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Separation of Pharmaceutical residues from wastewater

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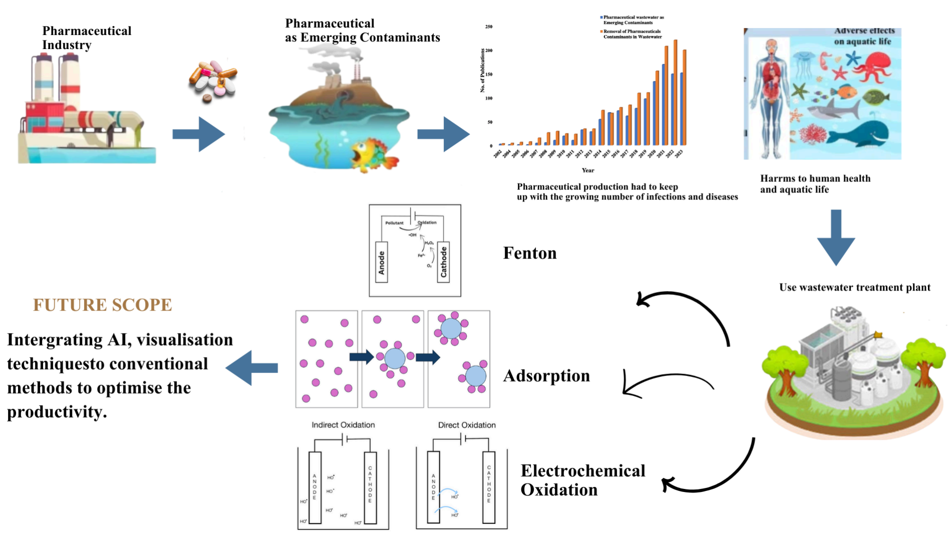
Graphical Abstract



Abstract

Pharmaceutical residues in wastewater threaten both aquatic ecosystems and human health. Approximately 80 % of the wastewater produced worldwide is discharged into the environment without treatment, and 26 % of 258 rivers surveyed in 104 countries have API levels that exceed safe limits, making advanced treatment urgently needed. Herein, three major separation methods for degrading or removing pharmaceutical pollutants are reviewed: Fenton oxidation, adsorption, and electrochemical oxidation. Under optimum conditions, reported efficiencies range from 74 % to 100 %; however, their efficacy usually declines under fluctuating pH and ionic strength and other complex wastewater matrices.

Each of these processes offers trade-offs in scalability, cost, and energy demand; full-scale implementation is further limited by such issues as sludge formation, adsorbent regeneration, and by-product toxicity. More recently, the integration of machine learning and physics-informed hybrid models has been shown to improve predictive accuracy and operational optimization over conventional kinetic approaches. The paper concludes by recommending AI-driven frameworks and immersive visualization for adaptive control of wastewater treatment systems that ensure sustainable, cost-effective, and data-transparent removal of pharmaceutical residues in concert with global water-quality and sustainable development goals.

Keywords: separation, pharmaceutical, impact, waste, water

1. Introduction

1.1 Background

Increased measures and remediation techniques must be developed to maintain pace with accelerated pharmaceutical production, a necessary response to the rapidly growing numbers of infections and diseases.[1] Unregulated water treatment can lead to pharmaceuticals contaminating water sources, posing significant health and environmental risks.

1.1.1 Pharmaceutical Contaminants in Water. Pharmaceuticals are common contaminants of wastewater and must traverse treatment facilities to avoid infiltrating water sources (i.e., rivers and lakes) or even drinking water supplies. Vinayagam et. al reported that the treatment efficiency of those pharmaceuticals, including atenolol, clofibric acid, carbamazepine, lincomycin, diclofenac, propranolol, acetylsalicylic acid, and mefenamic acid within wastewater is especially low, ~ 10-15%.[2] Hussain et. al also mention trends found by the OECD (Organization of Economic Co-operation and Development) that reports one third of four million prescriptions end up as waste in the USA.[3] Furthermore, despite Oceania having the lowest reported water pollution among other continents, Australia was found to have relatively high contamination levels of salicylic acid and paracetamol. It should be noted that in their article, Adedipe et. al highlighted that pharmaceutical residues in Oceania generally did not have many research publications, relative to the other continents. [4]

In a study by PNAS, 258 of the world's rivers were tested at 1,052 locations across 104 countries representing all continents, and the environmental influence of 471.4 million people. The highest contaminated sites were from middle to low-income areas with poor waste and wastewater management. Concentrations of at least one Active Pharmaceutical Ingredient (API) at 25.7% of sampling sites were greater than concentrations considered safe. Lahore, Pakistan, had the highest cumulative concentration of APIs at 70000 ng/L; Adelaide, Australia, was the highest-ranking Australian city, in the 30th percentile, with a concentration of ~580 ng/L, followed by Sydney at ~490 ng/L. [5]

1.1.2 Emerging Technology and AI. Traditional modelling approaches in separation processes, such as adsorption isotherms, kinetic models, and mechanistic equations, provided valuable insight into how systems behave. However, they often express significant drawbacks, such as reliance on many assumptions, sensitivity to specific operating conditions, and the challenge of accounting for uncertainties. As a result, their predictions can be poor in real-world applications, where processes have significant variability.

Machine learning frameworks trained on large multi-layered databases and AI can be harnessed to increase the optimization of separation processes, which can provide scenario-dependent predictions of the removability and efficiency. AI models can also handle non-linear relationships, are adaptable, and effective in depicting hidden trends that traditional methods would often miss. Overall, the integration of Machine Learning and AI increases the efficiency of wastewater treatment.

1.1.3 Aim of the Review. This review will explore previous studies and articles to evaluate and compare various separation techniques that have been proposed to treat pharmaceutical residue in wastewater, while also exploring the integration of AI and modelling techniques that were utilised. Through the comparative analysis of all current treatment methods, this report goes on to suggest future processes with ingrained AI, with justification of these techniques as well as discussing the research gaps prevalent in this study.

1.2 Importance and Challenges of Pharmaceutical Contaminants in Water

Purifying wastewater from pharmaceutical contamination is a crucial process that affects everyone with access to water. This section details multiple reasons to consolidate its significant importance.

1.2.1 Sustainability and Regulatory Pressure. In 2015, many countries and regions, particularly members of the United Nations, adopted the 2030 Agenda for Sustainable Development.[6] This global framework consists of 17 interconnected goals that aim to eradicate poverty and inequality, protect the planet, and promote justice, prosperity, and human well-being. At first glance, the treatment of pharmaceutical contaminants in wastewater directly aligns with three specific goals: SDG 3 (Good Health and Well-Being), SDG 6 (Clean Water and Sanitation), and SDG 14 (Life Below Water). Ensuring that pharmaceutical residues are effectively removed from wastewater reduces risks to human health, guarantees access to safe water, and protects aquatic ecosystems from harmful bioaccumulation. However, recent studies such as "*The Role of Wastewater Treatment in Achieving Sustainable Development Goals (SDGs) and Sustainability Guidelines*" suggest that wastewater treatment contributes to as many as 11 out of the 17 SDGs, far more than anticipated.[7] This reinforces the critical role of advanced treatment technologies in driving sustainable development and highlights the broader societal, environmental, and economic importance of addressing pharmaceutical pollution.

1.2.2 Environmental Protection. As discussed in Part 1.2.1, pharmaceutical contaminants in wastewater raise significant environmental concerns. Research has demonstrated that pharmaceuticals constitute a major class of emerging contaminants that adversely affect living organisms.[8] Their toxicity to aquatic life is evident through bioaccumulation in the tissues of aquatic animals, while chronic exposure can alter species behavior, reproduction, and growth, ultimately disrupting ecosystem balance. A critical challenge is that many pharmaceutical compounds are highly persistent, resisting natural degradation processes and thereby accumulating in water bodies over time. In Australia, this issue has been observed in local waterways: aquatic flora in river systems across South-Eastern Australia, even at considerable distances from the initial contamination sources, were found to contain pharmaceutical residues. Such findings highlight both the mobility and long-term ecological risks posed by pharmaceutical pollution.

1.2.3 Prevention of Antibiotic Resistance. Another increasingly important reason to prioritize the treatment of pharmaceutical contaminants in wastewater is the role of environmental antibiotic residues in driving the development of antibiotic-resistant bacteria. When antibiotics enter ecosystems through wastewater, they create selective pressures that accelerate bacterial adaptation and resistance.[9]

Pharmaceutical drugs, particularly antibiotics, can reach waterways through several pathways.[6] The most significant is human excretion: while antibiotics are consumed in vast quantities—estimated at 34.8 billion daily doses globally—up to 90% of the active compounds are excreted unchanged into the environment.[4] Healthcare facilities represent another major contributor, generating large volumes of concentrated pharmaceutical waste, with hospitals producing between 1,150 and 5,967 grams of residues daily.[10] Community and household sources also play a critical role, as improper disposal of unused or expired medicines introduces additional contamination into wastewater streams.[10]

Antimicrobial resistance (AMR) in 2019 was directly responsible for 1.92 million deaths, and contributed to a further 4.95 million deaths. This figure is projected to rise by 2050, partially due to wastewater, as the pharmaceutical industry continues to grow. [11]

The consequences of this contamination are profound. The release of antibiotics into aquatic environments fosters direct interactions between local bacterial populations and antimicrobial residues, facilitating the emergence of resistant strains. These resistant microbes can then spread through water systems, food chains, and direct contact between humans and animals, escalating the global health threat of AMR.[12]

Given the scale and severity of this issue, effective treatment of pharmaceutical wastewater is not only an environmental priority but also a critical safeguard against the acceleration of AMR. Without intervention, the unchecked spread of resistant strains could heighten the risk of a future global health crisis comparable to, or even exceeding, past pandemics.

1.2.4 Human Impact. A vast majority of wastewater globally is left untreated (80%), even while narrowing the scope to the developed world, wastewater treatment facilities are often unable to filter out dangerous antibiotics and other pharmaceutical waste, possibly leading to antibiotic resistance from continued exposure. This resistance could possibly lead to dangerous pandemics due to the development of superbugs, which is a large cause for concern for public health globally and also in Australia.[9]

Pharmaceuticals in drinking water can increase the risk of diseases, with antibiotic waste in water causing increased drug resistance to microorganisms, particularly pathogenic ones. It is estimated via upstream sources indicate nearly 5 million deaths were associated with antimicrobial-resistant pathogens in 2019, with projections rising to 10 million per year by 2050, with water systems cited as an important medium for dissemination.[13] This can also increase the incidence of breast and testicular cancer due to estrogen in water. Residual anti-cancer drugs in drinking water can penetrate the blood-placenta barrier, causing a teratogenic and embryotoxic effect, which has an especially dangerous impact on pregnant women.[14] Some antibiotics and other pharmaceutical waste pose a significant risk to those who suffer from kidney or liver diseases or failure. This is a particular concern due to the aging Australian population, who are more susceptible to these diseases and failures, with Chronic Kidney Disease recorded as a diagnosis for 2 million hospitalisations in 2021-2022.[15] Similarly, 1 in 3 Australians is affected by varying forms and seriousness of liver disease.[16] This indicates that pharmaceutical waste in waterways poses an increasing threat to both global and Australian society, especially those with underlying conditions and the vulnerable.

Furthermore, drinking water is a main source of endocrine-disrupting chemicals (EDC), these chemicals are associated with a number of diseases and disorders, such as reproductive and cardiovascular disorders, kidney disease, neurological disorders, autoimmune disorders, and cancer. EDCs play a large role in the pharmaceutical industry and, hence, are a sizable source of EDCs ending up in wastewater and effectively in drinking water.[17]

2. State-of-the-art Analysis

2.1 Current Treatment Methods of Pharmaceutical Waste in Water

There is a wide variety of chemical and physical processes used to separate harmful pharmaceutical waste from water, with varying costs and viability. With many different types of drug residue contaminating waste effluent, there are also several different types of separation processes that can be effective in purifying the water. Three common techniques are discussed in detail in this section.

2.1.1 Fenton. The Fenton process is one of the earliest and most widely used advanced oxidation processes (AOPs) for wastewater treatment.[18] It has been successfully applied to various waste streams, including textiles, agrochemicals, leachate, and other recalcitrant pollutants.[19] The process relies on ferrous iron (Fe^{2+}) as a catalyst and hydrogen peroxide (H_2O_2) as an oxidant to generate hydroxyl radicals (•OH)—highly reactive species capable of degrading a broad range of organic and inorganic pollutants.[20]

Fenton oxidation proceeds through a chain of reactions between Fe^{2+} and H_2O_2 under acidic conditions (typically pH 3–4) [20], resulting in the continuous formation of •OH. These radicals rapidly attack and oxidise organic contaminants (RH) in the water.[18] The simplified reaction mechanism is shown below:

Fenton Reaction:

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^{\cdot} + \bullet OH \quad (1).$$ [18]

Radical Attack on Pollutants:

$$RH + \bullet OH \rightarrow R + H_2O \, (2).$$ [18]

The performance of the Fenton process is affected by several operational parameters, including the ratio of Fenton's reagents (H_2O_2 to Fe^{2+}), solution pH, reaction time, temperature, initial contaminant concentration, and the nature of the wastewater matrix. Among these, the reagent ratio and pH are generally considered the most influential factors governing process efficiency.[18]

While the conventional Fenton process is highly effective, it presents several operational limitations. One major drawback is the requirement for strongly acidic conditions (typically pH 3–4), which increases chemical consumption and may necessitate post-treatment neutralization and the production of large amounts of iron sludge. The quantity of this sludge depends on the dosage and ratio of reagents used. Its handling and disposal pose environmental and economic challenges, as improper disposal may lead to secondary contamination and hinder resource recovery efforts.[19] To overcome these drawbacks and improve efficiency, several modified processes have been developed, namely Electro-Fenton (EF), Anodic Fenton (AF) [22], and Photo-Electro-Fenton (PEF).[23]

The Electro-Fenton process offers significant advantages, including low energy consumption, operational simplicity, and reduced reliance on externally supplied chemical reagents.[24] In this system, carbon-based cathodes are commonly used because of their high efficiency in oxygen reduction and their stability under acidic conditions.[25] As shown in Figure 1, at the cathode, hydrogen peroxide (H_2O_2) is generated in situ via the two-electron oxygen reduction reaction (ORR):

$$O_2 + 2H^+ + 2e^- \rightarrow H_2O_2 \quad (3).$$ [25]

The electrogenerated H_2O_2 subsequently reacts with externally added Fe^{2+} (as described in Equation 1) to form hydroxyl radicals (•OH) [22]. This in situ generation of H_2O_2 eliminates the need for transport and storage of concentrated peroxide solutions and enables enhanced recycling and reagent efficiency within the treatment process.[26]

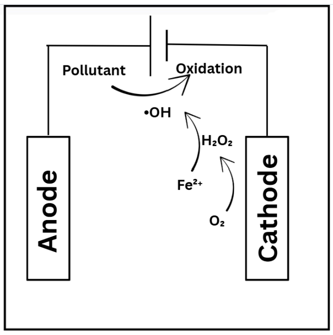


Figure 1. Schematic Diagram of Electro Fenton.

In anodic Fenton systems, pollutants can be degraded through two primary pathways. First, pollutants are directly oxidised at the anode surface via electron transfer. Second, advanced oxidation occurs via reactive oxygen species (ROS) generated from water oxidation at the anode surface. These reactions lead to the formation of hydroxyl radicals (•OH), which are highly effective in breaking down organic contaminants. The general surface reaction is:

$$M(Anode) + H_2O \rightarrow M(\bullet OH) + H^+ + e^- \quad (4).$$ [25]

Besides hydroxyl radicals (•OH), weaker oxidants such as hydrogen peroxide (H_2O_2) and ozone(O_3) are also formed from water oxidation, enhancing the overall oxidative capacity and complementing the classical Fenton reaction as shown in Equation 1.[27]

The efficiency of anodic Fenton processes depends on the mass transfer of pollutants to the electrode surface and the intrinsic properties of the anode material. Anodes are commonly classified as active (e.g., Ti, Pt) or non-active (e.g., boron-doped diamond (BDD), PbO_2). While both types can degrade antibiotics, non-active anodes(BDD) are generally preferred because they achieve greater mineralisation and produce fewer toxic byproducts. Despite the excellent oxidative performance of BDD, its high cost limits large-scale implementation. Consequently, mixed-metal oxide (MMO) or doped-metal oxide anodes are often explored as more cost-effective alternatives. [28]

The Photo-Electro-Fenton process integrates UV or visible light irradiation with the EF system to further boost degradation efficiency. Light irradiation accelerates the photoreduction of Fe^{3+} back to Fe^{2+}, thereby sustaining the catalytic cycle and reducing the need for excess iron addition.[29] A representative reaction is:

$$Fe^{3+} + H_2O_2 + h\nu \rightarrow Fe^{2+} + \bullet OOH + H^+ \quad (5)$$

In addition, UV irradiation promotes the direct photolysis of H_2O_2 to generate extra hydroxyl radicals (•OH), thereby enhancing the mineralization of recalcitrant organic pollutants.[30] PEF therefore combines the advantages of EF with light-driven radical production, offering higher removal efficiencies and reduced iron sludge formation compared to classical Fenton.

Based on a literature review by Jiang et al. (2022), recent advances in the removal of antibiotics in aqueous environments using Fenton processes have demonstrated high removal efficiencies. Reported performance using Photo-Electro-Fenton includes ~90% degradation of thiazole sulfate with a total organic carbon (TOC) removal of 75%. For tylosin, a degradation efficiency of 97.1% and TOC removal of 91.5% were achieved. Amoxicillin and cloxacillin exhibited chemical oxygen demand (COD) removal of 78.7% and TOC removal of 52.3%. Electro-Fenton systems have also shown excellent performance, with tetracycline achieving complete (100%) degradation and 97.2% removal efficiency under optimised conditions.[23] Overall, Fenton-based processes demonstrate strong potential for the degradation and mineralisation of pharmaceutical residue in wastewater.

2.1.2 Adsorption. Adsorption is an effective and prevalent separation technique where 'unwanted' molecules are selectively bound to the surface of an adsorbent and are removed from the source they were contaminating, a process overall driven by Van der Waals forces.[31]

The wide range of adsorbents offers this separation process versatility, creating an extensive range of drug residues that can be eliminated while meeting operational goals (i.e., sustainable, economic, etc.). A common adsorbent for the removal of antibiotics and other pharmaceuticals from water is Activated Carbon (AC). Its effectiveness is characterised by its "large surface area, large micro porosity, and high sorption capacity," and is proven to be "effective in removing organic pollutants at lower concentrations," with removal rates ranging from 74 to 100% when addressing antibiotics in aquatic environments specifically.[2] Neolaka et al substantiate that AC has high surface reactivity and good adsorption capacity, while also being inexpensive with low-maintenance and low energy requirements.[32] In addition, it is reported that granular activated carbon (GAC) could effectively remove simultaneously multiple pharmaceuticals from wastewater up to 52% by applying various isotherm and kinetic models under batch conditions, offering practical insights for realistic scenarios.[33]

Utilising adsorption as a separating technique still has a few disadvantages. For instance, after the contaminants have attached to the adsorbent and exhausted its adsorption capacity, it needs to either be regenerated or disposed of. Qin et al. established that a thermal or chemical regeneration of the adsorbent AC would be largely energy-inefficient, while a complete disposal would result in secondary wastes that would then require extra costs and energy to remove.[34] This concludes that, despite AC and other adsorbents being relatively cost and energy-efficient as separating agents, their removal could potentially make the process more expensive.

2.1.3 Electrochemical Oxidation. Electrochemical oxidation is an electrocatalytic process in which pollutants are decomposed or transformed to safer compounds through redox reactions at electrodes. A direct current is applied between the anode and cathode, which is then submerged in the wastewater. With the application of electric current, the water is oxidised at the anode either directly through electron transfer with the anode's surface, or indirectly through the production of a highly reactive radical species, namely the hydroxyl radical (OH•) (see figure 2). Whereas at the cathode, H^+ is reduced to hydrogen gas. [35]

The choices of electrode, composition of the electrolyte, and cell configuration are vital for the efficiency and cost of this process. Boron-doped Diamond (BDD) is the best anode to use as it promotes the highest oxidation, although it comes with a high cost. A mixed metal oxide is cheaper, although it is less stable and has a shorter longevity when compared to BDD, with PbO_2 as another option, although over time, Pb^{2+} will dissolve.[36]

Pharmaceutical waste is incredibly hard to treat with more conventional separation methods, although through the hydroxyl radical (OH•), degradation of the otherwise difficult-to-degrade pollutants can occur without the addition of other chemicals into the water. This process, with the use of different types of anodes, has been tested and used for the degradation of antibiotics. There are also limitations to the implementation and scalability of this process, including high cost, high energy consumption, and also efficiency, electrode cost, and lifetime, and possible by-product formation if certain compounds are present (e.g, Cl^- can create chlorinated species).[37,38]

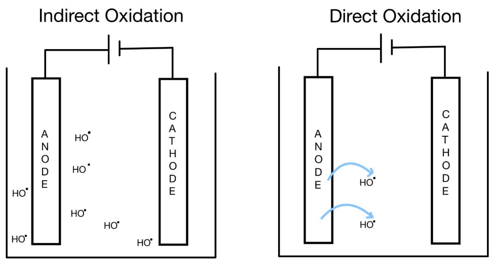


Figure 2. Schematic Diagram of the Electrochemical Oxidation Process

2.2 Integration of Emerging Technologies in Separation Process Studies

2.2.1 Current Modelling Methods.

Table 1. Summary of Models used in adsorption, Fenton, and Electrochemical oxidation technologies.

Method	Model used	Main Limitations
Adsorption	Langmuir/Freundlich, PFO/PSO kinetics, thermodynamics, and potential theory	Derivation in more than one approach => difference in the physical interpretation of the model parameters
Fenton	Classical kinetics, ML regressors (RFR, GPR, DTR, GAM) on experimental data	Mechanistic models in a narrow pH window
Electrochemical oxidation	Butler–Volmer, mass transfer	Many uncertainties and plant-specific parameters limit predictive certainty

Most of the water treatment processes that relate to the analysis of water movement are hard to observe directly. Therefore, classical mathematical and computational fluid dynamics (CFD) have long been a numerical procedure to calculate the properties of pharmaceutical contaminants under different treatment scenarios via mass balances, reaction kinetics, and transport phenomena. [39]

Over the years, a wide variety of equilibrium isotherm models (Langmuir, Freundlich, etc) in adsorption modelling have been built based on three fundamental approaches, which are kinetic consideration, thermodynamics, and potential theory, to estimate capacity and affinity, while uptake dynamics are fitted with pseudo-first-order and pseudo-second-order kinetic models. However, isotherm modeling is the derivation in more than one approach, thus leading to differences in the physical interpretation of the model parameters. [40]

Machine learning methods using experimental Fenton treatment data were proposed to mathematically demonstrate the effect of the hydrogen peroxide (H_2O_2) and iron sulfate ($FeSO_4$) dosage on dye and total organic carbon (TOC) concentration. It uses four regression techniques: Random Forest Regression (RFR), Gaussian Process Regression (GPR), Decision Tree Regression (DTR), and Generalized Additive Model (GAM), which are used to predict the dye and TOC concentration outputs of the Fenton process (Ergan et al., 2025). However, classical kinetics addresses the narrow pH range challenge, when performance drops quickly under varying conditions and robust operational parameters. [41]

In electrochemical separation processes, the model relates to the Butler-Volmer equation, electrode kinetics, and mass balance to give the total rate of the direct electrochemical processes. However, many factors influence these parameters in real-world wastewater-treatment processes, such as conditioning of the electrode surface or the presence of impurities in the electrolyte. This large number of parameters makes it impossible to carry out quantitative and reliable calculations on a theoretical basis for electrochemical oxidation or coagulation processes.[42]

2.2.2 Integration of AI Methods. Machine learning (ML) frameworks trained on large multi-layered databases, gathered from thousands of measurements across a large number of pharmaceuticals and wastewater treatment plants, can predict the removability of pharmaceutical waste and how effectively it can be done on-site. This model can also provide scenario-dependent predictions, which provide valuable guidance for optimising the treatment plant to ensure most of the pharmaceuticals are removed.

A study by Zhang et. al using 4000 measurements, 80 pharmaceuticals across 17 wastewater treatment plants as its database provided an accuracy of 0.81. Including more data points in the database would increase accuracy and indicate that ML integration can significantly improve pharmaceutical waste removal from water, as this method allows plants to be optimised without significant cost. [43]

In their article, Cairone et. al detail many advantages of AI modelling specific to Wastewater Treatment Plants (WWTPs). They explore the ability of AI models (through their ML algorithms) being able to handle complex and nonlinear relationships among factors involved in the whole treatment process. The AI models' adaptability, effective data management, and identification of hidden trends are other listed advantages that traditional mathematical models do not possess to the same degree.[44] Cairone et. al also detail and review how Nam et. al developed their own AI model to enable hourly predictions in Membrane Bioreactor (MBR) plants, which improved their energy efficiency by 12%, reduced membrane fouling by 26% and reduced operating costs by 16%, overall demonstrating how AI improved the performance of the MBR and aided their study.[45]

2.2.3 Role of Digital Technologies in Visualisations and Interactive Simulations. Digital technologies, including interactive visualisation tools, virtual simulations, and augmented or virtual reality (AR/VR), are increasingly being used in separation processes to enhance analysis and communication. Instead of relying on static tables or graphs, these interactive platforms allow users to adjust parameters in real time and observe how systems respond, offering a clearer view of behaviour under changing conditions. For instance, visualisation frameworks that integrate computational fluid dynamics (CFD) data allow researchers to virtually explore phenomena such as pollutant dispersion, mass transfer, or catalytic reactions inside reactors—processes which are often challenging to capture through conventional laboratory experiments.[46]

These technologies offer two main advantages. Firstly, they help minimise both experimental costs and potential risks by allowing different operating scenarios to be tested safely in a simulated environment before being applied in practice. Second, they make complex data more accessible through visual storytelling, which supports better understanding among researchers, policymakers, and stakeholders in wastewater management.[47] Recent studies show that interactive 3D models and digital twins of wastewater treatment plants can simulate how operational changes—like modifying flow rates or electrode configurations—affect performance, helping decision-makers plan more effectively.[48]

Overall, digital visualisation technologies complement classical modelling by connecting theory with practice. They enhance understanding of dynamic processes, make communication clearer, and support safer, more efficient experimentation in separation research.

2.3 Comparative Analysis

Table 2: Comparison between separation processes commonly used in pharmaceutical removal from wastewater.

	Separation Technique		
	Fenton	Adsorption	Electrochemical Oxidation
Cost	· High costs due to chemical handling, transportation, storage of reagents (H_2O_2 and homogeneous solution of iron ions), and sludge disposal · Costs are reduced in modified versions of Fenton, anodic Fenton, and photo-electro-fenton techniques.[49]	·Cost depends on the adsorbent type; low for activated alumina, but it can be unsustainable. Hence, cheap adsorbents are available, though other operational goals need to be considered to determine if it is feasible. [50]	· High initial cost for electrodes (especially BDD) · Moderate operational cost from electricity · Hard to degrade pollutants can increase the cost due to increased electricity.
Efficiency	· High efficiency in degrading a wide range of organic pollutants	· Adsorbent choice can be specialised depending on pollutants, providing high efficiency with low energy requirements	· High efficiency in the degradation of complex compounds like pharmaceuticals
Scalability	· Highly scalable due to short reaction time and straightforward operation setup. but limited by acidic pH (pH~3) requirement and safety of handling H_2O_2 and Fe^{2+}.	·Limited by the expensive and energy-intensive adsorbent disposal process · Scalability depends on pollutant and adsorbent type.	· Constrained by electrode cost, energy consumption. · Wastewater must also be somewhat conductive, which can be difficult on a large scale.
Environmental impact	· Produces large volumes of iron sludge · Non-toxic reagents are primarily used (H_2O_2 and Fe^{2+} salts).	· A wide adsorbent range allows sustainability flexibility, though some materials are costly or less efficient.	· No harmful chemical addition; environmentally safer, but may generate by-products under certain conditions.

Energy Requirements	· No direct electricity use but energy needed for reagent ((H_2O_2, Fe^{2+}) preparation and pH control; Electro-Fenton requires electrolysis.	· The pollutant removal stage has low energy requirements. · Adsorbent disposal/regeneration consumes a lot of energy, especially when meeting sustainability goals.	· High energy consumption, due to the electricity needed to conduct the reaction. · Some pollutants require additional energy due to the extra time needed to degrade compounds.

2.3.1 Understanding Wastewater Purification Through the Combination of Traditional Separation Processes with Modern Tools. AI-integrated modelling within articles often uncovers new and complex relationships between factors that could not have been discovered using other conventional mathematical methods. This ultimately leads to a greater understanding of how pharmaceutical residue is separated from wastewater using traditional techniques (i.e., Fenton, adsorption, and electrochemical oxidation) as it explains and accounts for hidden variables within experiments and provides an augmented analysis into how these techniques operate, thereby yielding more results for authors to discuss.

3. Challenges and Future Directions

3.1 Future Separation Processes

Advanced oxidation processes, while being a process that already exists, have thus far had scalability issues, although through its combination of multiple traditional techniques as well as the electrochemical oxidation process, it provides the most promise to eradicate pharmaceutical waste in waterways, indicating it is the most promising process to be implemented in the future.

Advanced oxidation processes (AOPs) involve harnessing radical chemistry to destroy pathogens and other organic and non-organic compounds (i.e, pharmaceuticals) in wastewater. Depending on the specific AOP used, a number of different techniques, such as ozonation, Fenton, and photo-Fenton processes, as well as photocatalysis, are implemented with the electrochemical oxidation process discussed in detail previously.[51,52]

These are relatively new processes that are not widely used to a large scale due to scalability issues such as the oxidation conversion efficiency, batch vs. continuous flow systems and location of radical production, as research has found for best results this must be completed in-situ, as well as the delivery systems for different components used in this method, and overall the high cost of scaling this process up to an industrial level. While advanced oxidation processes are difficult to scale up, some reports suggest that under the most ideal conditions (i.e. low dosages) 100% of pharmaceutical waste can be eliminated from water systems, as well as other difficult-to-remove organic and inorganic harmful compounds.[35]

As discussed in section 2.2.2, Machine Learning can be used to optimise a separation process before it is scaled to the industrial level, which cuts costs as the efficiency of separation will be higher, subsequently reducing energy consumption. Safe by-product disposal must also be considered, especially when harnessing advanced oxidation processes, which can form toxic by-products. This can be done through optimisation inside the column, or further separation after wastewater treatment is completed.[53] Ensuring regulatory compliance and reducing the overall cost of this process will ensure financial and legal needs are incorporated, increasing the viability of advanced oxidation processes to be more regularly harnessed in wastewater treatment in the future.

3.2 Research Gaps.

Although numerous studies have advanced the understanding of pharmaceutical wastewater treatment through Fenton oxidation, adsorption, and electrochemical oxidation, several research gaps remain across the literature examined.

In this article, most of the studies were carried out under controlled laboratory conditions; therefore, they fail to take into consideration the real-life systems, which are complex, large-scale, and under different conditions (pH instability, fluctuating influent composition). In the practical scope, although each method (Fenton oxidation, adsorption, and electrochemical oxidation) exhibits a high cost,[49] [50] which makes them economically challenging for large-scale implementation, combined treatment is shown as the most efficient method in terms of both treatment efficacy and cost.[54]

While classical models such as the Langmuir, Freundlich, and kinetic equations remain valuable for describing adsorption and reaction behaviours,[39] [41] they also have limitations that restrict their predictive accuracy under complex or variable operating conditions. Recent studies show that artificial intelligence and machine learning can help overcome some of these challenges by capturing nonlinear interactions and optimising process parameters.[40] [42] However, traditional modelling methods and AI tools are often used in parallel rather than truly integrated into a single hybrid framework. Furthermore, while artificial neural networks (ANNs) demonstrate considerable predictive accuracy, their application remains limited by computational demands and their inherent "black-box" behaviour. Because the internal reasoning behind their predictions is often opaque, engineers and decision-makers may find it challenging to interpret or justify the model outcomes—an important concern in safety-critical fields such as wastewater treatment. [55]

The majority of current literature reports pollutant removal efficiency as the primary metric of success (e.g., de Aguiar Pedott et al., 2024; Khan et al., 2023). This shows limitations in coupling treatment performance with ecotoxicological endpoints over time, such as the stability of adsorbents or electrodes, accumulation of residual iron sludge, and formation of secondary toxic by-products. Furthermore, few studies have examined the long-term performance of treatment systems or the potential toxicity of their effluents, even though such assessments are vital for understanding the true environmental safety and sustainability of these processes.[56]

3.3 Proposal and justification of new modelling techniques

Although traditional mechanistic and kinetic models have provided valuable insights into pharmaceutical wastewater treatment, their predictive capacity often fails under real-world variability. They depend heavily on idealised assumptions, narrow pH windows, and plant-specific parameters, limiting their generalisability and scalability.[36 37] Therefore, next-generation modelling frameworks should integrate AI-machine learning, physics-informed learning, and digital visualisation environments to enable adaptive, transparent, and data-driven wastewater management.

AI-driven hybrid modelling directly handles most of the limitations within classical mechanistic models. While the current models require over-simplified kinetics and pH-dependent assumptions, AI technologies provide performance with high accuracy by omitting the relationship between inputs and their corresponding outputs and complex mathematical formulas. Hence, an artificial neural network (ANN) could improve real-time monitoring, forecast treatment efficiency, optimize operating parameters, and enhance fouling control in order to transform membrane-based wastewater treatment. Also, by forecasting the required dosages and cleaning intervals, AI models can optimize the use of chemicals in cleaning processes, reducing the costs and minimising negative environmental impacts.[57]

Although ML and models above could highly improve the predictive accuracy in wastewater treatment applications, AI models often suffer from the "black-box" problem, where their internal decision logic remains opaque, limiting trust and regulatory adoption. Especially deep learning neural network approaches, which sacrifice transparency and interpretability for prediction accuracy. Therefore, this opacity can be problematic in the context of pharmacological separation when judgments about treatment optimization involve important factors like pH, electrode potential, or oxidant dosage.[57] Moreover, as AI models usually capture a wide range of factors influencing membrane fouling, this improves predictive performance. However, few studies sometimes overlook critical factors such as membrane characteristics, feed composition, and operating parameters—including key foulants like EPS, SMP, TEP, and BPC and do not consider pH, operating temperature, and filtration/backwashing protocols as input variables. To handle the limitations, Explainable AI (XAI) methods such as Shapley Additive Explanations (SHAP) and Layer-wise Relevance Propagation (LRP) could be deployed to quantify each variable's contribution to model output, enabling engineers to identify which factors most affect pollutant removal efficiency or energy consumption. [58]

Future research should move toward the development of hybrid models that combine many techniques, including both mathematical and artificial intelligence models, coupled with augmented or virtual reality (AR/VR) interfaces. This is still in its preliminary stages to establish better practices and refine methodologies in real wastewater treatment plants (WWTPs). Recent research visualises how an AI system makes decisions and predictions, and executes its actions, thereby making these models interpretable without sacrificing predictive power.[58] In the future scope, integrating interpretability frameworks within physics-informed machine learning (PIML) ensures predictions remain consistent with chemical and thermodynamic laws while providing traceable reasoning for decision-making, enhancing predictive reliability, operational safety, and global scalability.[59]

4. Conclusion

Overall, with the production and consumption of pharmaceuticals increasing, the human and environmental impact that occurs with inadequate separation techniques can cause global concern. Moving towards advanced oxidation hybrid processes with deeply ingrained AI and machine learning technologies to ensure optimal performance is inevitably where the field of pharmaceutical separation should head to ensure environmental and human safety.

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