropriateness, and cross-sector collaboration.	Provided recommendations for implementing EPV in clinical practice and public policy.
8	Quijano-Prieto & Orozco-Díaz (2025)	Colombia	Review	Environmental health perspective	Discussed the relationship between pharmaceutical pollution, public health, and environmental health.	Strengthened the environmental health perspective within EPV.
9	(Obando et al., 2026)	Ecuador	Systematic Review	Dermatological products and EPV	Poor management of dermatological product waste contributes to water pollution, endocrine disruption, and antimicrobial resistance.	Demonstrated the application of EPV in dermatology.
10	(Madikizela & Netshithothole, 2026)	South Africa	Review	Pharmaceutical residues in African water resources	Identified high occurrences of antibiotics, analgesics, and hormones in water resources and their impacts on aquatic organisms.	Provided evidence supporting environmental monitoring as a core component of EPV.
11	(Gómez-Oliván, 2026) (2026)	Mexico	Editorial Review	Ecopharmacovigilance and One Health	Explained that pharmaceutical residues in water	Expanded the EPV concept through the

					represent a key link between human, animal, and environmental health, highlighting the need for mechanistic ecotoxicological approaches.	integration of One Health and environmental toxicology.
12	(Arumugam et al., 2026)	Malaysia	Narrative Review	Pharmaceuticals in water	Described pharmaceuticals as emerging contaminants widely detected in surface water, groundwater, and drinking water, and discussed treatment technologies and environmental governance.	Provided scientific evidence supporting policies for pharmaceutical residue control within EPV implementation.
13	(Maculewicz et al., 2022).	Poland	Review	Transformation products of pharmaceuticals in the environment	Pharmaceutical degradation products may be equally or more toxic than parent compounds and may bioaccumulate.	Demonstrated that EPV should encompass metabolites and transformation products in addition to parent compounds.
14	(Roveri et al., 2026)	Latin America	Computational Study	Ecological Risk Assessment	AI-QSAR models improved the prediction accuracy of ecological risks associated with pharmaceuticals, particularly diclofenac, macrolides, and psychotropic drugs.	Highlighted the potential application of artificial intelligence in EPV and ERA.
15	(Madikizela & Netshithothole, 2026)	South Africa	Critical Review	NSAIDs and analgesics in marine environments	NSAIDs and their metabolites are widely detected in seawater, sediments, and coastal biota, posing toxicological risks	Expanded the scope of EPV to coastal and marine ecosystems.

					to marine organisms.	
16	(Khamkar et al., 2021a)	India	Narrative Review	Ecopharmacovigilance concepts	Described the definition, scope, implementation strategies, and relationship between EPV and pharmacovigilance.	Served as a primary conceptual reference for EPV.
17	(Oldenkamp et al., 2024)	Netherlands	Review	Regulatory Environmental Risk Assessment	Identified the need to update ERA frameworks and integrate environmental monitoring data into regulatory decision-making.	Provided a foundation for EPV policy development.
18	(Maculewicz et al., 2022)	Poland	Review	Bioaccumulation of pharmaceutical transformation products	Transformation products may exhibit greater toxicity than parent compounds.	Expanded the scope of EPV to include pharmaceutical metabolites.
19	(Cannata et al., 2024)	Netherlands–Sweden	Review	Prioritization of active pharmaceutical ingredients (APIs) for ERA	Prioritized 68 APIs for ecotoxicity testing and 66 APIs for environmental risk assessment.	Supported prioritization strategies for environmental monitoring within EPV.
20	(Helwig et al., 2024)	United Kingdom	Review	Strategies to reduce pharmaceutical residues	Emphasized eco-directed prescribing, precision medicine, medicine take-back programs, and advanced wastewater treatment technologies.	Proposed practical EPV implementation strategies in healthcare settings.
21	Welch et al. (2023)	Norway	Review	Environmental risk prediction of pharmaceuticals	Developed environmental risk prediction approaches based on Predicted Environmental Concentration (PEC).	Supported ERA for newly developed pharmaceuticals.
22	(Gurudiwan & Mire, 2024)	India	Review	Pharmaceuticals in aquatic environments	Reviewed environmental pathways, toxicity, and risk assessment of	Strengthened evidence of global pharmaceutical pollution.

					pharmaceuticals in aquatic ecosystems.	
23	(Punginelli et al., 2024)	Italy	Review	Effects of pharmaceuticals on marine fish	Pharmaceutical residues cause physiological, behavioral, and reproductive alterations in marine fish.	Added important biological evidence supporting EPV.
24	(Caban & Stepnowski, 2021)	Poland	Review	Mitigation of pharmaceutical pollution	Proposed green chemistry, pharmaceutical waste management, prescribing optimization, and wastewater treatment technologies.	Established the foundation of Green Pharmacy within EPV.
25	(Uluseker et al., 2025)	United Kingdom	Critical Review	Modeling the environmental fate of pharmaceuticals	Discussed predictive models for pharmaceutical distribution, degradation, and exposure across environmental compartments.	Supported the development of predictive models for EPV.
26	(Baaloudj et al., 2025)	Italy–South Africa	Review	Heterocyclic pharmaceuticals as emerging contaminants	Described the sources, persistence, toxicity, and remediation strategies of heterocyclic pharmaceuticals.	Expanded evidence regarding the ecological impacts of pharmaceuticals.
27	(Belle et al., 2025).	South Africa	Review	Pharmaceuticals of Emerging Concern	Identified azithromycin, dexamethasone, and prednisone as emerging contaminants posing risks to aquatic ecosystems.	Supported the need to expand environmental monitoring of pharmaceutical residues.
28	(Zampelli & Verna, 2025a)	Italy	Review	Environmental pollution caused by pharmaceuticals	Reviewed sources of pharmaceutical pollution, impacts on human health and the environment, and	Provided a comprehensive overview of pharmaceutical pollution.

					mitigation strategies.	
29	(Zhang et al., 2016)	China	Meta-analysis	Psychopharmaceuticals in surface waters	Demonstrated the global distribution of psychopharmaceuticals and their ecological risks to aquatic organisms.	Expanded the scope of EPV to psychiatric pharmaceuticals.
30	(Cristini et al., 2025)	Italy	Narrative Review	Prescribing appropriateness and environmental impacts	Integrated eco-directed prescribing, water quality monitoring, and regulatory frameworks within the One Health approach.	Connected clinical prescribing practices with the implementation of EPV.

DISCUSSION

Concept and Development of Ecopharmacovigilance

Ecopharmacovigilance (EPV) has evolved from the concept of pharmacovigilance to focus on the identification, assessment, monitoring, and prevention of the environmental impacts of pharmaceutical residues. Unlike conventional pharmacovigilance, which primarily emphasizes patient safety, EPV extends its scope to encompass the effects of pharmaceuticals on ecosystems throughout the pharmaceutical life cycle. The development of this concept has been driven by increasing evidence demonstrating the occurrence of pharmaceutical residues in various environmental compartments, including surface water, groundwater, sediments, and soils, where they may pose ecological risks and potential threats to public health (Khamkar et al., 2021b).

Several studies indicate that the successful implementation of EPV depends not only on monitoring pharmaceutical residues but also on integrating rational medicine use, pharmaceutical waste management, Environmental Risk Assessment (ERA), and the principles of green pharmacy. Furthermore, the One Health approach has reinforced the importance of EPV by recognizing the interdependence of human, animal, and environmental health. Consequently, EPV has emerged as an essential component of sustainable healthcare systems through multidisciplinary collaboration among healthcare professionals, regulatory agencies, the pharmaceutical industry, and researchers (Dikshit, 2024; Gómez-Oliván, 2026; Vitanza et al., 2025).

Sources of Pharmaceutical Residues and Their Environmental Impacts

The synthesized evidence indicates that pharmaceutical residues originate from multiple sources, including human and animal excretion, improper disposal of unused or expired medicines, hospital wastewater, pharmaceutical manufacturing, livestock production, and wastewater treatment plants that are unable to remove pharmaceutical compounds completely. Several classes of pharmaceuticals, including antibiotics, analgesics, hormones, non-steroidal anti-

inflammatory drugs (NSAIDs), and psychotropic medications, are among the most frequently detected contaminants in aquatic environments because of their widespread use and environmental persistence (Arumugam et al., 2026; Gurudiwan & Mire, 2024; Madikizela & Netshithothole, 2026).

Long-term environmental exposure to pharmaceutical residues may alter the physiology, behavior, reproduction, and growth of aquatic organisms while increasing the risk of bioaccumulation throughout the food chain. In addition to parent compounds, several studies have demonstrated that pharmaceutical metabolites and transformation products may exhibit toxicity comparable to or greater than that of the original compounds. These findings suggest that environmental monitoring should extend beyond parent pharmaceuticals to include metabolites and transformation products that may pose even greater ecological risks (Maculewicz et al., 2022; Madikizela & Netshithothole, 2026; Punginelli et al., 2024).

Beyond their ecological impacts, antibiotic residues in the environment contribute to the emergence and dissemination of antimicrobial resistance, which is currently recognized as one of the most significant global public health threats. Therefore, controlling pharmaceutical pollution through the implementation of EPV plays an important role in mitigating antimicrobial resistance while protecting environmental quality (Belle et al., 2025; Obando et al., 2026).

Environmental Risk Assessment and Environmental Monitoring

Environmental Risk Assessment (ERA) constitutes a fundamental component of EPV because it evaluates the potential environmental risks associated with pharmaceutical compounds before and after market authorization. Recent advances in analytical technologies, particularly liquid chromatography–tandem mass spectrometry (LC–MS/MS) and ultra-high-performance liquid chromatography (UHPLC), have substantially improved the sensitivity and accuracy of pharmaceutical residue detection across diverse environmental matrices. In parallel, predictive approaches such as Predicted Environmental Concentration (PEC) models and artificial intelligence-based quantitative structure–activity relationship (AI-QSAR) models are increasingly being applied to estimate the environmental distribution, persistence, and ecological risks of pharmaceutical compounds more efficiently (Inaudi et al., 2025; Roveri et al., 2026; Welch et al., 2023).

Despite these advances, several studies have identified important limitations in the current implementation of ERA, including insufficient environmental monitoring data, inconsistencies in regulatory requirements across countries, and inadequate integration between environmental monitoring outcomes and pharmacovigilance systems. Strengthening regulatory harmonization and expanding integrated environmental monitoring programs are therefore essential to improve the effectiveness of EPV implementation (Cannata et al., 2024; Oldenkamp et al., 2024).

Implementation of Ecopharmacovigilance Within the One Health Framework

The implementation of EPV requires active engagement from multiple stakeholders through the One Health framework, which integrates human, animal, and environmental health. Recommended strategies include eco-directed prescribing, rational medicine use, medicine take-back programs, improvements in pharmaceutical wastewater treatment technologies, and public education regarding the appropriate disposal of unused medicines (Cristini et al., 2025; Helwig et al., 2024).

Pharmacists play a strategic role in implementing EPV by educating patients, promoting the rational use of medicines, and supporting pharmaceutical waste management within healthcare facilities. Furthermore, collaboration among healthcare professionals, regulatory authorities, academic institutions, and the pharmaceutical industry is essential for developing evidence-based policies capable of reducing the release of pharmaceutical residues into the environment (Cristini et al., 2025; Nana Shashiashvili, 2025).

Challenges and Future Perspectives

Although interest in EPV continues to increase, its implementation still faces several challenges, including limited reporting of environmental impacts within existing pharmacovigilance systems, inadequate environmental monitoring infrastructure, insufficient regulatory harmonization, and limited public awareness regarding pharmaceutical waste management. Analysis of the VigiBase database indicates that reports related to environmental impacts remain substantially fewer than reports of adverse drug reactions in humans, highlighting the need for more comprehensive and integrated environmental reporting systems (Spilsbury et al., 2024).

Looking ahead, the future development of EPV is expected to be supported by digital technologies, artificial intelligence, and big data approaches for environmental monitoring and ecological risk prediction. Integrating EPV into pharmaceutical regulation, public health policies, and environmental protection strategies has the potential to establish a more sustainable pharmaceutical management system while contributing to the achievement of the Sustainable Development Goals (SDGs) through the One Health approach (Gómez-Oliván, 2026; Zampelli & Verna, 2025b).

CONCLUSIONS AND RECOMMENDATIONS

Ecopharmacovigilance has emerged as an increasingly important approach for addressing the environmental impacts of pharmaceutical residues through the integration of pharmacovigilance, Environmental Risk Assessment (ERA), green pharmacy, and the One Health framework. This review demonstrates that pharmaceutical residues originating from multiple sources—including human and veterinary medicine use, healthcare facility wastewater, pharmaceutical manufacturing, and the improper disposal of unused medicines—have become significant environmental contaminants capable of disrupting ecosystems, promoting bioaccumulation, and increasing the risk of antimicrobial resistance. Advances in analytical technologies, environmental risk assessment methodologies, and artificial intelligence have created valuable opportunities to

improve the monitoring, prediction, and management of pharmaceutical residues. However, the effective implementation of ecopharmacovigilance continues to face important challenges, including limited environmental monitoring systems, insufficient regulatory harmonization, inadequate reporting of environmental impacts, and the need for stronger interdisciplinary and cross-sectoral collaboration.

Strengthening regulatory frameworks, developing integrated environmental monitoring systems, promoting the rational use of medicines, implementing sustainable pharmaceutical waste management practices, and enhancing the role of healthcare professionals, particularly pharmacists, are essential to support the effective implementation of ecopharmacovigilance. These efforts are expected to reduce the environmental burden of pharmaceutical residues while contributing to sustainable healthcare systems in accordance with the One Health approach and the Sustainable Development Goals (SDGs). Future studies should focus on generating long-term environmental monitoring data, developing standardized ecopharmacovigilance indicators and environmental risk assessment methodologies, validating artificial intelligence–based predictive models, and evaluating the effectiveness of ecopharmacovigilance interventions and policies across different healthcare and environmental settings to strengthen the evidence base for sustainable pharmaceutical management.

FURTHER STUDY

This review has several limitations, including its reliance on published literature, variations in study methodologies, and differences in environmental monitoring approaches across regions, which may affect the generalizability of the findings. In addition, the rapidly evolving nature of ecopharmacovigilance may result in the emergence of new evidence beyond the review period. Future studies should focus on developing standardized environmental monitoring frameworks, evaluating the effectiveness of ecopharmacovigilance interventions in real-world settings, and strengthening the integration of environmental risk assessment with pharmaceutical regulatory policies. Further research is also needed to explore innovative technologies and One Health-based strategies to reduce pharmaceutical contamination and its ecological and public health impacts.

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