Heavy Metal Pollution in Water Supplies: Removal and Recovery

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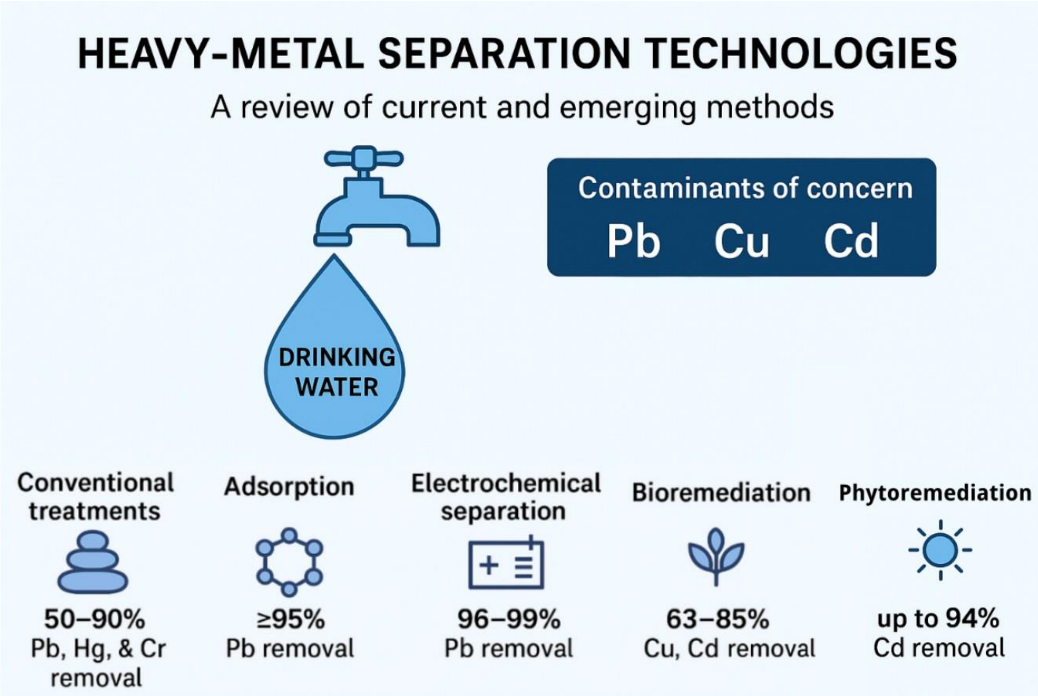

Abstract

Heavy metal contamination in drinking water represents one of the most critical environmental and public health challenges worldwide, affecting an estimated 200 million people annually. This review evaluates the evolution and current state of heavy-metal separation technologies, focusing on lead, copper, and cadmium as key contaminants of concern. Conventional treatment methods, such as coagulation and filtration, achieve 50–90% removal for metals like Pb^{2+}, Hg^{2+}, and Cr^{3+} under optimal conditions but perform poorly for Cd^{2+}, Ni^{2+}, and Zn^{2+}. Emerging strategies including adsorption, electrochemical separation, photoreduction, and bioremediation, offer enhanced selectivity and efficiency under specific conditions. Adsorption using nanostructured carbons and zeolites achieves lead removal efficiencies exceeding 95%, while permeable reactive barriers report maximum adsorption capacities up to 476 mg/g. Electrocoagulation can achieve 96–99% Pb^{2+} removal at current densities of 5–10 mA/cm^2 and pH 5, whereas electrodialysis achieves ~75% Pb^{2+} removal under pilot-scale conditions (5 mg/L initial concentration, 0.6 V per cell pair, 4-hour batch time). Bioremediation of Cu^{2+} using bacteria, fungi, and algae achieves 63–85% removal in batch studies, while cadmium photoreduction using bismuth/sulphur co-doped carbon quantum dots reaches up to 94% removal at pH 8, 10 mg/L initial concentration, and 120 minutes contact time. Despite technological progress, achieving sub-µg/L metal concentrations under complex water chemistries continues to challenge current methods. Economic feasibility, secondary waste generation, and system resilience under dynamic contamination events remain major barriers. Future research must prioritise integrated, adaptive separation systems that couple advanced materials with digital optimisation, balancing performance with sustainability and energy efficiency. Such cross-disciplinary innovation is essential to ensure universal access to safe drinking water in the face of accelerating industrialisation, population growth, and climate uncertainty.

1 Introduction

Heavy metal contamination of drinking water poses serious risks to human and ecological health. Water supplies are particularly vulnerable to the downstream effects of increased metal pollution produced by the expanding global economy. It is currently estimated that over 200 million people are exposed to dangerously contaminated drinking water annually [1, 2]. Environmental heavy metal pollution from anthropogenic sources greatly exceeds natural sources, and it has been shown that the amount of lead mined and introduced into urban environments is over 100 times greater than lead introduced through natural leaching [3, 4]. This accelerating threat demands separations infrastructure and technology keeps pace with the growing risk.

1.1 Defining Heavy Metals

Heavy metals evade precise definition, but for this paper we define heavy metals as metals with a high atomic weight and a density at least five times greater than that of water [5, 6]. The heavy metals linked most often with human poisoning are lead, mercury, arsenic and cadmium [7]. The physical and chemical properties of heavy metals present unique challenges for separation and pose significant risks to humans and the environment.

1.2 Human health Impacts

Heavy metals pose two distinct risks – to public health and to the health of the broader ecosystem. When ingested by humans, heavy metals can induce remarkable toxicity at low doses [8]. Several, such as arsenic and cadmium, are well established carcinogens [1]. Lead is particularly harmful to the development of the nervous system in children, causing neurological and developmental impairments [9]. More broadly, exposure of heavy metals has been linked to cardiovascular disease, kidney damage and elevated blood pressure, highlighting the severe impact on human health. [10]. The risk of heavy metals is not confined to adverse health impacts; heavy metals present an equally significant threat to the broader environment.

1.3 Ecological and Environmental Impacts

Heavy metals pose risks to ecosystems through bioaccumulation and food chain transfer. Bioaccumulation is a major concern because, unlike many organic pollutants, heavy metals do not degrade over time. The accumulation first manifests in soils and sediments, with contamination spreading into plants and animals and terrestrial organisms, disrupting biological functions and normal growth [11, 12]. In aquatic systems, metals are transferred up the food chain, disrupting the growth, reproduction, and physiology of fish and other marine life [13]. More broadly, heavy metals persist within both terrestrial and aquatic environments, contributing to long-term ecosystem decline [12]. Separations technologies are vital in maintaining not only public health, but in ensuring ecological sustainability into the future.

1.4 Separation of Heavy Metals

Because heavy metals persist and accumulate, effective separation processes are essential to ensure safe drinking water remains accessible worldwide. In most contexts, heavy metals levels are naturally below contamination guidelines. The primary risk, as seen historically, is posed by human activity. Broadly speaking, separation can be understood in two forms: preventive and reactive.

The first is preventative separation under normal operating conditions. Given typically low levels, heavy metals are not explicitly targeted by water treatment plants but may be incidentally removed by coagulation or filtration [14]. Additionally, some metal contamination, such as lead and copper, originates from leaching in the plumbing system itself, after intended treatment has occurred [15]. This type of contamination is currently not treated through chemical separation, but rather expensive infrastructure replacements.

The second is in reactive separation under exceptional contamination events. This is required in areas without conventional treatment facilities, such as developing regions where people drink and bathe directly from rivers and streams. Contamination of these bodies of water often go unnoticed and untreated, resulting in significant human exposure and harmful ecological effects. In developed nations, reactive separation may also be required when treatment plants are overwhelmed or when a new pollutant source drives concentrations above safe limits. In such cases, immediate separative action is required to ensure access to clean and safe water is reinstated as soon as possible [16]. Historically, heavy metal contamination has been widespread, yet existing separations technologies have proven to slow or impractical for efficient mitigation of the contamination risks.

1.5 Historical and Contemporary Case Studies

There are numerous diverse historical examples of heavy metal contaminated drinking water, originating from two main sources. In developed nations, one of the most persistent risks has come from the plumbing system itself. Lead pipes and fittings have long been used in water infrastructure, and under specific conditions they may leach dangerous amounts of lead into the water supply [17]. This type of disaster occurred in Flint, Michigan in 2014, when a change in municipal water supply from Lake Huron to the Flint River increased erosion, causing widespread lead leaching from pipes [18]. The event remains one of the most significant environmental contamination crises in recent history [19]. To prevent similar disasters, modern utilities often use corrosion-control measures such as orthophosphate dosing, which reduces leaching [17].

The greatest risk currently is seen in developing nations. This stems from hazardous and unsafe practices in industrial processes such as mining and smelting. Heavy metals discharged into rivers and streams can contaminate drinking water, especially in regions lacking centralized water treatment infrastructure and water quality monitoring. Communities in Ghana, for example, have faced severe lead and mercury contamination of the Bonsa River due to illegal mining [20]. Similarly, in Bangladesh, waters surrounding a key granite mining region were found to contain dangerously high levels of heavy metals requiring immediate action [21]. These water sources are vital to the function and daily lives of the communities they serve, highlighting the unique vulnerability to contamination events seen in these regions.

Australia has also not been immune to metal contaminated water. Studies have documented widespread copper and lead contamination in household drinking water across New South Wales [22]. In South Australia, a 2018 survey reported that 89% of tested rainwater tanks contained lead levels exceeding national drinking water guidelines in at least one sample [23]. This reinforces the risk of metal contamination through leaching from water infrastructure. Contamination of town water supplies has also been seen near the Cadia gold mine in NSW, with elevated selenium and nickel levels [24].

These cases underscore the diversity of the problem, ranging from illegal mining induced contamination in rural Africa to rainwater tank leaching in regional Australia. These cases underscore the need for adaptable separations technologies capable of addressing the scope and severity of risks posed by drinking water contamination.

1.6 Evolution of Treatment technologies

The separation of heavy metals from drinking water has evolved significantly, though major gaps remain. Conventional water treatment plants are not designed to target metals, focusing instead on turbidity, pathogens, and nutrients [25]. Some metals are incidentally removed during coagulation and filtration if incorporated into suspended solids, but this approach is neither reliable nor sufficient in high contamination events [26]. Coagulation and flocculation followed by sedimentation with ferric chloride or alum has been used for more than a century, achieving 50-90% removal for species such as Pb^{2+}, Hg^{2+}, and Cr^{3+}, but performing poorly for cadmium, nickel, and zinc [27]. Preventive measures such as orthophosphate dosing have been especially important in developed nations, forming insoluble phosphate scales inside pipes to reduce lead leaching [28].

Adsorption using activated carbon and the deployment of ion exchange resins have introduced greater selectivity, while reverse osmosis (RO) and nanofiltration (NF) membranes have offered near complete removal of multiple metals [29]. Although RO is most associated with desalination, the removal of bulk salts from seawater and brackish sources, similar membrane principles have been adapted for trace-level heavy-metal separation. Unlike desalination, which targets total dissolved solids in the gL^{-1} range, heavy-metal removal aims to selectively reject toxic ions such as Pb^{2+}, Cd^{2+} and Hg^{2+} present at far lower (μg/L) concentrations, often with correspondingly lower energy demands. Typical RO systems require 2-6 kWh/m^3 of treated water and can achieve > 95% metal rejection under low-NOM conditions [30, 31]. Ion exchange processes can achieve comparable removal efficiencies but produce concentrated brines and spent regenerants that must be managed sustainably [31, 32]. Electrocoagulation (EC) and electrodialysis (ED) have also emerged as hybrid or polishing options for metal removal. Electrocoagulation can reach 90-99% Pb^{2+} removal at current densities of 5-10 mA/cm^2 using iron or aluminium electrodes although performance declines with increasing organic matter or competing ions [32, 33]. All membrane-based systems remain susceptible to fouling and require significant operational oversight.

These limitations highlight that while conventional and modern processes can reduce heavy-metal concentrations, they remain energy-intensive and generate secondary waste streams. Continued innovation toward more selective, resilient, and sustainable separation systems is therefore essential, leading to the challenges and research gaps discussed in section 1.7.

1.7 Current Challenges and Research Gaps

Today, despite decades of progress, several persistent challenges remain. Achieving sub μg/L concentrations for metals such as lead and arsenic remains difficult in high NOM waters without incurring prohibitive energy or chemical costs. Treatment systems also lack robustness to sudden contamination spikes from events such as mining spills, infrastructure failures, or corrosion incidents. In addition, residual waste streams such as brines, sludges, and exhausted sorbents risk creating secondary pollution if not properly managed. For example, residual sludges from Fe-based coagulation can reach 0.3-0.5 kg/m^3 of treated water, creating significant disposal burdens [34].

These gaps underscore the need for advanced separation strategies that are both selective and effective as well as resilient, energy-efficient, and sustainable. There is a growing imperative to develop integrated, adaptive systems capable of maintaining safe water quality under dynamic and resource-constrained conditions. To address these challenges, this review identifies key research directions and evaluates emerging separation methods through a series of guiding questions.

1.8 Scope of this Review

This review evaluates the state-of-the-art in separation methodologies for heavy metals in drinking water, focusing on the challenges of meeting sufficiently low concentration targets under realistic conditions of NOM, variable pH, and aging infrastructure. Emphasis is placed on energy and chemical usage, robustness to fouling and transients, and the management of residual waste, and the discussion is framed by three guiding questions.

1. How can existing and emerging separation methods be optimised to achieve sub-μg/L metal concentrations under complex water chemistries (e.g. high NOM, mixed contaminants, variable pH)?
2. How can digital and modelling tools, including machine learning, process simulation, and data-driven control, enhance predictive capability, operational efficiency, and design of adaptive separation systems?

3. How can advanced separation technologies be scaled and integrated into real-world drinking-water systems while maintaining sustainability across energy use, residuals management, and infrastructure constraints?

Accordingly, these three overarching research questions guide the evaluation of separation technologies, digital optimisation approaches, and implementation challenges. Together, these questions frame the discussion from the molecular to the system scale, moving from process performance under complex water chemistries, to the integration of data-driven tools, and finally to the translation of these technologies into real-world drinking-water contexts.

Finally, this paper contributes to the UN Sustainable Development Goal (SDG) 6: Clean Water and Sanitation, by addressing the need for safe and sustainable drinking water through improved heavy metal separation technologies. It also contributes to SDG 3: Good Health and Well-Being, by mitigating the severe health risks posed by toxic metal exposure, and SDG 12: Responsible Consumption and Production, by promoting energy-efficient, low-waste treatment methods that reduce environmental impact.

2 Analysis of current State-of-the-Art Separation Technologies

2.1 Lead (Pb)

2.1.1 Physicochemical Separation

Physio-chemical approaches refer to methods that exploit the physical and chemical properties of substances to separate components in a mixture. In the context of lead, specifically in the form of Pb^{2+}, recent studies indicate that Adsorption and Permeable Reactive Barriers (PRB's) are particularly effective remediation techniques.

Adsorption is a physiochemical process in which solute molecules are transferred from the bulk phase of a fluid onto the surface of a solid substrate, driven either by van der Waals forces (physisorption) or by the formation of chemical bonds (chemisorption) [35]. In practice, adsorption is applied either in batch systems, where adsorbents are mixed with contaminated water, or in fixed-bed columns, where water passes through a packed layer of adsorbent and Pb^{2+} ions are retained on the surface. This method offers several advantages, including low operational costs, ease of implementation, a high degree of purification, high profitability and straightforward system design, making it a widely employed technique for the removal of Pb^{2+} from aqueous solutions [36]. Traditionally, activated carbons, natural and synthetic zeolites, and ion-exchange resins have been widely used as adsorption materials. However, modern research has shifted towards developing highly efficient adsorbents based on carbon nanomaterials, such as carbon nanotubes, nanofibers, graphene, and graphene oxide (GO), due to their large specific surface area and high thermal and electrochemical stability [37]. A key limitation of adsorption is that its removal efficiency is strongly influenced by multiple parameters, including pH, contact time, adsorbent dose, initial concentration, and temperature, which can complicate process optimisation [36]. To address these challenges, machine learning models, such as artificial neural networks (ANN), support vector regression (SVR), and multivariate linear regression (MLR), can been applied to accurately model optimise adsorption performance. These models capture nonlinear dependencies between process variables and adsorption capacity, allowing accurate performance prediction and data-driven optimisation for the design of high-efficiency biosorbents, reducing experimental effort and improving scalability [38].

Permeable reactive barriers (PRBs) operationalise adsorption in situ, extending this mechanism into a subsurface system for groundwater remediation. Using a ZSM-5 / Silica Aerogel composite (25% ZSM-5 / 75% SA) adsorbent enabled a max adsorption capacity of ~476.2 mg/g over a range of pH (3-11), with an initial Pb^{2+} concentration of
50 mg/L, contact time of 60 min, and an adsorbent dose of 0.05 g in 100 mL [39]. PRBs are passive remediation systems developed to intercept and treat contaminated groundwater, offering low cost, and broad applicability [40]. PRBs installation involves placing a permanent, semi-permanent or replaceable reactive media in the subsurface across the flow of groundwater, where it intercepts the contaminated plume and transform the pollutants over the reactive media into less harmful compounds [40, 41]. Depending on the barrier's composition, contaminants may be adsorbed, precipitated, or chemically transformed, facilitating their removal from the groundwater [42]. In the case of Pb^{2+} separation, activated carbons or zeolites - a class of crystalline naturally occurring aluminosilicate minerals - are commonly used as the reactive substrate embedded within the PRB [43, 44]. The primary limitation of PRBs is their reduced efficiency in treating complex contaminant mixtures, as pollutants often coexist rather than occurring in isolation, particularly in the presence of organic compounds [link]. Although research in this area is currently limited, machine learning approaches, such as compositional data analysis combined with k-means or hierarchical clustering, hold potential for classifying geochemical associations, identifying natural co-contaminants of lead, and guiding the design of more efficient separation strategies [44].

2.1.2 Electrochemical Separation Methodologies

Electrochemical approaches employ electric fields or electrode reactions to remove lead (Pb^{2+}) from aqueous solutions. These methods offer high removal efficiencies and can be integrated with other treatment technologies for enhanced performance. The most widely applied electrochemical techniques include electrocoagulation (EC) and electrodialysis (ED).

Electrocoagulation (EC) involves in situ generation of coagulant ions at sacrificial electrodes, commonly iron, aluminium, or zinc. These ions destabilize dissolved metals, suspended solids, and organic matter, forming flocs that can be separated by sedimentation or filtration [45, 46]. A study on Pb^{2+} removal from battery manufacturing wastewater using alternating current at a current density of 6 mA/cm² with iron electrodes obtained a 96.7% removal, indicating that under ideal conditions EC can achieve Pb^{2+} removal efficiencies exceeding 95%, using iron rod electrodes, direct current (6 mA/cm²), 30-40 min reaction time, pH 5, and mixing rate of 200 rpm [47]. The main advantages of EC include simultaneous pollutant removal and metal recovery. However limitations still arise, including electrode passivation and energy requirements, which are influenced by water chemistry and operational parameters [48].

Electrodialysis (ED) is another electrochemical approach which employs cation and anion-exchange membranes to selectively transport ions under an electric field, effectively separating Pb^{2+} from aqueous matrices [49]. Traditionally ED technology is utilised the field of water desalination, however recent developments in membrane design, including multi-section ED cells and improved ion-selective materials, have enhanced efficiency, selectivity, and applicability to complex wastewater streams [49]. The application of ED to Pb^{2+} removal offers many advantages, including high separation efficiency for positively and negatively charged ions, effectiveness at low metal concentrations, and low operating pressure [50]. Despite these benefits, ED efficiency is not yet comparable to EC, with pilot-scale studies using an anion exchange membrane (AEM: PC SA) and a cation exchange membrane (CEM: PC SK) achieving ~75% Pb^{2+} removal in a pilot scale plant using an applied voltage of 0.6 V per cell pair (across 66 pairs), 2 cm/s velocity, 4 hour batch time, initial Pb^{2+} concentration of 5 mg/L and pH 1.6-2.9 [51]. ED and similar membrane-based desalination systems are also associated with high significant energy requirements and sensitivity to operational parameters, which can limit their large-scale applicability [52].

2.2 Copper (Cu) – Bioremediation

Emerging research on separation technologies for copper are largely focussed on bioremediation utilises biological agents such as plants and microbes to remove or lessen the effects of environmental pollutants [53]. In the context of copper pollution, particularly in the form of cupric ions Cu^{2+}, engineered strains of *Escherichia coli* and the green alga *Chlamydomonas reinhardtii* have shown great potential as low-cost and eco-friendly bioremediation agents.

2.2.1 Bacterial Bioremediation

Escherichia coli (*E. coli*) is a type of bacteria that naturally possesses several copper efflux systems to survive when exposed to toxic levels of copper [54]. One such system is regulated by the CueR protein, which controls the transcription of copper tolerance genes, CopA, a P-type ATPase located on the cytoplasmic membrane, and CueO, a multi-copper oxidase [55]. In this system, CopA exports Cu^{+} from the cytoplasm to the periplasm [56], and CueO converts periplasmic Cu^{+} to the less toxic form Cu^{2+} [57]. Recent advances in genetic engineering have leveraged these mechanisms to enhance bioaccumulation, the process by which copper ions are actively transported and sequestered within the cell [58].

Specifically, wild-type E. coli strains can be modified via recombinant DNA technology to remove or downregulate efflux pathways, while introducing plasmids encoding both copper-sensing and copper-binding elements. These modifications enable the bacteria to bind Cu^{2+} ions and actively accumulate them within the cell, thereby reducing copper concentrations in the surrounding aqueous environment [59]. This bioremediation approach allows for high selectivity for copper ions with minimal generation of secondary chemical waste, however it exhibits slower kinetics relative to physicochemical methods, and may be susceptible to fluctuations in environmental parameters such as pH and temperature [60].

2.2.2 Fungal Bioremediation

Fungal bioremediation has also gained recent traction for heavy metal removal, due to the natural metabolic capabilities of fungi to degrade and detoxify a wide array of pollutants [61]. Fungal species such as Trichoderma, or *Penicillium simplicissimum* have ability to remove copper through simultaneous surface adsorption and intracellular bioaccumulation. In this process, biosorption occurs whereby functional groups on the fungal cell wall passively bind Cu^{2+} ions, while intracellular sequestration simultaneously occurs within the cytoplasm and vacuoles [62]. In batch studies, actively growing T. lixii CR700 was reported to remove up to 84.6% of Cu^{2+} at an initial concentration of 10 mg/L [63], whereas *P. simplicissimum* achieved approximately 63% Cu^{2+} removal at an initial concentration of 100 mg/L [64]. These fungi are capable of maintaining removal activity across varying pH values and in the presence of co-occurring contaminants, however, large-scale implementation requires careful management of metal-laden fungal biomass to prevent secondary contamination, as it can be hazardous if not properly handled [61, 64].

2.2.3 Algal Bioremediation

Green algae, such as *Chlamydomonas reinhardtii*, have also demonstrated significant potential for copper bioremediation. C. reinhardtii removes Cu^{2+} through both biosorption to cell wall components and intracellular bioaccumulation, while simultaneously facilitating the biosynthesis of valuable sub-10 nm copper nanoparticles (Cu NPs) [65]. The effectiveness of this copper removal depends largely on algal viability, as active metabolic processes enable reduction of Cu^{2+} to Cu NPs and proper intracellular accumulation [66]. In batch experiments with wastewater-like nutrient media containing 10 mg/L Cu^{2+}, viable *C. reinhardtii* removed ~20-30 % of initial Cu^{2+} under experimental conditions, depending on light and growth parameters, while forming well-dispersed, polydisperse Cu NPs [67]. Altough this is a relatively low removal rate compared to the other bioremediation agents, *C. reinhardtii* offers the advantage of simultaneously producing recoverable copper nanoparticles in a low-cost and environmentally sustainable manner.

2.3 Cadmium (Cd)

2.3.1 Photoreduction of Cadmium

Cadmium can be removed from water through photoreduction, where it is reduced from its toxic ionic form, Cd^{2+}, to its metallic form, Cd, from water by reacting it with reactive oxygen species. This often occurs in conjunction with the use of a catalyst to maximise the amount of Cd^{2+} that can be reduced in a system by reducing charge recombination and providing active sites for the reduction process. A significant amount of research in Cd^{2+} reduction is focussed on producing and optimising these catalysts and the reaction conditions, depending on the desired application. There is research focussed on the removal of Cd^{2+} under visible-solar light, with a range of catalysts being used, such as Eosin Y-sensitised titanium dioxide in triethanolamine, or bismuth/sulphur co-doped carbon quantum dots [68]. Other research focused on the removal of Cd^{2+} under ultraviolet light, with different catalysts being developed, such as bentonite-supported Zn oxide (ZnO/BT), or adsorption into MnO_2 by sulphite–sulphate cycling [69, 70]. Additionally, reaction conditions such as pH, temperature and reactant concentrations, as well as the presence of other chemical additives, greatly affect the success of Cd^{2+} removal by these catalysts. The photocatalytic activity of the Sulphur and bismuth co-doped carbon quantum dot (S,Bi-CQDs) catalyst was investigated under the addition of scavenger solvents, including ethanediamine, formaldehyde, acetic acid, and methanol. At 300ppm, ethanediamine improved the effectiveness of Cd^{2+} removal by the Bi/S catalyst, reaching a maximum removal of 94% at pH 8.0, initial Cd^{2+} concentration of 10mg and contact time of 120 minutes, temperature of 25 °C [71, 72].

Photoreduction techniques have been in use and developed for water purification since the 1970s, with the optimisation of reaction conditions and production of catalysts in a range of systems remaining a large area of research [73]. In recent years, machine learning and AI are increasingly being used for optimising Cd^{2+} photoreduction techniques, greatly assisting in the speed in which research and development can take place. Machine learning has produced a greater understanding of what features of catalysts and photooxidative conditions are most important for maximising the removal of pollutants. One study used machine learning to determine the optimal pH levels for sulphite–sulphate cycling in radical-based photoreduction processes, while machine learning is also being used to determine and map sources of cadmium pollution, allowing for a targeted response to cadmium pollution at its source [74, 75, 76]. Another study used AI assisted machine learning to investigate the important parameters for cadmium reduction using a UV/malathion/sulphite reaction [77]. The study used Gradient Boosting Regression, Support Vector Regression, and Genetic Algorithm to successfully identify optimal reduction conditions, and develop a model capable of regulating UV intensity and sulphite and Malathion concentration to maximise cadmium reduction efficiency, highlighting the importance of AI in enhancing research and development for environmental protection.

2.3.2 Phytoremediation of Cadmium

Plants are known to absorb cadmium present in soil, with the bioavailability of cadmium largely dependent on soil conditions such as acidity, chelating agents, soil layer structure and the microbial profiles, with the irrigation of cadmium contaminated water causing cadmium to be deposited in soil [78]. Cadmium accumulation in plants is highly toxic, reducing uptake and movement of nutrients and water, increasing oxidative stress, and disrupting metabolism pathways [79]. The ability for plants to absorb cadmium can be exploited to reverse cadmium contamination, with research focusing on how to prevent the toxic effects that cadmium has on plant growth and nutrient uptake or enhance the natural ability for plants to uptake cadmium.

Recent development in phytoremediation has determined that dosing plants with combinations of hormones can improve the ability of the plant to uptake cadmium, among other pollutants [80]. These phytohormone combinations were investigated to determine their effect on plants already classified as cadmium hyperaccumulators such as *Bidens Pilosa* and found that certain combinations of phytohormones could modulate key physiological responses, significantly increasing cadmium phytoremediation of soil. One study found that cultivating soil nitrate reductase producing rhizobacteria drives a strong symbiotic relationship, significantly increasing a plant's ability to phytoremediate soil [81]. To avoid the uptake of cadmium by edible plants, cross breeding and genetic modification are being explored, intending to produce non-edible plants that are hyperaccumulators of cadmium, reducing the concentration of bioavailable cadmium in agricultural areas [82, 83]. Since effective phytoremediation relies on the survival and stable growth of plants in soil containing heavy metal contamination, effective methods to stabilise plant growth and bioavailability of cadmium are necessary to effectively phytoremediate cadmium contamination [83]. In high concentrations, heavy metals can inhibit plant growth, preventing phytoremediation. Biochar can be added to soil to supplement phytoremediation, where its porous structure enables adsorption of heavy metals, reducing the concentration of heavy metals that are available for immediate biosorption, while its carbon-based physicochemical properties improve water retention and soil fertility, promoting plant growth [84, 85]. Machine learning has assisted the development of biochar assisted phytoremediation, with one study using neural networks to investigate 24 soil characteristics and predict and optimise the efficiency of cadmium fixation by biochar in soil, providing valuable insights that can guide further research and optimisation of biochar applications in soil remediation [86]. Studies on the large-scale or industrial application of phytoremediation and photoreduction for cadmium removal remain rudimentary, with current known reaction and activation conditions not notable.

3 Discussion of Challenges and Future Perspectives

3.1 General Identified Challenges

Within the field of heavy-metal remediation in water systems, multiple challenges exist and continue to be identified as technology further develops. On a broad scale, the most prevalent consideration is economic, with scale-up of many remediation technologies being an expensive process, for newly advanced techniques in particular.

3.1.1 Data Availability and Monitoring

One common challenge across most water treatment systems is the lack of data availability and insufficient monitoring. Traditional in-situ sampling methods are costly and time-consuming, leading to a general lack of consistent monitoring. Heavy metal contaminants often exhibit a dynamic nature, with sudden influxes occuring without the real-time monitoring required to detect these changes early. Such influxes could occur due to natural events such as flooding, which can wash agricultural or industrial contaminants into waterways [12]. Improper waste management can also cause sudden contamination, with the discharge of mining or manufacturing byproducts directly entering water systems. Advancements are being made however, with researchers in Nanchang, China developing remote sensing methodologies to detect heavy metals in aquatic environments, using the reflectance and absorbance characteristics of these elements [87].

3.1.2 Emerging Contaminants

There are also a number of emerging contaminants that utility systems and treatment plants aren't designed to handle. These are synthetic or naturally occurring substances, that are not commonly detected within an environment. [88]. Prominent examples of these contaminants include pharmaceuticals, pesticides, surfactants and fire retardants. Further dangers to public health and the aquatic environment arise from these contaminants, with the extent of these impacts considerably under-researched. For example, PFAS (forever chemicals), have recently been identified in tap water around the Greater Sydney Area. The current studies of these chemicals in Australia are sparse, highlighting the need for further assessment, and more frequent monitoring [89].

3.1.3 Climate Change and Population Growth

It is important to address the increasingly releveant discourse surrounding climate change, and the rapidly growing global population. As global population continues to grow, so too does the demand for treated water. This demand is also now coming from regions further away from the existing central infrastructure. The combination of rapid urban development with the uncertainty of climate change, particularly flooding events, means there is rising concerns about urban water quality risks.

3.2 Challenges associated with Lead Separation

3.2.1 Adsorption

Adsorption capacity refers to the quantity of adsorbate that a given mass of adsorbent can capture in specific conditions. [90]. This capacity is strongly influenced by a range of factors, which includes the properties of the adsorbent and adsorbate respectively, as well as the process conditions. One of the main limitations of this technique is the adsorption capacity in most applications is still relatively low compared to the concentration of contaminants. This correlates to large expenses to effectively remove the required amounts of adsorbate. Furthermore, with the vast range of influencing factors impacting the adsorption process, it can a complex process to optimise. Addressing this problem could integrate machine learning models such as ANNs and various regression models. These could offer process optimisation in terms of parameter tuning, as well as improved predictive modelling, capturing the complex and non-linear relationships within this technique.

3.2.2 Electrochemical techniques

It is important to address the inherently higher energy demand of the electrochemical techniques discussed. There is a baseline energy required to produce an electric current, which can further increase with certain factors and reaction conditions. For electrocoagulation this includes current density, heavy metal concentration, and reaction time [91]. For electrodialysis, the energy requirement depends on salinity and membrane resistance. In terms of the removal of lead from water, adsorption is the far less energy intensive option as it Is primarily pump driven. Whilst energy demand is not the only factor when implementing these separation techniques, it is a prominent feasibility consideration.

Whilst electrocoagulation offers the advantage of simultaneous removal of heavy metals and other pollutants, there are numerous constraints that are required for the successful removal of Pb^{2+} to a high degree. Tight pH control is required, and the process is severely inhibited by the presence of competing ions such as Cd^{2+}, Zn^{2+} and Ni^{2+} [91]. This presents challenges in real-life water systems, in comparison to the idealised experimental conditions that produce these high efficiencies.

Currently, electrodialysis has had limited applications in waterway treatment due to problems associated with the membranes. This includes membrane fouling, scaling and concentration polarisation [92]. Like other removal techniques discussed, pH has a significant impact on the efficiency of electrodialysis. There is a small pH range to which concentration polarisation, current efficiency (number of ions through the membrane relative to the electric potential difference) and energy consumption are optimised [93]. This pH range is estimated to be optimal between pH 3 and pH 6. The applied voltage is also an important factor to balance, as the membrane can undergo ion exchange when the voltage is too low, and regeneration when it is too high.

Furthermore, the generation of secondary pollution is an issue in for electrodialysis based processes. Several toxic and hazardous organic, and inorganic chemicals are required in these processes, as cleaning and pH control agents [94]. Therefore, the application of electrodialysis on a wider scale remains a technical and economical challenge, not yet feasible compared to other techniques.

3.3 *Challenges associated with Copper Separation*

3.3.1 *Bioremediation*

There are several hurdles surrounding the wider-scale implementation of bioremediation for the removal of copper from water. In general, there is a high dependency of this process on a variety of environmental factors, such as pH, temperature, and the concentration of the heavy-metal contaminant. Whilst copper is an essential micronutrient, vital to life, it can also become toxic at elevated levels. Many of the microorganisms used in the bioremediation process have a sensitivity tolerance, above which the microbial activity is limited, and eventually the concentration can become toxic. Other environmental conditions can also lead to inefficiencies via bioremediation, such as hyper-salinity and acidic conditions [95]

As an emerging separation technology, many of the longer-term impacts of this technique are yet to be studied. There are a range of potential secondary risks, such as contaminant desorption, nanoparticle release, and ecotoxic impacts that still need to be assessed, to ensure long-term environmental safety [84].

3.4 *Challenges associated with Cadmium Separation*

3.4.1 *Photocatalytic Reduction of Cadmium*

The feasibility of Cd removal via photoreduction is most significantly limited by the catalysts used, and their properties. For example, ZnO based systems rely primarily on UV light for reduction, but UV is only 4-8% of natural sunlight [96]. A much larger proportion of sunlight is made up of visible wavelengths, yet the catalyst systems that rely on these wavelengths are still maturing in terms of cost and catalyst stability when applied to Cadmium. Furthermore, ZnO based catalysts are prone to photo-corrosion under UV light, meaning the breakdown of the crystal lattice and a loss of photocatalytic effectiveness [97]. Further research is still required to raise the photostability of many catalyst systems when exposed to prolonged light irradiation.

3.4.2 *Phytoremediation of Cadmium*

Despite adequate levels of research into phytoremediation, there are significant constraints associated with adoption in field. One of the main risks is the uptake of Cadmium into edible plants, entering the food chain and posing danger to human and animal health. Genetic modification is being explored, with the intention of producing a plant that is a hyperaccumulator of Cd and not edible, therefore reducing the bioavailable concentration of Cd in agricultural areas.

In comparison to other separation techniques, phytoremediation is considered quite a slow process, with large variability in performance between real-life sites. It is a promising option when tested experimentally, but in when implemented in real water systems the results have been inconsistent, and scaling strategies are immature and unproven. There is also limited understanding of the longer-term environmental risks of this method, in terms of human and ecological health.

There is potential for further development of this technique, extending the process to metal recovery as well, termed phytoextraction. This dual benefit is a prime example of the circular approach that could be implemented in a range of current technologies and practices, moving towards a more sustainable future society.

3.5 *Future Perspectives*

3.5.1 *Implementing Circular Approaches*

One consideration for the future is around aligning with the approach of Circular Economies. The traditional, linear model of find, use, dispose, is being shifted to focus on the recovery and repurposing of resources. In the context of contaminated waterways, valuable heavy metals can be recovered, alongside treatment materials which can be reused.

In terms of tackling the challenge of population growth, and the rising demand for water in regional population centres, the transition to modular systems could also be considered. This could involve more compact, mobile separation units for small or crisis-affected communities. Potentially a closed-loop system, a modular system could follow the principles of a circular approach, reusing treatment materials like adsorbents, minimising the discharge of byproducts. This would mean less dependence on centralized infrastructure, making treated water accessible for everyone, and on a much shorter timeframe than the full development of treatment plants.

3.5.2 *Infrastructure and Asset Management*

As seen in the case of the Flint Water crisis, proactive management of water-related infrastructure is pivotal in ensuring ongoing safety and success. Effective asset management by governments and other stakeholders is required, with careful consideration of budgeting, climate risk, growing populations and public policy. There is a strong argument in this sense to incorporate the use of artificial intelligence into this process, modelling the lifetime of assets to better understand the system and the early signs of degradation. Furthermore, with the uncertainty surrounding climate-related risks, machine learning models could be implemented to forecast demand and system operation under future scenarios, providing operators with more information regarding risk, resource allocation and optimisation [98].

4 Conclusion

Heavy metal contamination of drinking water continues to pose a significant environmental and public health concern in many regions of the world. Difficulties such as industrialisation, population growth and ageing infrastructure are becoming increasily prevalent, driving the need for improved separation technologies that are both efficient and sustainable.

Conventional physicochemical techniques, including coagulation, adsorption and membrane separation, have demonstrated high removal efficiencies under controlled conditions, yet remain limited by high energy demand, maintenance requirements and secondary waste generation. Recent advances in electrochemical, biological and photocatalytic techniques have emerged as potential options, but remain costly, difficult to scale, and sensitive to environmental conditions. Future approaches must prioritise systems that are modular, resilient and aligned with circular economy principles. This includes the recovery and reuse of valuable by-products, the regeneration of treatment materials, and the minimisation of process waste. The integration of digital tools, including artificial intelligence and machine learning, presents a further opportunity to enhance process optimisation, predictive maintenance and adaptive control of treatment systems.

In summary, the sustainable removal of heavy metals from water systems will require continued collaboration across the engineering, materials, digital, and government fields, ensuring access to safe water through adaptive and resource-efficient treatment strategies.

Author Contributions

J. Dahdah produced part of section 2, the abstract, graphical abstract; M. Finlayson produced section 3 and 4; S. Jirsa contributed to section 1; B. Lynch contributed to section 1; A. Whitehouse contributed to section 2; B. Binwal and J. Kambanis provided task direction and project assistance, and Dr. Gobinath Rajarathnam provided conceptual direction, research and writing guiding frameworks, facilitated project resources, and direct project supervision.

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AI Declaration

We acknowledge the use of ChatGPT 5.0 (https://chatgpt.com/) to assist in the production of the graphical abstract. It was given prompts and instructions on what to include, including colours, imagery and words and instructed to produce the graphical abstract. ChatGPT was also used for grammar and format

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Production of Diesel Fuel from Hydrocarbon Wastes Utilising Pyrolytic Distillation Recovery

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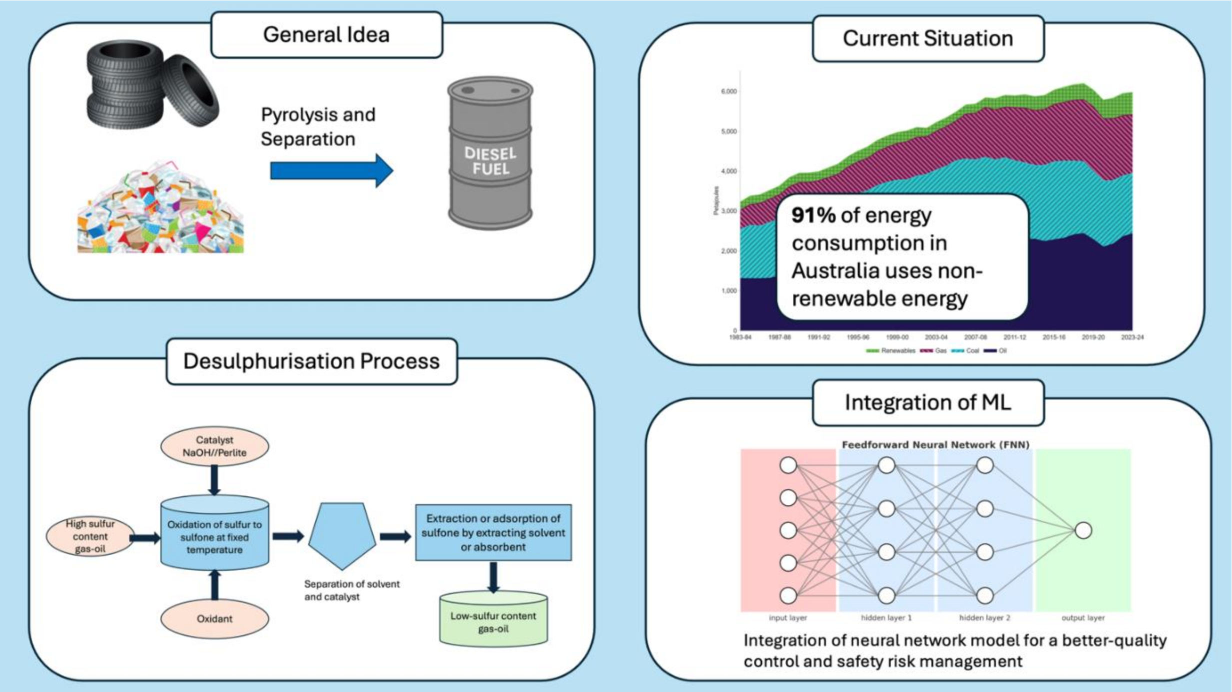
Graphical Abstract



1. Abstract

Pyrolytic separation is an innovative solution to produce diesel fuel via the thermal decomposition of hydrocarbon wastes such as tyres and plastics, achieved by treating the wastes at high temperature in the absence of oxygen. There are numerous studies on factors such as operating temperature and catalyst choice, which must be optimised to design a sophisticated system. In addition, integrating AI and other emerging digital technologies enables real time dynamic control and kinetic analysis with accuracy significantly higher than past empirical models, allowing better quality control and enhanced safety risk management. Although the technology is currently at laboratory scale, it has strong potential to contribute to Australia's sustainability by reducing waste and producing energy simultaneously. While there are limitations that need to be addressed, various advanced technologies could effectively mitigate issues including yield recovery, energy intensity, and sulphur or metal contamination.

Keywords: Pyrolytic distillation, hydrocarbon waste, Diesel, thermal decomposition, Artificial intelligence (AI)

2. Introduction

With the introduction and its extremely expeditious growth of artificial intelligence (AI) in recent years, the globalisation of the markets and trading is accelerating faster than ever. Whether at a macro or micro scale, this is resulting in a huge increase in the demand for transportation of goods around the world. Particularly in Australia, where the fundamentals of the economy are supported by the exportation of minerals and natural gases, 1,558.2 million tonnes of goods were exported by sea, with a growth rate of 1.5% per annum[1]. The use of diesel fuel is essential to support the growth of the Australian economy, with total consumption of 1,269.9 PJ in FY23/24 equating to 21.2% of the nation's net energy consumption[2]. However, at the same time, it is a fundamental global mission to reduce the use of fossil fuels in order to achieve Australia's target of creating a net zero society by 2050 for a sustainable future[3]. As the consumption of diesel fuel produces an enormous amount of greenhouse gases (GHG), which contribute to global warming, it is crucial to come up with innovative strategies that would reduce the use of diesel produced directly from fossil fuels. Several initiatives for solving these two issues simultaneously have been explored, including the implementation of electric vehicles and hydrogen fuel cells, the production of biodiesel, and energy-recovery techniques[4,5]. Among these, energy-recovery techniques, particularly using hydrocarbon wastes to produce diesel fuel, have captured attention. This is mainly due to the high yield potential in the wastes, environmental friendliness from reducing waste, as well as the limited release of greenhouse gases, which provides an implementation of a circular economy to enhance sustainability[6].

The energy recovery from hydrocarbon wastes uses streams that consist of a high density of carbon and are originally made from fossil fuels, with examples including tyres, plastics and lubricating oils. Currently in Australia, only a small proportion of hydrocarbon waste is recovered (either reused, recycled or energy-recovered). For example, in FY23/24 the plastic and tyre recovery rates were 14.1% and 66% (including export of waste tyres for energy recovery), with the remainder disposed of in landfill[7,8]. In Australia, there is the nation's first waste-to-energy recovery station operating in Kwinana, WA, which is a facility expected to process 460,000 tonnes of landfill and generate 38 MW of electricity every year[9,10]. Although this could potentially accelerate the energy recovery of wastes, currently there are no other facilities projected for energy recovery in the nation. From a legal perspective, there have been some developments in legislation for the disposal and recovery of hydrocarbon wastes. However, their contribution to the circular economy is quite limited. For example, from October 2021 the federal government amended the Recycling and Waste Reduction Act 2020, which now regulates the exportation of waste tyres, requiring companies to have a waste-export licence to do so and for the tyres to be processed into shreds of less than 150 mm[11]. However, despite this, burying waste tyres on mine sites is still standard practice across the nation, which is often regulated at state jurisdiction level under long-standing legislation, such as the Environmental Protection Act 1994 in Queensland[12].

Based on this current situation, the journal will explore the potential implications of energy and resource recovery from hydrocarbons, utilising a pyrolytic distillation system for diesel fuel production. The pyrolytic separation of hydrocarbons is a well-known process, where hydrocarbon wastes are thermally decomposed as they are treated with intensive heat in the absence of oxygen[13]. More specifically, the long polymer chains of wastes such as polyethylene and polyisoprene are broken down into paraffins and naphthenes, the main components of diesel fuel, which are then extracted through a series of separation methods[14]. The first half of the journal will investigate the innovative methods that have been researched to optimise the entire process. This includes consideration of factors such as yield, purification and quality control. Additionally, the potential integration of AI or other machine-learning models will also be investigated, as it can make a significant contribution to system prediction, which could consequently result in improved dynamic control and kinetic analysis of the system. Based on the innovative systems that have been researched, the second half of the journal will consider their actual feasibility in Australia, with a series of careful evaluations including economic, physical and environmental factors over varying time spans. This includes identifying possible challenges, risk assessment of contaminants, scalability and the energy intensity required during the separation process, each with realistic solutions to address them.

3. State of the Art in Advanced Separation Strategies

3.1 Current Methodologies

Through an analysis of 23 different papers on pyrolytic distillation in diesel recovery the main two sources that were prevalent were tires and plastics. All papers have shared the same fundamental process of pyrolytic distillation. This is the heating of materials to high temperatures in the absence of oxygen decomposing the source material[15]. From here the products can then be separated and filtered to extract only the liquid component[16]. The liquid can then be distilled to separate the diesel. However, there are various challenges depending on the source of the fuel and optimising efficiency.

3.1.1 Plastic Pyrolysis

70% of the papers investigated are congruent with the pyrolysis of plastics being optimised at 580°C and separation at 180°C. However, these papers differ slightly with varying techniques and the use of catalysts. Additionally, there are several environmental concerns regarding the production of chloride and organohalides. These compounds are produced at high temperatures which corrodes metal, causes catalyst poisoning and fouling[17]. Additionally, the chlorinated pyrolysis oils risk forming dioxins/furans, high chloride wastewater and toxic combustion products (HCl & phosgene)[18]. To mitigate these issues first a rapid quench should be used to condense the HCl. Next a scrubber can be used immediately after the quench to neutralise the acid and remove lighter chlorinated organics. Finally, bag houses are used to remove particulate matter before the gases can be released to the atmosphere[19].

3.1.1.1Plastic Fuel Quality

There a several key specifications that make a hydrocarbon solution diesel and more specifically one that can be used in combustion engines. According to EN 590 diesel should have the following properties, a density of 820kg/m^3, cetane index of 46, minimum viscosity of 1.3 cSt, CFPP of -10°C - 0°C and a FAME value of up to 7%[20]. Fuel that is extracted through plastic pyrolysis for the purpose of being used for diesel unfortunately must be further refined. This is evident with Gala et al (2020) which shows that the distillate didn't conform with traditional diesel with post-consumer white plastic waste producing a diesel with a density of 791 kg/m^3, viscosity of 1.89 cSt and a CFPP of 22°C[21]. Similarly, Jahirul et al (2022) indicate that the limiting factor for the diesel to be used in cars is the flash point of 78 °Cmin^{-1}vs standard diesel of of 61.5 °Cmin^{-1} if using polypropylene[22]. However, these properties can be fixed through various techniques such as dilution and hydrotreating. Mustayen et al (2023) indicates the benefits of using a mixture with ultra-low sulphur diesel (ULSD) as a 20% mixture resulted in a 3.9%-4.74% increase in thermal brake efficiency, a 3% increase in torque and power and a 14.51% decrease in CO emissions. This results in an increased cetane number of 48.4 and viscosity of 2.75 cSt whilst decreasing density of 840 kg/m^3 for a 20% volume mixture of ULSD[23]. Bezergianni et al. (2017) found that hydrotreating improved the flash point from 48°C to 52.5°C and reduced sulphur content from 43 to 12 mg/kg[24].

3.1.1.2 Distillation Optimisation

Wiriyaumpaiwong & Jamradloedluk (2017) optimised the distillation column for the separation of plastic pyrolysis oil. Their findings found the optimal reboiler temperature was 180°C separating a diesel oil with a density of 817.5 kg/m^3, a viscosity of 3.62 cSt and a calorific value of 36382.9 kJ/kg[25]. As such, the diesel still contains some heavy impurities and may need to be further refined to meet certification. However, Thahir et al. investigated the use of a refinery distillation bubble cap plate column indicating that it decreases the ash and wax content. This allows for the kerosene and gasoline type fuels to be directly applicable however, still require diesel fuel to be recycled again to meet the specifications[26]. Meanwhile, Jahirul et al (2022) utilises vacuum distillation which improves quality and whilst maintaining a yield of 57% with polypropylene producing a diesel which meets all diesel specifications[27].

3.1.1.3 Plastic Pyrolysis Optimisation

Kassargy et al (2017) found that the use of a 10:1 USY zeolite to plastic ratio during pyrolysis caused an increase in yield to 70%. Polypropylene favoured carbon lengths 5-11 and polyethylene favoured carbon lengths of 10-13[28]. Jahirul et al (2023) also highlights the use of high-density polyethylene and polypropylene are ideal for diesel extraction with yields of 57% and 53.7% respetctively[27]. However, Kassargy et al (2017) indicate the need for further fractionation for gasoline and diesel to meet standards[29]. Contrastingly, Wang et al. (2021) suggests that a nickel catalyst shows more potential for deriving diesel from plastic compared to the USY zeolite catalyst. This is due to the high heating value of 45 MJ/kg and H/C ratio of 1.94[30].

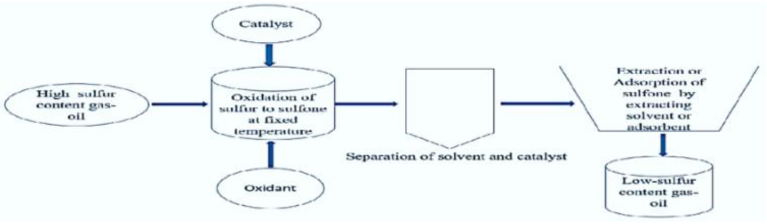


Figure 1: process diagram of the desulphurisation process

3.1.2.1 Tyre Pyrolysis Purification

The main challenge that all papers elucidate is the high sulphur content of the tires. As such, the general desulphurisation process can be seen in Figure 1 highlighting that the primary investigation will be the catalyst. Yildiz & Aydin (2023) indicate the most effective catalyst was Perlite decreasing the sulphur content by 25.3%. However, they also indicate that the sulphur content is heavily dependent on the temperature of pyrolysis[31]. This is in line with Aydin & İlkılıç (2012) who indicate that sulphur can be minimized at 0.825% by undergoing pyrolysis at 550°C with a liquid yield of 39.18%. However, the yield can be maximised at 500°C with a yield of 40.26% and only a minor change in sulphur content of

0.83%[32]. Contrastingly, Yildiz & Aydin (2023) findings show that the maximum diesel yield of 42% is collected when the reaction is at 300°C[31]. This large difference is likely due to the heating conditions such as different residence times and heat transfer rates. However, they both indicate the need to consider the end use of the diesel and whether it will be subject to regulations. As a greater amount of diesel can be extracted at lower temperatures, however, will have a larger sulphur content. Furthermore, Aydin & İlkılıç (2012) indicate that the most effective catalyst was NaOH decreasing sulphur content by 83.75%[32]. Additionally, Ayanoğlu & Yumrutaş (2016) use CaO and Zeolite indicating that 10% wt CaO produces a diesel like fuel with a density of 830 kg/m^3, viscosity 3.12 cSt and a HHV of 42.18 compared to standard 42.7[33]. It is therefore evident that NaOH is the most effective as both papers conclude that CaO underperforms compared to their counter parts. However, the optimal temperature appears to be at 500°C but is clearly dependent on the rate of heat transfer and residence times[33]. As such, it is imperative that future studies focus less on temperature as it is inconsistent and instead focus on measure of heat transfer for greater consistency and comparability.

3.1.2.2 Tyre Separation/Pyrolysis Techniques

Ayanoğlu & Yumrutaş (2016) investigated the use of a rotary kiln reactor as it provides more uniform heating with better mixing reducing impurities. This is affirmed with the properties of the heavies having a density of 827 kg/m^3, viscosity 3.16 cSt and a HHV of 42.548. In addition, it improved yield whilst resulting in less carbon black[34]. Meanwhile, Costa & Santos (2019) indicate the possibility to use steam to flash distil the liquid. Flash distillation favours time and energy over yield, however, the article indicates that it is only effective at separating the light component[35]. As such, it is not suitable for diesel production but in the extraction of petrol a comparative analysis is required to determine whether flash distillation is more economically effective. Meanwhile the traditional distillation has been explored through a pilot scale distillation plant by Martines et al (2023) which concludes ideal operating conditions are a reflux ratio of 2.4 with a reboiler temperature of 250°C[36]. As such, yield would be maximised by using multiple stage distillation and a rotary kiln.

3.2 Integration of Emerging Technologies

In recent years, the integration of various emerging technologies, such as artificial intelligence (AI), machine learning (ML) and deep learning (DL) have significantly improved and transformed separation processes. These technologies offer improvements to prediction accuracy through shifting previous reliance on process-specific empirical relations to more versatile analysis of feedstock mixes. It also allows for enhanced analysis of thermal behaviour and chemical kinetics that allows for real-time analysis and improved system control. Generally, this allows for improved scalability, efficiency and maintenance, however, they have common drawbacks of higher capital investments and are often limited by data scarcity.

3.2.1 Improved Prediction Accuracy and Non-Empirical Analysis.

AI has shown strong potential in improving the prediction accuracy of yield volume and properties in thermochemical separation processes such as pyrolytic distillation. This has been achieved through continuous real-time analysis of feedstock characterization data (such as through proximate and ultimate analysis) and operating conditions to support modelling software such as Aspen Plus. This approach allows for more accurate predictions through avoiding costly and time-consuming empirical experiments. This is shown through consistently higher R^2 values than empirical correlations (up to 0.9759 for HHV predictions)[37]. This also allows for handling of more complex feedstock blends using distillation conditions as input features. For example, through using the feedstock, catalysts and operating conditions as numeric features in an ANN model, the hydrogen richness of syngas was able to be predicted in a range of various feedstock blends[37]. This has also been beneficial in petrochemical pyrolysis, where complex plastics and oils are difficult to characterize due their ranges of molecular complexity. AI can correlate molecular structures to physiochemical properties for more accurate predictions in hydrocarbon pyrolysis[38]. However, this is limited by the quality of input data for the models as for some feedstocks there is data scarcity, limiting applicability[37,39]. An additional limitation is the non-uniformity of data sets in broader applications, emphasizing the future need for data integrity and standardization[40]. Furthermore, there are computational limitations of analysis methods such as ultimate analysis. While these methods have superior accuracy, they are more demanding, resulting in slower computation time and greater energy requirements. This limits the versatility of these models in systems where faster computation is required, though this is being addressed through experimentation with hybrid models with DL networks.

3.2.2 Dynamic Control and Kinetic Analysis

These technologies also allow for more dynamic control and optimisation as traditional kinetic modelling methods require understanding of complex thermal phenomena and kinetic parameters. These are found from empirical experiments, increasing the time and resource costs and drastically reducing their applicability in unseen scenarios. The use of AI, such as through FNN and SVM models, bypasses these requirements and can directly correlate real-time data to observed trends.

From this, kinetic data (reaction order, activation energy and pre-exponential factor) can be reliably found by training these models on feedstock composition and thermal data. This can improve performance with more adaptive and predictive responses to system conditions when integrated into modelling software[37]. Further studies also show how sensitivity analysis can be integrated with AI models to improve prediction quality at a wider range of operating conditions previously limited by practical empirical testing, improving the versatility and computational efficiency of these models[40]. For example, through combining historical CFD trends with real-time data in a LSTM network, reactor mass flow rates were able to be solved up to 30% faster, improving real-time prediction accuracy and computational efficiency[39]. An additional point is how ANNs can be hybridized with traditional kinetic models to greatly improve generalization and accuracy. These systems combine white boxes (based upon physical laws) which grounds simulation behaviour in known laws, while the black box (experimental ML models) models are applied to find unknown values in a more complex system through non-linear analysis of subtle complexities that are normally simplified out of analytical solutions[41]. However, these models can often be overwhelmed by unstandardized data with high dimensions. This is significant for pyrolytic distillation as thermogravimetric analysis (TGA) data is often used in these systems, which results in time-dependent data, increasing data complexity. DL algorithms have been implemented into these systems to improve the real-time analysis of temporal input data. The use of Bi-LSTM DL models has allowed for far stronger predictive accuracy in time-dependent systems, with R^2 values of 0.998 compared to EML which typically have a score of around 0.885. However, DL takes considerably more computational resources (for example the Bi-LSTM model had 86 million parameters and took 40 minutes to train), reducing their applicability in smaller-scale systems, encouraging the use of specialized hybrid models[42]. The real time analysis also allows for the implementation of predictive maintenance. Trends of potential failures and performance deterioration can be identified based upon real-time input data with non-linear analysis of process parameters[38]. This improves economical long-term feasibility of these systems by reducing downtime and improving resource efficiency that previous first-principle software could not handle in real time[43,44].

3.2.3 Model Architecture

To ensure robustness in AI systems, various sensor data is required to ensure accurate data acquisition. Though it will vary, key sensors would record temperature, pressure, stream flows, duty, pressure drops, stream density and spectroscopic data, as well as other specific variables for each case. The goal of this array of information is to enable soft sensing approaches, where difficult variables such as stream composition and volatility and inferred from empirical relations to more easily collected data[45]. Additionally, to maintain predictive accuracy across varying conditions and systems, a structured validation plan is critical to prevent model drift. In industry, there are a few current approaches to this, the most common is through using rollback rules[46] and rolling-window calibrations[47]. In these cases, periodic retraining is conducted using the most recent operational data analysed against historical trends. This allows for the implementation of automated rollback triggers when drift occurs (for example continued prediction errors against standard thresholds), reverting to the last validated models. In systems that have more feedstock and operating condition variability, cross-campaign checks are used to validate models under different profiles and seasonal trends when there is larger variation. These measures allow for continuous accuracy validation to prevent model drifting and ensure model learning at a reduced risk of runaway error. Examining the future of model architecture, industry standards are learning towards hybrid approaches pursuing the ANN white-black box models discussed above to leverage physical laws for interpretability and accuracy while exploiting AI for non-linear complexity[38], as well investing into predictive maintenance.

3.2.4 Conclusion

In evaluation, the integration of AI, ML and DL into pyrolytic distillation enables real-time analysis and control of complex systems, bypassing the limitations of traditional empirical methods. AI driven models not only enhance scalability and energy efficiency but also support predictive maintenance, improving operational reliability and reducing resource waste. Challenges remain in data standardization, computational demands and data availability. The development of physical analysis with AI hybrid models allows for a well-rounded solution. As the field continues to evolve, the strategic implementation of AI technologies will be critical in advancing separation science toward more accurate and environmentally efficient solutions.

3.3 Comparative Analysis

While the idea surrounding pyrolysis of waste streams to create diesel fuel is a fantastic way to improve overall circular economic practices, there are limitations that currently prevent their scale up and implementation. A common problem surrounding recycling practices is the high variance in both composition and quality of waste input streams. This makes it difficult for both current physical pyrolysis methods to produce effective and quality product, and for emerging simulation and analysis using AI, ML and DL, to accurately measure and predict required inputs and outputs.

3.3.1 Strengths of pyrolysis for diesel synthesis.

The opportunity to use pyrolysis as a synthesis pathway for diesel is an important area currently in research. If a successful method is developed, it will be an extremely effective practice at improving the circularity of international trade, as there is minimal use of the extremely large plastic and tyre waste streams present. Further, this practice would be beneficial in reducing the stress on the current diesel synthesis, with Kelkar[48] analysing that there are only enough petrochemical oil resources to meet the demands of the population for approximately the next 50 years. Ncube et al[49] cited that a cumulative amount of approximately 6300 Mt of plastic waste has been generated up to 2015, with generation increasing exponentially with each year. From that, only an estimated 9% was recycled, and 79% was thrown into landfill. This means that with an effective recycling program and method of recovery from landfill, there is a large resource that can be used for a feed stream. This ideal provides solutions to two of the most important issues currently effecting our economy: a way to reduce dependence on the ever-depleting natural petrochemical resources and a way to make use of the ever-increasing plastic waste stream that is a result of modern industrialisation.

3.3.2 *Limitations of pyrolysis for diesel synthesis*.

Aside from the idealistic goals of using waste streams to synthesise diesel by pyrolysis, there are many difficulties that make its practicality difficult. Firstly, the need for a consistent quality feedstock of recycled waste streams is essential if its implementation can be viable. The recycling practices currently set up in both industrial and community systems do not produce quality feed at a large enough scale to ensure the effectiveness of a pyrolytic diesel system would be optimal. Whilst the feasibility by looking at the sheer volume of plastic waste being produced seems ideal, incorrect recycling practices make obtaining a stable feed difficult, with Ragert et al[50] citing that worldwide 150 Mt of plastic annually ends up in landfill rather than recycling, approximately half of all plastic waste. Further, these waste streams that are being recycled are a heterogenous mixture of multiple different plastics and additives. Common plastics like PET, PVC and PE all have different properties and additives requiring different approaches, meaning for an effective pyrolysis to occur our streams would have to be separated and refined to ensure fuel quality, adding more energy and process requirements. As an example, Qureshi et al[51] specifically raises the case of PVC, citing difficulties in its thermal degradation pathway as many of its chlorinated intermediates cause corrosion to the reactor and leave the product halogenated, resulting in a practice that would need constant repair, cleaning and replacement. Additionally, these difficult feedstock materials and additives lead to issues surrounding the pollutants that are a byproduct of their pyrolysis. Often additives such as flame retardants and dyes are added to plastics and tyres for benefit in their initial use, but these additives can be toxic, environmentally damaging and difficult to remove. Tyres have many additives on top of their synthetic rubber compound to improve durability, thermal resistance and traction. A common practice in tyre manufacture is vulcanization, which adds sulphur to create disulphide cross linking between polymer chains, improving strength. These bonds are incredibly strong, making the removal of the sulphur additives difficult. The most common practice for removal is Hydrosulphurisation (HDS), but this process is very energy intensive and not economically viable on a larger scale, with Hossain et al[52] stating that in testing at optimal conditions (250°C, 2 Bar) only a sulphur removal of 87.8% could be achieved (noting that this is before pyrolysis can occur, adding additional stages and energy requirements to the system). For the compounds that cannot be removed from the feed stream, this causes problems with the emissions in pyrolysis. Pivato et al[53] researched into the emissions of various pyrolysis plants and found that waste tyre pyrolysis generated large amounts of NO_x and SO_2 gasses which are harmful to the environment. Further development of both processes and recycling practices are needed for effective implementation of the systems into current synthetic pathways.

3.3.3 Strengths of emerging prediction and simulation tools (Artificial intelligence and software).

In recent years, significant advancements in the areas of computer and data science have brought to light the extremely useful potential of artificial intelligence and simulation software as a way of optimising processes in an extremely broad application. For pyrolysis in particular, the development of simulation software and pyrolysis-based predictive models are providing promising results for implementation into industry, optimising process economy and efficiency. An example of application can be seen in an article by Ayub et al[54], where multiple ANN and ML models were given literature data (composed from 280 individual experiments) and trained to predict pyrolysis outputs (such as oil and gas yields and optimal reactor conditions). Models such as CatBoost Regressor (CatB) and Extreme Gradient Boosting (XGB) were seen to perform extremely well at predicting outputs, with R^2 value ranges of 0.92-0.98 and 0.91-0.98 respectively over various pyrolytic scenarios. This is a perfect example of what with further development could revolutionize how we approach pyrolytic process plants. The implementation of AI based subsystems into the design process will reduce the time requirements for design and allow for systems to be developed with incredible optimisation of both feed streams and reactor conditions, lowering both chemical and energy wastes. Further, the use of simulation software also is beneficial in the optimisation of design process and plant conditions. In a study by Ismail et al[55], the Aspen Plus® software was tasked with simulating a flowsheet model of waste tyre pyrolysis, which was then verified by comparison to experimental data done by Olazar et al[56]. The model was able to predict the outputs with decent accuracy comparatively to experimental data, but its true benefit could be seen in its modelling of energy requirements and adjustments with a change in reactor condition.

3.3.4 Limitations of emerging prediction and simulation tools (Artificial intelligence and software).

Whilst the implementation of artificial intelligence and simulation software into the pyrolytic plant design process hold much promise, it is important to understand the limitations of such tools. Though AI models have an incredible power for predictability, they are limited in their understanding and are tailored to be optimised for a finite dataset, meaning it is important for engineers using these systems to understand their applicability and proper training. A research review done by Muravyev et al[57] looked into over 100 papers that applied ANN for analysis, with a large proportion of these papers being models used to predict pyrolytic outcomes. They found that in observing these models, though they seemed effective over domains similar to their testing conditions, there was no evidence of their effectiveness upon scaleup and extrapolation. It is important to remember that these models are based on a limited set of conditions, and so extrapolation can be extremely inaccurate (due to model overfitting), limiting model effectiveness when trying to generalise and scale up process plants for industry. Further it is important to acknowledge that these models do not hold the capacity to identify if their entire dataset is invalid, nor can the understand economic repercussions for their estimations (for example, a model may suggest large amounts of a resource that is not easily accessible and therefore isn't economically viable). Overall, the limitations of AI integration into pyrolytic design must be actively supervised by human intervention.

3.3.5 Combination of traditional pyrolytic systems with modern tools

As discussed in paragraphs beforehand, the implementation of modern tools such as Artificial intelligence are limited to prediction and simulation. Traditional methods are still required for pyrolysis, but these modern tools can be used for their optimisation of conditions, yield and energy requirements. The combination of modern tools in design, and traditional process plants and methods in practicality are the future of how we can develop systems that minimise waste and grow a more circular green economy.

4. Challenges and Future Perspectives

4.1 Identified Challenges

This section of the report will outline and define the key barriers that are faced by advanced separation techniques when upgrading pyrolysis liquids to diesel-range fuels. The responses to these challenges will then be outlined in Section 4.2 (Role of Advanced and emerging Separations techniques for mitigating challenges and future directions.)

4.1.1 Sulphur and other contaminants that survive distillation

As outlined in section 3.1, one of the greatest challenges faced when upgrading pyrolysis liquids to diesel-range fuels is the high levels of sulphur contaminants within tyres and mixed-plastic pyrolysis liquids. This is noted as a common problem throughout a majority papers on pyrolysis oils. Serefentse et al (2019) highlighting that on average pyrolysis oils contain 1.6% sulphur[58], this is further backed by Hossain et al (2021) who states the sulphur content in pyrolysis oils to be >1%[59]. These numbers are far above general standards, while the aforementioned papers outline environmental limits to be <0.1 wt% (1000ppm) Sulphur, Australian laws are much stricter with the Fuel Quality Standards Determination 2025 requiring sulphur content of ≤ 0.001 wt% (10ppm)[60].

Sulphur can survive through distillation as the sulphur species within the waste tires and lubricating oils convert into stable heteroaromatic sulphur compounds (benzothiophene, and dibenzothiophene) during pyrolysis. These thiophenic compounds are chemically stable and thermally resistant with their boiling points being close to those of middle-distillate hydrocarbons of diesel fuel[61]. Betiha et al (2018) defines the boiling point range of diesel fuel to be 160–380 °C, whilst benzothiophene and dibenzothiophene have boiling points of 221-222 °C and 332-333 °C respectively, both clearly falling within the boiling point range of diesel fuel[62]. Thus, because of the boiling point overlap vacuum/fractional distillation transfers a large portion of these species into the target product. This is problematic as it can lead to SO2 and SO3 emissions, which cause harms that have been known for many years. Kikuchi outlined in 2001, SO2 is a chronic respiratory irritant and an acid rain precursor, while SO3 is both toxic and corrosive, forming sulfuric acid aerosols that penetrate deep into lungs and damage infrastructure[63]. Thus, while section 3.2 highlights emerging data-driven monitoring, it is clear the intrinsic volatility and thermal stability of these contaminants especially sulphur remains a big obstacle.

4.1.2 Feedstock variability and chemical complexity

An additional complexity faced is the heterogeneous nature of waste streams. It is important to consider the variability and complexity of the waste feedstock, as waste plastics, lubricating oils and tires all drastically differ in their chemical composition, additives, and degradation levels. These variabilities lead to inconsistent pyrolysis yields and fuel quality as it becomes difficult to treat waste streams because of shifts in boiling distributions, stability and the contaminant species profile from one batch to the next[64]. Additionally, waste engine oils often contain metals (Zn, Ca, Fe, Cu, P) from additives and wear particles which can get into the pyrolysis oils poisoning catalysts and reducing performance[65]. In separations, consistency is pivotal, thus it is vital to be able to address waste feedstocks and impurities.

4.1.3 Scalability and operability limits

Transitioning to the emerging technologies as discussed in section 3.2 brings many challenges, one of the main ones being, what works in a lab may not work the same to a larger scale. Transitioning from bench and pilot scales to industry scale raises many new problems and knowledge gaps. As Mong et al (2022) brought up "scaled-up pyrolysis plant are scarce", which can introduce issue with cost, knowledge of real-life yield and safety[66]. These problems arise as large reactors may struggle with non-uniform heating of bulky wastes leading to incomplete pyrolysis or over-cracking. Furthermore, real long-term use will lead to coking and fouling of reactor surfaces not accounted for in pilot tests which will clog pipes and reduce heat transfer efficiency. Thus, when columns are built to scale, important factors that would not be considered or able to be tested during lab runs must be regarded during construction processes. Even when columns are properly sized and designed as per section 3.1.2.2, real life operation constraints will still lower effective capacity and inflate specific energy because units must be run conservatively to protect uptime[67].

4.1.4 Energy intensity in separation process

Producing diesel from pyrolysis oils usually requires multi-stage or vacuum distillation as well as post-distillation clean up. Each of these stages requires highly energy intensive heating and cooling cycles[68], which if not addressed could potentially offset any environmental benefit of using waste feedstock in the first place. It can then become an issue of balance, higher temperatures improve distillation recovery but accelerate cracking and coking, reducing product quality. Meanwhile running at milder conditions lowers degradation but requires larger energy input to maintain vacuum efficiency and multiple separation steps[69]. Thus, balance must be found to manage the high energy intensity whilst maximising recovery and quality while simultaneously creating a new environmental benefit.

4.1.5 Product stability and engine compatibility

A final challenge that is important to examine during design is the product stability. Even when normal specs are met Pyrolysis oils from plastics, tires, or waste oils are prone to oxidation, polymerization, and gum formation during storage as they can be aromatic and olefin-rich[70]. These reactions can cause increased acidity, viscosity and insolubility thus reducing overall long term stability due to poor atomization and incomplete combustion in engines[71]. Thus it is evident during design, the challenge is to account for long term stability and not just immediate post-processing compliance.

4.2 Role of Advanced and emerging Separations techniques for mitigating challenges and future directions.

This section explains how advanced and emerging separation processes will combat the issues prevalent in part 4.1 such as methods of purifications and management of waste streams for environmental considerations. Additionally, alternative methods are analysed to observe methods of reducing energy requirements to ensure unstable pyrolysis liquids derived from tire and plastic waste into controlled and economically viable sources of fuel currently and in the future. Furthermore, scalability limits and feedstock variably can be combated using machine models learning. This allows the plant to be kept stable through sensors and can be optimised so fuel quality remains high despite possible feed changes. Finally, for future directions, we highlight integrating electrified heat and heat-pump recovery, using low impact and regenerable media, modularising units for flexible capacity, and embedding life-cycle assessment driven targets into control to balance compliance and cost.

4.2.1 Desulfurization techniques for Regulatory and Environmental Considerations

Advanced separations encounter hurdles for tyre and plastic fuels which is managing the low sulphur amounts and ensuring appropriate volatility (boiling curve) for predictable ignition times and more stable combustion. For example, in Australia diesel sulphur concentration must be less than 10mg/kg and have tight volatility limits of 95% recovered diesel to be under 360°C Celsius[72]. This achieved through fractional distillation to isolate the middle distillate (diesel) cut, aligning the desired product volatility with the required specifications. Then vacuum distillation is conducted allowing liquids to boil at lower temperatures due to the lower pressure (below atmospheric) in the system allowing for a gentler and precise separation, preventing cracking and undesired heavy molecules ending up in the distillate. Furthermore, post distillation polishing such as oxidative desulfurization (ODS) combined with ionic-liquid (IL) extractions allows for refractory thiophenols which are normally resistant to removal to be oxidised to sulfones that are then readily removed[73].

4.2.2 Energy viability of separation

The pyrolytic distillation process accounts for approximately 40% of the total energy consumption of most refinery and chemical plants, thus the economics and carbon dioxide emissions are heavily dependent on the efficiency of the separation[74]. Additionally Heat Integrated distillation moves heat internally from the rectifying to the stripping section, as this method has reported to reduce energy requirements by 70%[75] which is extremely effective especially when working with energy intensive processes like pyrolysis and diesel separation. Recent Australian-led studies further show that integrating vacuum distillation with modest downstream hydrotreatment can produce diesel-range streams at larger scales, improving plant utilization and production for higher quality diesel which is more profitable than the export of raw pyrolysis oil[76]. Distillation fixes volatility while hydrotreatment removes sulphur and nitrogen and saturates olefins in one pass, which tightens stability. In mixed-plastic oils this combination has produced diesel properties that comfortably clear the target window, with a cetane index around 58 and sulphur about 2.5 mg kg^{-1} against a 10 mg kg^{-1} limit, alongside acceptable density and viscosity[77]. On the energy side, hydrotreatment adds hydrogen duty however, the upstream pyrolysis step dominates at roughly 8.87 kWh per litre for tyre-derived oil thus choosing a polishing route that avoids oxidant and ionic-liquid make-up maintains the energy use while simplifying waste handling and making compliance easier to sustain[77].

4.2.3 Data, operability and machine learning challenges.

For machine learning, many limitations, such as data constraints and hallucination of predictions when extrapolating data, which is done through pairing process knowledge with modern data science. Soft sensors allow for real-time control and monitoring of the plant, resulting in lower operational costs and time required for pilot testing for certain process conditions. However, each plant produces different data sets with soft sensors, resulting in problematic predictions for the machine learning model if applied to other plants. However, instead of remaking the model and feeding new datasets, Transfer learning (TL) can be utilised[78]. Transfer learning is a method that uses the previous model but not its data to form a new learning model for a specific plant, which allows for a smaller training data set to be required. Another way to cope with dataset shift across feedstocks, is to adopt transfer domain adaptation techniques to allow the soft sensors to be transferred to a new plant while accounting for the condition changes, improving reliability through scale-up changes within the process design. Furthermore, more machine learning operations such as Data contracts (checks and quarantines bad sensor/lab data before it reaches the model) and live monitoring (Tracks soft sensor MAE and drift scores) are used to maintain accuracy and handle many variables considered in the process. This allows for real-time analysis of the drift and accuracy of the model, giving alerts when the model starts to hallucinate or give inaccurate predictions[79]. Also, industrial data science guidance can allow for constraints to the model with the process knowledge and desired specifications for diesel to limit bias and achieve a maintainable and reliable deployment of the ML model for long-term usage[80].

5. Conclusion and Recommendations

This research journal has clearly shown that there is a significant potential to produce recovered diesel fuels from hydrocarbon wastes such as tyres, plastics and lubricating oils through thermal decomposition using pyrolytic separation. From the literature review, key design conditions such as temperature, catalyst choice, reactor design and contaminant removal are essential to improve economic and energetical viability of these systems. Key metrics such as yield recovery, energy intensity and SO_x and carbon emissions are highly dependent on these designs, exemplifying their importance. Additionally, the use of AI and other emerging technologies combined could allow for real time prediction and kinetic analysis, replacing the classical models that utilise time-consuming and costly empirical relations. Improved prediction accuracy of the system would allow for a more precise dynamic control and kinetic analysis, improving the reliability of the system with enhanced quality control and safety risk management.

Furthermore, various challenges and limitations that would affect the viability of the system have been identified. Examples of the limiting factors include the sulphur and metal contamination in the diesel product, energy intensity during the pyrolysis and finally product instability caused by fluctuating waste feedstocks. To overcome these challenges and meet safety legislation, some emerging innovations have also been explored to improve the overall effectiveness of pyrolytic systems. Examples include hydrotreatment to saturate olefins in one pass to enhance reaction stability, oxidative desulfurisation using the ionic liquid extractions and the adaptation of transfer learning models to allow for real time analysis and the implementation of validation plans to prevent model drift.

Despite some possible challenges, the thermal recovery of hydrocarbon wastes into diesel fuel has huge potential to contribute to the realisation of a circular economy by simultaneously achieving waste reduction and energy production. Implementation of such technology in industry is essential in order to achieve Australia's goal of net zero society by 2050.

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Separation of Pharmaceutical residues from wastewater

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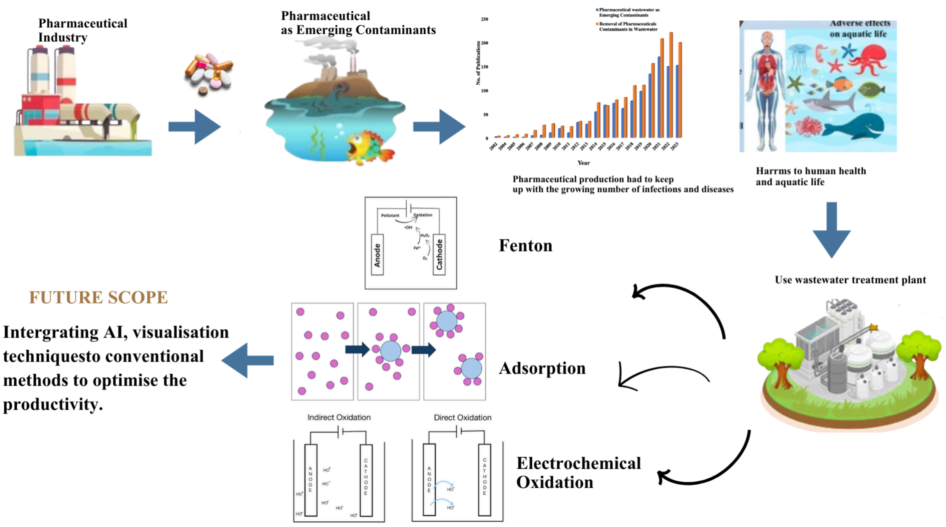
Graphical Abstract



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]

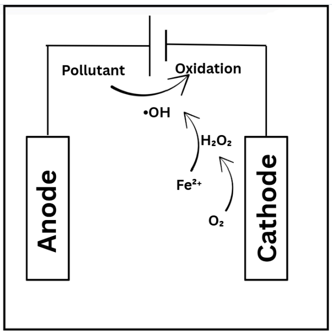


Figure 1. Schematic Diagram of Electro Fenton.

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]

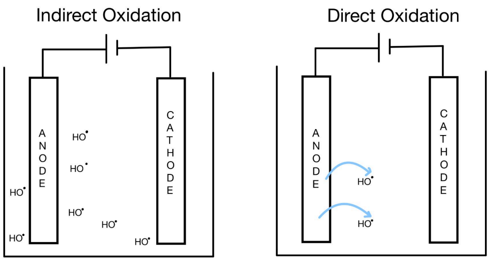


Figure 2. Schematic Diagram of the Electrochemical Oxidation Process

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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Illicit drug purification: Detection and removal of fentanyl analogues from narcotics supply chains

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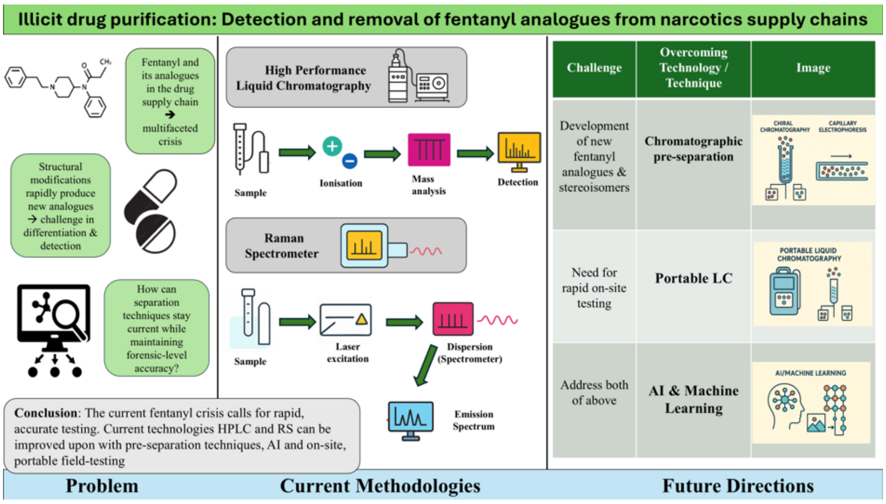
Graphical Abstract



Challenge	Overcoming Technology / Technique	Image
Development of new fentanyl analogues & stereoisomers	Chromatographic pre-separation	CHIRAL CHROMATOGRAPHY CAPILLARY ELECTROPHORESIS
Need for rapid on-site testing	Portable LC	PORTABLE LIQUID CHROMATOGRAPHY
Address both of above	AI & Machine Learning	AI/MACHINE LEARNING

Conclusion: The current fentanyl crisis calls for rapid, accurate testing. Current technologies HPLC and RS can be improved upon with pre-separation techniques, AI and on-site, portable field-testing

Abstract

Recently, the rate of unintentional overdose deaths in Australia has far surpassed that of population growth, reflecting a public health crisis partially driven by illicit production of fentanyl and analogues, which demand rapid and reliable separation for detection and removal. This review critically investigates current and emerging techniques for the detection of compounds, considers social and legal implications, and examines the potential of Artificial intelligence (AI) to transform fentanyl detection from a reactive to predictive science. Presumptive field methods such as Raman spectroscopy and fentanyl test strips provide near-immediate, qualitative results, aiding emergency response, while laboratory techniques, including coupled mass spectrometry and chromatography, offer superior quantitative precision. Fentanyl's structural flexibility enables the continual emergence of novel analogues, challenging identification, which relies on preexisting compound libraries, making detection impossible in the field and time-consuming in laboratories. AI offers a promising solution, whereby convolutional neural networks and machine learning can identify and predict unknown compounds. Emerging advancements focus on developing accurate algorithms and improving field-deployable chromatographic systems to ensure forensic-level accuracy. By bridging analytical chemistry, AI, and health policy, separation strategies have the potential to enhance detection and removal of fentanyl analogues, mitigating societal and individual harms of synthetic opioids.

Keywords: Fentanyl detection; Fentanyl analogues; Separation techniques; Mass spectrometry; Artificial intelligence; Public health; Illicit drug detection; Machine learning; Mass Spectrometry; High Performance Liquid Chromatography; Immunoassays; Raman Spectroscopy

1. Introduction

1.1 Context: Illicit Fentanyl Analogues - A crisis

The proliferation of fentanyl and its analogues in the illicit drug supply chain have triggered a multifaceted crisis around the world, fuelling the need for sophisticated separation processes, regulation, healthcare policies, and harm reduction strategies to effectively combat this issue. Fentanyl is a highly potent synthetic opioid (depressant) that is 50-100x more potent than morphine,[1] often used in a pharmaceutical setting for severe pain management, anaesthesia, and analgesia. Fentanyl misuse and illicit manufacturing has been a prevalent issue since the 1970s,[2] and in recent years structural variations on the main drug, otherwise known as analogues, are becoming increasingly apparent due to lower costs and stronger potencies. One such example, carfentanil, a common analogue is 50 times stronger than fentanyl.[2] Fentanyl and its analogues all share the same core structural characteristics, comprising of a piperidine ring, amide group, N-Phenyl group (aniline), and phenethyl group. Disparities between analogues resultingly arise from interchanging functional group substituents at these 4 key bonding sites, driving a significant challenge in specific differentiation between analogues and the identification of new ones, as structural modifications can be easily and rapidly generated. Historically, fentanyl analogues have been 'cut' into other drugs,[1] enhancing drug strength, and creating powerful, potentially lethal biological interactions when being unknowingly ingested. This fuelled the US opioid crisis and today has resulted in majority of deaths from opioids being from unintentional overdose from fentanyl and its analogues cut into heroin, cocaine, Xanax and other drugs. Recently demand for novel psychoactive substances (NPS) in the form of fentanyl analogues in the pure form has arisen, exacerbating existing problems in detection, prevention, harm reduction, and healthcare responses worldwide.[3]

1.2 Relevance: Individual and Societal Impacts - Sizing of the problem

The impacts of fentanyl and its analogues are multifaceted and profound, the effects of their sale and consumption are felt in various social contexts such as crime and violence, environmental sustainability, the economy, health, politics, and economic cost. Currently the opioid crisis is preventing the continuous improvement and achievement of the UN Sustainable Development Goals, the detection and removal of fentanyl analogues from narcotics supply chains is thus indispensable in promoting health and well-being (SDG 3) and reducing inequalities (SDG 10).

On a global scale, the likelihood of fatally overdosing on fentanyl overpasses the likelihood of death from a motor vehicle related accident.[2] Despite signs of a slowing fentanyl market in recent years based of seizure levels,[4] this is still a large societal cost. The use and abuse of fentanyl's, both prescription and illicit, is concentrated in North America, as novel synthetic opioids have become a drug of choice in both manufacturing and consumption patterns, reflecting a generalised trend in the favour of higher potency drugs. As such, overdose deaths are overrepresented in the US, whereby in 2023, 72,000, or nearly 70% of drug overdose deaths were estimated to involve illegally manufactured fentanyl.[5] In 2023, more than 390 million lethal doses of fentanyl were seized in the US alone,[6] with half of all pills containing lethal doses. One of the main issues in the response and reduction of fentanyl use is the tracing of manufacturing origin or where the drug was obtained, due to the evolving illicit drug market, whereby anonymity is enhanced due to cryptocurrencies, e-commerce, and online servers.[1]

Although Australia has not experienced the same scale of fentanyl-driven mortality as North America, the increasing detection of fentanyl analogues amongst the drug market and supply chain has prompted rising concern amongst policymakers, law enforcement, and healthcare. Fentanyl usage and abuse represent a significant social cost, whereby in 2022/23 opioids were projected to have a combined social and economic cost of $18.4bn and contributed to the largest proportion of overdoses, sitting at 43.9% of deaths in 2023.[7] Many studies have concluded that death from overdose is both avoidable and inexplicitly linked to the environment in which it occurs,[5] therefore harm minimisation and preventative techniques achieved through separation processes should be at the forefront of public health policy in Australia to minimize individual, societal, and economic cost, and promote global sustainable development. A challenge also lies in preexisting legal regulations and societal viewpoints, whereby stigma and punitive policies can prevent harm reduction and individuals accessing support services. As such, Australia must align with the UNs recommendation for a comprehensive approach which places individuals at the centre of policy making, to effectively address the issue.

1.3 Literature review on existing and emerging methods

Separation processes act as the bridging force between law enforcement, policy makers, and healthcare providers in the fight to address and prevent fentanyl-based overdose, whereby both laboratory and in field methods are utilised to match different analytical requirements and separate fentanyl analogues from other narcotics. Majority of methods used are not specific to fentanyl or its derivatives, rather they are used among most drug separation situations. Due to the complex mixture of compounds often found in illicit substances, sensitive and selective processes are used. Laboratory processes consist of comparatively higher sensitivity and accuracy as opposed to field methods, evolving from the use of gas chromatography (GC) aided with mass spectroscopy (MS) to liquid chromatography (LC), aided with in tandem mass spectroscopy (LC/MS).[8] In field detection is primarily achieved through portable spectroscopic devices, namely Fentanyl testing strips, and a Raman spectrometer, which are made intended to inform emergency operators immediately, allowing for actionable results to be produced in time-sensitive situations.[9] While these devices are not comparable in terms of sensitivity and performance with laboratory techniques, these is growing recondition that due the proliferation of unintentional fentanyl use and overdose, these methods should be the priority for future development and implementation.

Artificial Intelligence (AI) and Machine Learning (ML) offer a unique opportunity to transform responses to clandestine manufacturing of fentanyl and its use from reactive to proactive. By leveraging data processing techniques, deep learning and generative models, AI can be trained on current fentanyl analogues, chemical properties of drugs, and mass spectrometry outputs to identify new substances and predict potential further analogues.[10,11] Thus, the proficient and strategic implementation of AI has the potential to enhance drug discovery, strengthen detection capabilities, and reduce testing time.

Current research on fentanyl detection faces several limitations. Laboratory methods are forensically reliable but can be slow especially with rapidly emerging analogues. AI shows some promise for screening and prediction but remains underutilised and unvalidated for routine forensic use. Portable devices enable fast field testing but can be unreliable and potentially legally inadmissible.

This raises key questions:

- How can separation methods be adapted to stay current with the constant development of new fentanyl analogues while maintaining forensic-level accuracy?
- What strategies will allow ML/AI models to not only be helpful in fentanyl detection but still be robust, explainable and admissible in forensic workplaces?
- What innovations in microfluidic or portable separation technologies could provide rapid, reliable, and admissible on-site screening for fentanyl analogues?
- How should separation processes balance harm-reduction goals (field testing for public safety) with evidentiary standards in criminal justice?

1.4 Ethical removal, purification, and end-of-life handling (forensic & harm-reduction)

Effective separation in this context does not end at identification, ethical practice requires safe handling after analytical processes to prevent secondary exposure, and other consequences. Implementing ethical and sustainable methods for removing and disposing of fentanyl analogues is crucial to prevent negative environmental impact and ensure long-term safety of users and first responders, directly supporting SDG15 by promoting the protection of ecosystems from pollution, and aligning with ESG principles.

Separation workflows should focus on containment, this includes closed preparations, appropriate personal protective equipment (PPE) and minimal sample size.[12] Biological Safety Cabinets (BSCs) have been recommended however this only applies to laboratory settings and not field testing.[13] During such a process, it is important to keep evidence logs to preserve chain-of-custody and prevent diversion.

Decontamination post analysis is also crucial. Decontamination must avoid aerosolisation and use controlled, wet cleaning with clear clean and dirty zones within the lab. PPE should be disposed into sealed tamper-evident waste.[14] Field testing should have a focus on consistency and simplicity, this could include sealed containment for wipes and PPE, pre-moistened wipes, return-to-lab protocols along with measures to respond to symptoms of overdose such as having ready access to naloxone.[15] These practices reduce risk without compromising on courtroom admissibility or downstream laboratory confirmation.

The final obligation is disposal. Opioid containing wastes such as used sorbents, PPE, residual extracts should be segregated and labelled as high-risk material until they reach an endpoint, usually high temperature incineration. Discharge to drains or general waste streams should be avoided unless consistent with environmental and controlled-substance regulations.[16]

Organisations should implement policies and training to comply with such measures. Removal, cleanup and disposal can be integral features of testing while complying with analytical quality, public-health protection and legal defensibility.

1.5 Scope and objectives

This review examines separation methods for fentanyl analogues with a focus on laboratory methods, AI approaches and portable technologies, while considering social and legal implications. It covers experimental methods such as chromatography, electrophoresis, and sample preparation; computational strategies for optimisation, anomaly detection, and analogue generation; and field-deployable technologies for harm-reduction and forensic use.

This review aims to assess current methods, including laboratory separations such as chromatography, electrophoresis and sample prep strategies with performance benchmarks (e.g. sensitivity, specificity, turnaround time) and admissibility notes. Field deployable screening such as immunoassay strips, Raman and emerging microfluidics is also studied with an emphasis on triage accuracy, potential false positives and how they can be confirmed in a lab downstream. This review also explores AI/ML approaches including model design for analogue detection and prediction in ways relevant to broader societal challenges.

This review does not cover detailed synthetic routes for fentanyl or any of its analogues, clinical pharmacotherapy such as dosing regimens, supply chain and markets for fentanyl nor any consumer level handling for “DIY” or “at home” processing. Where referenced, these topics are only included to provide context or frame analytical requirements.

2. State-of-the-Art in Advanced Separation Strategies

2.1 Current Methodologies

Historically, GC coupled with MS (GC/MS) was the predominant method for separation and identification of fentanyl and fentanyl analogues, yet this has been replaced primarily by LC coupled with MS (LC/MS) or often high-performance liquid chromatography (HPLC). This is due to the necessity of the analyte in GC needing to be volatile and thermally stable, yet many fentanyl analogues have a relatively low volatile and are thermally labile (decompose under high temperatures) thus not suitable for separation via GC.[3] LC relies on the same principles as GC, where the separation occurs due to the level of interaction between the analyte and the stationary phase, yet the mobile phase is a solvent that carries the analyte, and it is driven through the stationary phase by a high-pressure pump. Within the analyte, the molecules that have a higher interaction with the stationary phase have a higher retention time and the molecules separate into elution peaks.[17]

Whilst HPLC is the primary method for separation of fentanyl and its analogues, mass spectroscopy is the method used to analyse the sample as it has very high sensitivity (can detect very small amounts), requires low purity for analysis and is highly specific. Mass spec is primarily used as it allows for the identification of the molecular mass of the molecules and the fragmentation patterns (especially in MS/MS). Since these analogues often vary via addition of side chains, replacement of hetero-atoms in cyclic structures, substitution of different atoms with halogens and functional group alteration, often fragmentation occurs at identical points for between analogues. Zhang, 2022 found that fentanyl forms fragments either side of the piperidine ring structure (N-αC and N-4C) forming MS peaks at 188.14 and 105.07. Between fentanyl analogues, depending on side chains added, the analogues formed peaks at 188.14 +R1 +R2 and 105.07 +R1 where R1 and R2 denote side chains.[18] Furthermore, fentanyl analogues with similar retention times were able to be differentiated via fragmentation patterns providing a heavy advantage to the coupling of HPLC and MS. The usefulness of these fragmentation patterns leads to the usage of MS/MS where the precursor ion is separated with an initial mass spectroscopy, then collided with an inert gas to further fragment the ion, then these fragments are analysed.[19]

Samples however can not be directly placed into GC,HPLC or MS as often contain impurities that are insoluble and can lead to damage of the instruments or tamper results and thus need to be prepared for analysis. Often solid phase extraction is done such as microextraction by packed sorbent as it offers the best selectivity in comparison to methods such as liquid-liquid extraction as well as its small sample and solvent requirements.[20] The sorbent is chosen to interact well with the target molecule so that it can be adsorbed to the surface of the sorbent. The analyte material is passed through carried by a weak solvent (a solvent that does not strongly interact with the sorbent). It is then washed with a strong solvent do desorb the analyte from the sorbent and collect it essentially purifying the sample and allowing for accurate analysis.[21]

Raman spectroscopy relies on the stokes and anti-stokes scattering of light depending on the vibrational modes of the molecules. Unlike Rayleigh scattering where the emitted light has the same wavelength as the absorbed, in stokes and anti-stokes, the emitted light has a larger or smaller wavelength depending if it increases or decreases the vibrational energy of the bonds. This produces a characteristic Raman emittance pattern of a molecule that can be used to determine the molecule.[5] Raman spectroscopy (RS) can compare the spectrum produced by the compound to a library of spectrums to determine if fentanyl analogues are present in the sample however this raises some key issues with (RS). Often drugs are laced with fentanyl and its analogues rather than purely fentanyl and thus exists in very small amounts. The detectable limit of lab grade Raman spectrophotometer's is 25 mcg/ml and thus for small traces of fentanyl or its analogues, this method will unable to detect it.[5] Depending on the other compounds present within the sample tested, they can also interfere with the spectrum observed and further reduce the detectable limits of RS. Furthermore, as (RS) must compare the measured spectrum to a library and search for a match within that library to identify the compound, it is only able to identify compounds with measured Raman spectrums. Resultantly, it can not detect fentanyl analogues that have not previously been measured and detected in a laboratory.

Irrespective of these drawbacks, handheld RS still appears to be one of the major emerging technologies in drug detection. The most primary of its advantages is its capability of determining the percentage composition of a sample not just detecting if compounds are present.[22] Its ability to detect samples through packaging material (plastic, glass, etc.) makes it highly advantageous in comparison to immunoassays which must come into physical contact with the substance.[22]

Fentanyl test strips are immunoassays which are able to detect the presence of trace amounts of fentanyl or its analogues in a sample. They utilise specific antibodies for the compound for detection by stimulating an immune response to the compound within animals which will change colour on a test strip if the antibody binds.[22] Since these antibodies are proteins, they function primarily through structure where the overall structure of the protein creates amino acid motifs at specific locations to selectively bind with the fentanyl and its functional groups. Whilst these immunoassays are very simple to use not requiring any expert opinion and are quick and relatively cheap to implement, they have a few drawbacks. They can lead to false positives as similar narcotics that are not fentanyl can bind to it due to structural similarities and lead to a false positive detection of the drug.[23] However, this can be advantageous in the case of fentanyl analogues detection where even if the immunoassay is not designed for a specific analogue, its structural similarity can still cause the antibody to bind and thus trigger detection. This leads to the development of broad range immunoassays that are not built for any specific molecule rather attempting to bind to the structural similarities between analogues however this is not foolproof and can cause no detection of the compounds.

Through the implementation of technologies, especially in a field context, methods such as the fentanyl testing strip and Raman spectrometer have the potential to reduce overdose deaths and help users and responders make informed decisions, overall improving health outcomes and aligning with UN SDG 3. Furthermore, these methods actively protect vulnerable communities, whereby structural vulnerabilities have been found to increase exposure to adverse health outcomes.[24] Cost-efficient and portable instruments will extend the capabilities of scientistic and health care professions in regional and resource limited settings, where communities who can be disproportionately affected by drug addiction and unsafe substances. These efforts align with UN goal 11 (reduced inequality).

2.2 Emerging Technologies

Artificial intelligence provides a potent opportunity to the separation field as it provides the capability to accelerate pattern and anomaly identification and ability to identify insights, patterns and knowledge without human interaction.[25] AI utilises machine learning, deep learning and neural networks to automate analysis of large data sets, improve the consistency and accuracy of analysis and to complete optimisation of experiments, particularly through the identification in noise in datasets.[25] The predominate strategy for separation classification is convolutional neural networks (CNN), allowing for an input 'neuron' to be connected to an output 'neuron', allowing for a more wholistic approach to data classification.[26]

Most prominently, CNNs have been used in tandem with LC-MS to identify components due to CNN's improved sensitivity and selectivity.[25] CNN models such as 'MST Tracer', act as a machine learning model for peptide feature identification.[27] Peptides each produce multiple trails after signal peaks, collectively labelled a peptide feature. In instances that noise to signal ratios are minimal, peptide feature identification is difficult and poses a challenge. This iteration of CNN conducts a comparative analysis on past databases and using CNN, identifies the new 'input' neurons to decipher the most correct output neurons. Similarly, other models have been similarly generated for other medicinal purposes with 100% sensitivity and 93.18% specificity.[28] The development of successful models is promising for separation processes in the identification of fentanyl analogues as similar models may be applied to the fentanyl analogue dataset. However, a limiting factor to creating a model for fentanyl analogue identification may lie within a lack of data. AI may address this through the ability to generate an expansion on current databases.

Integration of ML frameworks must be conscious of dataset bias and design considerations that must consider the nature of drug analysis. Cost sensitive modelling should suggest a penalty matrix for design that outweighs false negatives in comparison to false positives.[29] The detrimental consequences of undetected fentanyl presence; possibly leading to overdoses, deaths or the movement of lethal drugs in a community and in contrast with a false positive that may trigger further testing and waste resources; however, the potential detriment is at a greater cost than the cost of additional resources.[30]

It should be noted that emerging advancements with AI and Machine learning do result if significant water and energy usage, thus diverting from sustainable ESG practices and global decarbonisation efforts. To mitigate these adverse effects, it is strongly recommended that these technologies should be run using renewable energy and recycled water to minimise the effect on overall sustainability.

2.3 Comparative Analysis of Current Methodologies

The widespread integration of traditional methods that rely on LC-MS/MS, often in tandem with SPE or LLE for extraction, is well documented and often cited for laboratory and clinical adoption.[3] However, emerging technologies in Raman spectroscopy are gaining attention due to the high true positive and accuracy rates.[5,22]

Table 1: Comparison of Fentanyl Separation and Detection Methods

Method	Setting	Purpose	Speed	Sensitivity	Cost
Fentanyl Test Strips	Field	Presumptive, consumer, single use	Instant (seconds)	Qualitative, dependent on brand. Requires at least 1µg/mL [Rodriguez, 2023; green, 2020].	Low (~$1 each)
Raman Spectroscopy	Field	Presumptive/Screening, clinical and law enforcement	Fast (minutes)	Qualitative/Semi-quantitative/. Requires at least 25µg/mL [Green, 2020].	High ($35,000+)
GC-MS / LC-MS/MS	Lab	Confirmatory/ Quantitative, research, identification	Slow (hours)	Quantitative. Requires at least 3.1µg/mL [green, 2020].	High (lab equipment)

Novel approaches to drug testing are first outlined in Kranenburg et al.'s findings, using a chemometric-based cocaine detection using a handheld Raman spectrometer.[22] A barrier to implementation is the lack of previous work on chemometric based detection, however it is apparent that the strength of existing studies supersedes reluctance as implementation of the Raman spectrometer is suggested as a solution in clinical drug detection settings as a quick and accurate method of drug detection.[22,31] Despite the high specificity and reliability of handheld devices, a primary drawback is poor detectability at lower concentrations or in more structurally complicated analogues.[5,22,23] A primary benefit to machine learning is the ability to identify analogues which were not present in the training set, particularly the improvement in discrimination comparative to manual spectra comparison.[32] The implementation of Cooman et al's CNN model demonstrated overall accuracy of 98.4%, expanding the capabilities of existing technologies.[32]

Fentanyl test strips are a promising frontline tool due to high accessibility, low cost, portability and high analytical reliability.[33,34] Modern FTS exhibit high sensitivity at concentrations at 1µg/mL, and up to 200ng/mL, dependent on the brand of fentanyl test strip,[35] whilst maintaining minimal cross reactivity in the presence of other substances.[33] Although the reliability and accessibility of these tests are pertinent for harm reduction for people who use drugs (PWUD), most FTS are designed for laboratory matrices such as urine rather than substances in aqueous assays.[35]

Further usability difficulties including confusing instructions, poor packaging design and hard to open foil strips remain limitations to further widespread implementation of FTS within PWUD.[36] These limitations emphasise design flaws which limit the interpretability and accessibility of such techniques by the user. The integration of machine learning methods such as CNN algorithms that interpret lateral flow assays may be similarly applied to FTS.[37] These CNN based algorithms automatically read and quantify test lines using smartphone camera, compensating for factors such as poor lighting, user error or other environmental factors.

Beyond improving the interpretation for the user, the integration of machine learning may allow for data aggregation that could further contribute to general geographic data and supply trends which could contribute to predictive modelling. However, the integration of machine learning must be tightly monitored to ensure the anonymity and privacy of users is respected. Ultimately, the success of novel technologies is contingent on the practical ability for implementation; ensuring that operator proficiency, chain of custody and maintenance of equipment are rigorously monitored. Traditional separation methods are reliant on highly trained analysts, routine calibration and adherence to established laboratory operating procedure.[38] The high barrier to entry testing using traditional laboratory methods means adequate training of operators may take years. Although simpler testing devices such as Raman spectroscopy reduce operator training needs and processing complexity, calibration records of these devices should be maintained to ensure the reliability of results. Similarly, FTS are designed to be inherently simpler than a laboratory scale method but must be scaled to ensure that the methodology of results garnered are conclusive the experience of PWUD.[36]

3. Challenges and Future Perspectives

3.1 Identified Challenges

In field and laboratory detection is paramount for addressing the proliferation of illicit manufacturing, and consumption of fentanyl and its analogues; however significant challenges exist in the application of separation methods in an efficient and cost-effective way. While laboratory methods such as LC-MS/MS are often considered the gold standard for identification of fentanyl and analogues, they still have drawbacks due to the rapid pace at which new analogues are being produced, with slow turnaround times, limiting the ability of these processes to act in a preventative way.[23] While favoured due to quick turnaround time and low cost, in field methods do not come without drawbacks, whereby efficiency and response time improvements come at the cost of lost precision, reliability, and quantitative methods. Further, as these methods rely on a library of identified compounds, this complicates and increases lead time in the identification of novel compounds.

Extending from the physical methodology of separation, legal regulation and societal acceptance of in field drug testing and harm prevention methods remain a key challenge, whereby in Australia statewide discrepancies exist. An inherent tension exists within the optimal policy response as disagreements exist between the prioritisation of reducing the size of the drug market verse reducing the harm associated with their use.[2] From a social standpoint, there is growing recognition that harm reduction methods such as drug checking facilities and safe consumption spaces should be at the forefront of policy where in field testing methods would be employed. However, legal issues arise in navigating liabilities of allowing this occurrence, as well as managing perceptions of condoning and supporting drug use, both of which inhibit the application of on-the-spot drug testing. This has been seen recently in Queensland, as of September 2025 the government passed legislation banning pill testing despite evidence in favour of doing so in terms of harm reduction.[39] Another significant challenge is the complexity of the illicit fentanyl market, whereby trade and production of precursor chemicals being extremely hard to regulate and monitor as they are used in a variety of other pharmaceuticals.[2]

There is growing recognition that buyer-seller relationship predominately occurs via online black market, significantly obscuring the ability of law enforcement to trace back to manufacturing origin.[1] This issue is compounded due to the global complexity of the supply chain, whereby chemicals and different stages of production occur in different countries worldwide. Resultingly, separation processes is unable to address some of the main drivers of the fentanyl and analogue challenge, although it can play a preventative role in detection, other policies, technologies, and regulations are required to adequately address the issue at the source.

3.2 Role of Separations in Addressing These Challenges

Advanced separation techniques are critical to overcome challenges surrounding the rapid emergence of new analogues and balancing this through cost-effective but efficient methods. A present issue concerns novel fentanyl analogues with added chiral centres that evade MS detection, as MS alone cannot distinguish between stereoisomers.[40] An advanced separation technique, chiral chromatography such as LC with chiral stationary phases or capillary electrophoresis are able to resolve the stereoisomers prior to MS detection.[40] Although more intensive, both these methods enhance the capacity of accurate, early detection and appropriate responses.

Further to this, current in field-testing can incur more false positives due to lower precisions and reliability from a short turnaround time. A chromatographic pre-separation of the sample before conducting MS is sometimes required. For example, the compound of cyclopropylfentanyl; crotonylfentanyl, methacrylfentanyl all have the same mass and similar fragmentation patterns.[39] Chromatographic separation was demonstrated by Lee et al., 2019 to be necessary for absolute confirmation and certainty of identification, hence this method can similarly be considered for other fentanyl analogue isomer series.[39] These pre-separation techniques have the potential to increase reliability and reduce false positives with field testing, whilst also addressing the rapid emergence of new fentanyl analogues and stereoisomers.

Furthermore, separation techniques alongside with emerging models, for example, a linear algebra-based algorithm developed at Johns Hopkins University, has demonstrated an ability to analyse spectra from unknown substances.[41] From a mass spectrum of fentanyl analogues and 300,000 non-fentanyl compounds, it was able to find combinations of spectra that best reconstruct mass spectra of unknown substances.[42] These models and advanced separation techniques have a great role in overcoming challenges associated with illicit drug purification.

3.3 Future Directions

As previously outlined, there is a societal need for efficient and accurate testing, particularly concerning overdose prevention whereby immediate drug identification is needed. Current implemented LC-MS/MS methods are typically slower and more resource intensive. Emerging technology, miniaturised, and field-portable LC have potential to provide robust on-site analysis that allows for rapid decision making.[43] These would reduce issues arising from sample degradation, contamination, or long-term sample storage, significant financial savings as well as reduce reagent consumption and waste generation.[43,44] Past and present application of this technology has shown potential in the field of nutrient monitoring. More recently, improvements to open-tubular columns and pillar array columns have been made to enhance extraction selectivity and produce ultra-high-resolution separations.[45] The integration of artificial intelligence and machine learning has been an increasing trend in research, to optimise column design, separation conditions and data analysis to ultimately enable faster method development.[45] The primary obstacle facing this technology is the need for proper training with regards to handling small volumes and flow rates.[41] This would allow for a more widespread adoption and rapid development of miniaturised technologies that are crucial to the proliferation of fentanyl and its analogues.

In conjunction with the above technologies, an integration of AI for optimisation and analysis is a critical direction for future separations workflow, particular to overcome the constantly evolving fentanyl analogues. Machine-learning is platform with the potential for this. Through training algorithms on data and patten recognition from a data base of known fentanyl analogues would allow for the identification of novel ones with high accuracy.[41] These systems, alongside developing in-field technologies, assist with driving rapid and portable testing to prioritise the wellbeing and safety of the wider population.

4. Conclusion and Recommendations

Current separation techniques such as HPLC, LC–MS, and Raman spectroscopy provide robust means of detecting fentanyl analogues, acting as cornerstones for drug policy and harm reduction worldwide. However, the rapid emergence of novel compounds starkly outpaces the discovery of in field and laboratory methods. This discrepancy emphasises the necessity for advancements in reliable novel analogue testing methods. Overall, whilst the established methods provide a robust scientific basis for further advancements, successful harm reduction is ultimately contingent on legal regulations, government policy and public health professionals; out of the scope of the discussed scientific methods. Effective regulation, destigmatisation, education, and data-driven policy and implementation are essential for translating analytical findings into tangible social benefit. The integration of AI predictive methods into current analytical findings will further strengthen current models whilst simultaneously aiding in the discovery and analysis of novel analogues. The implementation of current and future technologies support SDG 3 (Good Health and Wellbeing) and SDG 10 (Reduced Inequalities) by promoting equitable access to harm-reduction technologies. Alignment with furthering SDG goals further supports the development of a sustainable future.

Avenues for future research should prioritise the feasibility of implementing novel methods and developing the most effective regulatory framework that supports emerging technologies. A potent barrier to innovation includes the outdated legislation and the persistent stigma towards drug users. Focusing on maintaining individual autonomy, minimising environmental impact, removing specific regulatory barriers, and ensuring scalable solutions is essential for successful harm reduction, improving health outcomes, and saving lives.

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Communities at Risk: PFAS Contamination Near Industrial Sites and Separation Strategies

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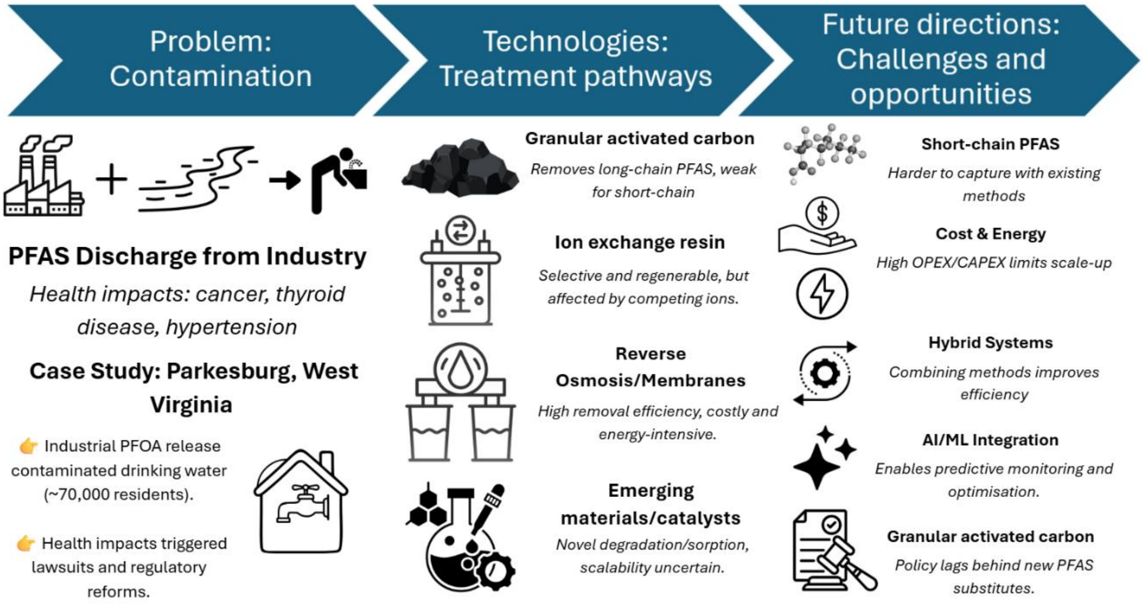
Graphical Abstract



Abstract

This review examines the growing challenge of per- and polyfluoroalkyl substances (PFAS) contamination in small communities located near chemical production facilities, with particular attention to perfluorooctanoic acid (PFOA). The case of Parkersburg, West Virginia highlights the scale of the problem, where adverse health outcomes and community exposure culminated in over USD \$670 million in remediation and legal settlements.[1] To mitigate these risks, multiple separation technologies have been evaluated, including granular activated carbon (GAC), ion exchange resins, and high-pressure membrane processes such as reverse osmosis and nanofiltration. Emerging nanomaterials are also being investigated for their high selectivity and adsorption capacity.[2] However, significant challenges remain in addressing short-chain PFAS, scaling up pilot processes, managing energy and cost demands, and preventing harmful treatment by-products. Integrating artificial intelligence and machine learning (AI/ML) into monitoring and optimisation frameworks offers opportunities to improve system efficiency and predictive maintenance.[3] Beyond technical considerations, PFAS remediation has far-reaching environmental, societal and economic implications, from reducing long-term health burdens to preventing the continued degradation of local water systems. Additionally, effective PFAS remediation advances progress toward several United

Nations Sustainable Development Goals, particularly SDG 3 (Good Health and Well-Being), SDG 6 (Clean Water and Sanitation), and SDG 12 (Responsible Consumption and Production).[4]

Keywords: PFAS, Separation, GAC, Ion Exchange Resin, Reverse Osmosis

1. Introduction

1.1 Context and relevance

Per- and polyfluoroalkyl substances, including compounds such as PFOA, are a class of synthetic chemicals with strong carbon-fluorine bonds that make them extremely stable, persistent and non-biodegradable. Since the 1950s, they have been widely used in non-stick cookware, waterproof fabrics, food packaging, firefighting foams, and industrial coatings, earning the term “forever chemicals”.[3] Figure 1 illustrates the chemical structure of common PFAS molecules.

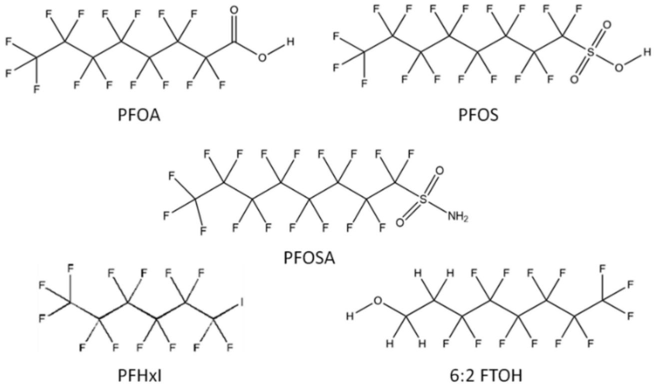


Figure 1 – PFAS structure of common molecules[5]

PFAS enter the environment through multiple pathways, including industrial discharges and wastewater from manufacturing. Conventional wastewater treatment processes redistribute rather than remove PFAS, and PFAS from land-applied biosolids, landfills, and fire-fighting foam sites can leach into the surface and groundwater.[3] Contaminated water supplies have become the primary route of human exposure, with PFAS accumulating in drinking water, and subsequently, in human bodies over time.[3]

1.2 Parkersburg, West Virgina case study

The Parkersburg, West Virginia case involved decades of PFOA (C8) discharges from DuPont’s Washington Works Teflon facility into the Ohio River and connected aquifers, contaminating municipal water, soils, and resident’s blood. The C8 health project linked this exposure to increased risks of thyroid disease, high cholesterol, pregnancy-induced hypertension, and kidney and testicular cancers, affecting approximately 300,000 residents and downstream communities.[1] Substantial social and economic impacts were experienced, including USD $670 million in settlements and ongoing costs for monitoring, remediation, and healthcare.

1.3 Size of the problem

While this review will focus on high concentration PFAS exposure, it must be acknowledged that low level PFAS exposure is a widespread and global problem. A recent study by the Australian Bureau of Statistics found PFOA at detectable levels in 99.1% of males and 98.3% of females. While Australia has relatively high PFAS concentrations, average levels of PFOA were lower than in the US, Canada and Europe.[6] If these levels are extrapolated to the world population, they indicate that PFAS such as PFOA are a potential threat to almost every human. High concentrations of PFAS can also be found in groundwater worldwide as can be seen in Figure 2. The health impact of these high concentration sites is difficult to estimate as both the number of people affected, and the magnitude of exposure vary from site to site and studies have not been conducted for every location. As a substitute for health data, an estimate based on number of exposure sites must be used. In Europe alone, the forever pollution project estimates more than 23000 contaminated sites and more than 2100 ‘hotspots’ where contamination levels exceed 100 ng/L. As these hotspot sites exceed safe limits significantly, they are far more dangerous and are likely responsible for the majority of PFAS related harm, both social and economic. A portion of this cost, specifically the price to remove all PFAS from the environment, was estimated by the same project as €95 billion over 20 years if only long chain PFAS were removed and production ceased immediately, or €2 trillion over the next 20 years if short and ultra-short chain PFAS were included in the removal and emissions continued (SDG12).[7] As this cost is currently not viable for most countries to bear, efforts should be focused on high concentration sites where removal efforts are more effective and have a higher impact.

1.4 Scope and Objectives

This review focuses on separation techniques used to remove PFAS, including PFOA, from drinking water in small communities located near chemical manufacturing facilities, where ingestion via water is the dominant exposure pathway. Grounded in the Parkersburg, West Virginia case study, the scope encompasses established and emerging technologies, including Granular Activated Carbon (GAC), anion exchange

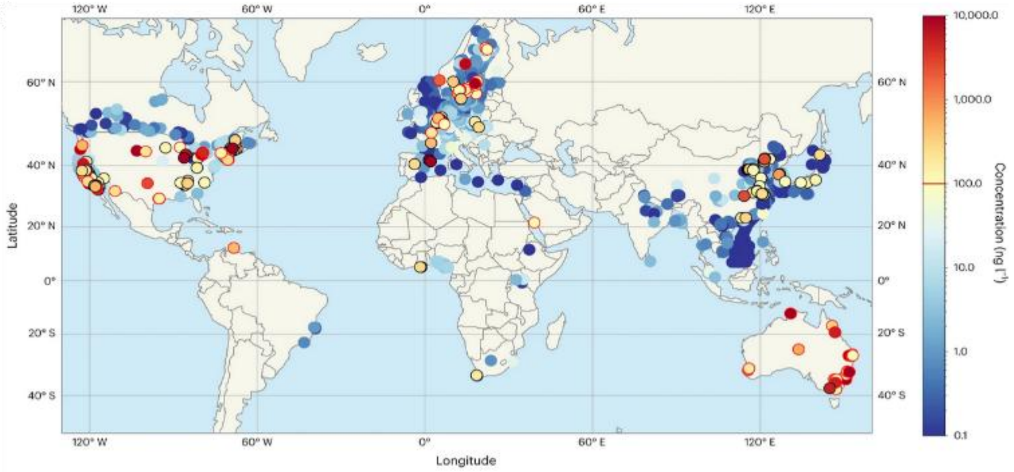


Figure 2: Groundwater PFAS levels globally, sites with PFAS levels above the EU limit for drinking water are circled in red for known contamination sources and black for unknown.[8]

resins, reverse osmosis, and novel sorbents or catalytic materials, with attention to relevant limitations and benefits, whilst examining real world case studies of these technologies. Topics beyond the scope of this review include destructive PFAS degradation processes such as electrochemical oxidation and plasma treatment, which, while promising fall outside the focus of separation-based techniques.[2]

Objectives:

1. Comparing current and emerging PFAS separation technologies assessing their effectiveness across long and short chain species, cost, energy requirements, and sustainability.
2. Evaluating the role of AI/ML in optimising treatment processes, including predictive modelling, monitoring, and hybrid system design.
3. Identifying key challenges and research gaps, including the removal of short term PFAS, scalability limitations, costs, and treatment by-products.
4. Quantifying the social and economic impacts of PFAS contamination in high-risk communities, including potential healthcare savings, remediation costs, and long-term benefits of early intervention.

1.5 Literature Overview

- Key findings from studies:
    - GAC (2.1.1): Effective for long-chain PFAS removal, but diminishing efficacy for short-chain variants
    - Ion Exchange Resins (2.1.2): Targeted removal, regenerable, but may be less effective for short-chain
    - RO (2.1.3): broad removal capabilities but expensive/energy intensive
    - Emerging materials/techniques
- Gaps in current research
    - Limited methods for short chain PFAS
    - Challenges in scale-up
    - Need for integration of predictive technologies to optimise treatment processes (AI)
- Major research questions:
    - How can short chained PFAS effectively be addressed?
    - How can hybrid systems (two or more PFAS removal techniques) be used to capitaliase on their strengths and compensate for limitations.
    - In what ways can AI/ML improve monitoring and optimisation of separation processes?
    - How can sustainability considerations (energy consumption, cost, waste management) be incorporated into treatment design?
    - Where should PFAS removal systems be implemented? (Point of production, general water treatment or point of use)

2. State of the Art in Advanced Separation Strategies

2.1 Current Methodologies

2.1.1 Granular Activated Carbon

Granular Activated Carbon (GAC) is a common resource used to separate PFAS from water and soil. It is carbon filtration made from raw organic materials that are carbon rich. Heat is used to activate the surface area of the carbon and remove chemicals that are dissolved in water.[9] It is a porous nonselective, hydrophobic adsorbent and is extremely effective due to its high surface area and microporous structure enabling it to trap and hold harmful compounds.

In South Australia a company called Bygen has deployed this method of PFAS removal by integrating GAC into a wetland system as part of a pilot project targeting PFAS contamination.[10] Over the 8-month trial, Bygen's GAC showed a significant increase in PFAS adsorption, from initially undetectable levels to over 1000 ng/g. In comparison, biochar, which is a carbon-rich material also used in soil purification, was used in the same trial only to capture around 100-200 ng/g of PFAS.

Bygen's GAC is made from organic waste materials like nut shells (almond, walnut, hazelnut) and sustainably sourced wood.[10] Through a controlled thermal activation process, these materials are converted into a microporous carbon that efficiently captures long-chain PFAS compounds like PFOA and PFOS, preventing their spread in the environment.

The total amount of water that passes through GAC filters significantly impacts both the filter's lifespan and the likelihood of PFAS breakthrough. As more water flows through the filter which is measured in bed volumes BVs, PFAS are adsorbed at different depths depending on how strongly they bind to the carbon.

At low bed volumes (2,600 BVs), most pollutants are captured in the top layer of the GAC filter. As the number of treated bed volumes increases to around 7,300 BVs and beyond , the adsorption continues at varying rates, with certain PFAS compounds moving faster and reaching the bottom of the filter bed earlier than others. This uneven movement means that weaker-binding PFAS compounds may break through the filter earlier, reducing overall filtration process effectiveness over time. Monitoring and frequently replacing the GAC is crucial in order to maintaining effective PFAS removal**.**

2.1.2 Ion Exchange Resins

Ion exchange resins are a practical and innovative technology for removing PFAS from contaminated water. Ion exchange resins are porous, polymer-based beads that swap charged ions from water with ions attached to the resin's surface. In anion exchange, negatively charged ions on the resin are replaced by other negatively charged contaminants in the water: such as PFAS.[11] Ion exchange resins have proven highly effective at capturing PFAS, which are also negatively charged.

These ion exchange resins work through a combination of hydrophobic and electrostatic interactions, making them particularly effective at targeting both short- and long-chain PFAS compounds. Because most PFAS molecules are anionic with low pKa values, strong-base anion exchange resins are especially well-suited for this task.

As opposed to other treatment technologies like (GAC), ion exchange offers both operational and financial advantages. Many systems use single-use resins, which securely binds PFAS and allows the used material to be safely disposed of in a landfill.

A case study, titled '*PFAS removal The forever chemical now has an expiration date* (published in the AWA Water e-Journal), tracked the performance of a regenerable ion exchange system between 2019 and 2023.[12] The treated water, taken from a site with significant PFAS contamination, showed incoming concentrations averaging around 16 µg/L, with occasional peaks surpassing 60 µg/L. The treatment train included a pre-treatment stage designed to remove competing ions such as nitrate, sulfate, and bicarbonate, as well as natural organic matter (NOM), which can reduce the resin's PFAS adsorption capacity. While not designed specifically for PFAS removal, this pre-treatment step did help lower total PFAS concentrations from roughly 10 µg/L to 4 µg/L before the water even reached the resin beds.

Throughout the operational period, the RIEX resin system performed well. Water passing through the lead and lag resin vessels showed marked reductions in PFAS concentration. This case study demonstrates that ion exchange resins, when properly supported by a tailored pre-treatment process and regeneration strategy, can provide a reliable and cost-effective solution for PFAS removal.

2.1.3 Membrane Processes (RO/NF)

High-pressure membrane processes, such as nanofiltration (NF) and reverse osmosis (RO), are among the most effective technologies available for removing long chain PFAS from water. This removal system works by forcing water through a semi-permeable membrane under high pressure and physically separating PFAS molecules based on size and charge. They have shown a strong performance in eliminating long-chain PFAS, such as PFOA and PFOS, which are among the most studied.

However, the effectiveness of these membranes in removing shorter-chain or lesser-known PFAS compounds is uncertain. Removal efficiency can vary depending on several factors, including membrane type, water chemistry (such as pH and the presence of salts or organic matter), and operating conditions.[13] Despite the high removal rates, these systems come with significant challenges, especially high energy costs and expensive structures. These factors limit their use in large-scale industry as a viable separation method.

Some newer research explores hybrid approaches, combining RO or NF with either destructive treatments (like advanced oxidation) or non-destructive treatments (such as activated carbon or ion exchange), aiming to enhance PFAS removal while reducing costs and membrane fouling.[14]

Reverse osmosis (RO) is an extremely effective method for PFAS removal. However, the management of the concentrate and brine waste remains a significant challenge. The brine and wastewater generated by this process can have detrimental environmental impacts. This by-product contains high concentrations of contaminants and salts that can negatively affect biodiversity when improperly disposed of. To reduce the environmental impact of this waste, several technologies have been explored. One of these advances is known as Zero Liquid Discharge (ZLD). This approach aims to eliminate liquid waste by recovering water and reducing the brine volume, while solidifying the dissolved contaminants. The process recovers clean water and leaves behind only solid waste, which can then be disposed of in a more sustainable manner.

2.1.4 Emerging Materials

In the search for more effective and sustainable ways to separate PFAS from water, researchers in South Australia have been developing new materials that go beyond just capturing and removing PFAS but aim to break the compound down entirely.[15] A team at the University of Adelaide has created a promising method involving a metal sulfide powder activated by UV light. When mixed with a PFAS-contaminated solution and exposed to UV, the photocatalyst becomes energised, triggering a reaction that begins to break apart the extremely strong carbon-fluorine bonds in PFAS molecules. Early trials have shown this process is particularly effective at degrading long-chain PFAS like PFOS and PFOA, which are known for their high toxicity and persistence. The team is now working on shifting from UV to natural sunlight as the energy source, with the aim of making the process more cost-effective and scalable for real-world use.

Alongside this, Australian company OLEOLOGY has introduced a new filtration and polishing technology using MyCelx media, which has been approved through in-field use across the country. This system captures PFAS to below detectable limits, all within a compact, lower-cost setup. Unlike traditional granular activated carbon or high-pressure membranes, which often require large infrastructure and higher operating costs, MyCelx offers a smaller footprint and proven performance across a wider spectrum of contaminants.[12]

There is growing interest in integrating emerging technologies with existing systems, such as using covalent organic frameworks (COFs) to enhance membrane-based separation, or exploring resin regeneration methods to reduce waste and improve sustainability in ion exchange processes.[16]

2.2 Integration of Emerging Technologies

According to the European Journal of Sustainable research, AI has already been seen as an effective tool for environmental sustainability management, tracking pollution and modelling the climate among many other applications yet its uses within the scope of PFAS mitigation remains relatively unexplored.[17] The implementation of AI contains the potential to be a pivotal tool in terms of mapping PFAS hotspots and predicting migration patterns in real-time as well as optimising remediation. Further AI driven sensing technologies and spectral analysis could significantly improve early detection of PFAS within agricultural soils, already showing valuable applications to reduce bioaccumulation of PFAS within food sources.

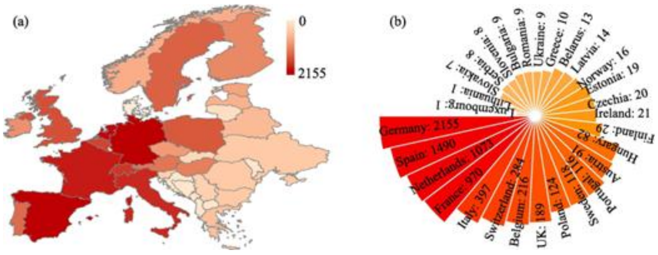


Figure 3: Heat map showing ML predicted PFAS

Machine learning (ML) based technologies that utilise AI have been identified as powerful tools for enhancing PFAS monitoring, source identification and remediation.[18] These technologies offer accuracies of up to 96% when classifying PFAS sources and show great promise in areas specifically using large data sets to identify relationships between physical, chemical and biological factors that otherwise require extensive experimentation to quantify. For this reason, artificial neural networks (ANN) and random forest (RF) technologies are useful to minimise reliance on experimental procedures and directly make predictions and observations about a wide array of PFAS characteristics such as source types, LD50 values, ionisation efficiency and many more. However, despite the vast applications of these technologies they rely on high quality datasets to be trained on, one of the largest challenges for the applications of these techniques moving forwards is having large amounts of high-quality data to further train them on to yield more optimal results.[19] Despite this technology still being developed and emerging there are case studies available for interpretation. One study focussing on Europe used machine learning models to interpret and predict high risk PFAS contaminated water sources and the people who would be affected by them at high-risk levels exceeding the 100ng/L safety limit guideline for European drinking water.[20] Conducted in May 2025 this case study is on the breaking edge of applying machine learning to predict and scope the challenging problem of PFAS contaminated water sources and their movements. Using this model they estimated nearly 8,000 individuals within Europe are affected by higher than acceptable PFAS contaminant levels and also importantly found a threshold distance of 4.1-4.9km from contaminated water sources that within which the water sources pose risk for elevated PFAS levels. Using data of 20 different PFAS contaminants and 9,985 sites across Europe this case study sets an exemplary model of how machine learning can be used to great advantage in analysing large data sets and finding trends in contributing factors to get results in a field that is historically poorly understood. The heat map of elevated PFAS concentrations predicted by this study can be found in Figure 3 and shows which countries have the most individuals above the acceptable risk threshold. Further ways to strengthen or ensure this technology develops in the right direction would be to implement some validation methods for the ML models. This could include human oversight of the models and also cross-testing predicted sites values with actually measured values. That is using a validation set of data that the machine has not been trained on. By utilising these methods to ensure the models develop accurately under the guidance of human oversight and validation they show potential to be a valuable resource in PFAS contamination movement and tracking

2.3 Comparative Analysis

RO and NF membranes are both highly viable solutions for PFAS removal. In a pilot-scale closed-circuit membrane filtration system, tap water spiked with PFAS was treated, achieving a recovery rate of up to 97%. The study compared the performance of NF and RO membranes, with PFAS removal by NF corresponding to a log removal value (LRV) of approximately 1.8, while RO achieved a higher LRV of 2.3.[21] For NF membranes with larger pore sizes, removal rates dropped significantly under high recovery conditions or in more challenging water matrices. Generally, NF removal of PFAS compounds falls within the 1–2 LRV range, whereas RO often achieves 2 log or higher LRV under favourable conditions. Because of its higher LRV, RO is more suitable when regulatory limits for PFAS are extremely stringent. However, NF may be acceptable in situations where PFAS concentrations are higher or when used as part of a multi-step treatment process.[22]

The adsorption capacity of ion exchange (IX) resins compared to granular activated carbon (GAC) showed that IX resins have a higher initial removal efficiency at lower pH and with dosages up to 6.0 g/L of water. Removal effectiveness decreased at higher IX dosages due to the desorption of previously adsorbed compounds. In contrast, GAC exhibited a consistent increase in removal efficiency with increased dosage, suggesting a more stable and predictable capacity range. Both treatment methods performed better at lower temperatures and after 12 hours of contact time.[23] While IX offers higher selectivity and capacity for certain compounds, it is highly sensitive to water chemistry. GAC provides more scalable and reliable performance across a range of conditions. Overall, IX may be preferable for targeted PFAS removal, while GAC is a more versatile option with broader operational usage for full-scale drinking water application.[24]

Table 1: Comparison of PFAS Treatment Technologies by Cost, Effectiveness, and Sustainability

Separation Method	**Cost**	**Effectiveness**	**Sustainability**
Granular Activated Carbon (GAC)	Relatively low cost depending on source material of carbon	High for long-chain PFAS	Uses organic waste- low emissions, 1 to 80 kg of CO_2 eq./g PFAS removed. Disposal and replacement required.[25]
Ion Exchange Resins	Lower than GAC in operational costs. [26]	Very effective for both short- and long-chain PFAS More selective and longer bed life than GAC[27]	Regenerable options available but some single-use resins go to landfill.
Nanofiltration / Reverse Osmosis (NF/RO)	High cost: energy-intensive operations and expensive infrastructure.	Excellent for long-chain PFAS; effectiveness for short-chain PFAS is less certain.	Membrane requires frequent maintenance. Energy use limits sustainability[28]
Metal sulphide powder	Estimated US $50-200/g[29]	Promising for PFAS degradation, especially long-chain types	Sustainable if shifted from UV to natural sunlight as the energy source

3. Challenges and Future Perspectives

3.1 Identified challenges

The vast diversity of PFAS and PFAS related compounds introduces significant challenges for detection, separation, and regulation. With nearly 15000 varieties identified,[20] individually crafted solutions are not viable, and datasets of sufficient size and quality are not currently available for ML solutions. As such, detection and separation systems must be generalised to be effective against many variations of PFAS.

Regulatory challenges are also presented by the variety of PFAS, as more countries implement bans or limits on the use of common varieties such as PFOA, PFOS and PFHxS, other compounds such as HFPO-DA (commonly GenX), ADONA, F–53B and 6:2 FTAB are becoming more prevalent as replacements.[30] As these are relatively recent developments, there is far less research on their health or environmental impacts (SDG3, SDG6). Despite this, they have all been found at significant levels globally,[31–34] and both GenX and ADONA have been found to affect gene expression in thyroid cells.[35] Current regulations are unable to keep up with development of these chemicals, and individualised bans only lead to the use of less researched alternatives, many of which have similar impact.[30]

Despite this potential harm from PFAS replacement options, it is essential to find replacements that are able to effectively fill the roles of PFAS in industrial and consumer applications. This presents another significant challenge, as the properties of PFAS that make them industrially relevant are the same that cause their bioaccumulation and harmful effects. One study found potentially suitable alternatives for PFAS for 40 applications, but identified 83 uses for which no alternative could be found.[36] If PFAS are to be phased out completely, this challenge must be addressed by further research into safer alternatives.

3.2 Roles of separation techniques in addressing challenges

Advanced separation techniques are paramount in overcoming the challenges presented by PFAS contamination, as varied techniques enable effective detection and removal of the persistent pollutants. Conventional analytical methods, that were popular in the past, such as gas chromatography, struggled to capture both structural diversity and the scarce concentrations that PFAS occur at environmentally. A notable 2024 study highlighted that the singular method, liquid chromatography-mass spectrometry (LC-MS), had proven successful for rapid separation and identification of all chain lengths (including ultra short) of PFAS.[37] This technology provides comprehensive monitoring at environmentally plausible concentrations (≈1 μg/L), however the limitation of small scale injection volume (20 μL) largely limits the technique to detection.[37]

Considering treatment, nanofiltration has shown remarkable performance, achieving a 99.61% targeted rejection rates of short-chain PFAS at 100 μg/L levels, with efficiency varying in accordance with applied pressures. This elucidates the promise of a membrane-based approach; to address the harder separation of smaller, agile PFAS that often bypass conventional treatment. However, scalability and energy requirements remain significant challenges.

Beyond separation, secure storage and disposal of concentrated PFAS waste are essential, as inadequate management risks environmental re-entry.[38] Hence, separation must be integrated with sustainable downstream strategies – to promote the ESG requirements and SDGs. It serves two functions: minimising risk through PFAS removal and enabling precise monitoring to support regulation and treatment evaluation.

3.3 – Current and Prospective Regulatory Solutions

Currently, the manufacture, import, and export of PFOA, PFOS, and PFHxS is prohibited in Australia due to their status as schedule 7 chemicals[39] under the industrial chemicals environmental management instrument. Guidelines for drinking water have also been updated for various PFAS and are summarised in table *2* below.

Table 2: Summary of Australian and US drinking water guidelines for PFAS concentration*[40,41]*

PFAS Derivative	Australian Guideline (ng/L)	US Guideline (ng/L)
PFOS	8	4
PFOA	200	4
PFHxS	30	10
PFBS	1000	No value set
GenX	No value set	10

While these are significant steps towards reducing the public health risk from PFAS, they are heavily focused on only a few specific varieties. This limited approach could cause significant harm if emerging PFAS are found to have similar or worse health effects. While new PFAS in Australia are automatically categorised as medium to high risk to human health[42] and must obtain an assessment certificate, the test data for the assessment is provided by the chemical manufacturer, introducing a significant opportunity for biased or incorrect data to be submitted, as was the case with DuPont's manufacture of PFAS in the 1970s[43] which led to the case of Parkersburg, West Virginia. Unfortunately, there is no apparent solution for this, new chemicals must be manufactured both to replace hazardous or banned materials and to allow for scientific advancement, and the government lacks the resources to perform independent health studies for every new chemical to be manufactured.

3.4 Future directions

Incremental advances in separation methodologies hold potential to significantly enhance PFAS management. One priority lies in developing accessible on-site detection techniques. Optical and electrochemical sensors have potential for rapid and cost-conscious monitoring of PFAS in environmental matrices. Nevertheless, current systems lack sufficient selectivity across PFAS subclasses and the sensitivity required to detect trace concentrations.[44]

Improving these capabilities enables more responsive field-based monitoring and support regulatory enforcement. Considering this, high-temperature incineration remains the only proven large-scale option for highly contaminated media such as aqueous film-forming foams (AFFF), polluted soils, and biosolids. This approach is costly and environmentally burdensome, underscoring the need for alternatives.[45] Emerging combinant strategies such as ion-exchange with electrochemical, hydrothermal, sonolysis, or plasma-based processes warrant further investigation to establish viable, scalable routes for PFAS destruction. Collectively, these incremental refinements could improve both detection and treatment, offering more sustainable and effective management frameworks.

4. Conclusions and recommendations

The persistence and toxicity of PFAS present one of the most pressing global water contamination challenges. The case of Parkersburg, West Virginia, where unregulated industrial discharges contaminated drinking water supplies, illustrates the severe local health and economic consequences that arise in the absence of effective separation strategies.

This review has assessed the performance of established and emerging approaches. Granular activated carbon methods remain reliable for long-chain PFAS but are limited by regeneration issues and poor removal of shorter-chain analogues, ion exchange lacks this weakness to short chain PFAS but faces the same issues with regeneration and waste generation. Membrane processes such as reverse osmosis and nanofiltration provide broad removal albeit more uncertain with short-chain species but require high energy and infrastructure inputs. Novel hybrid and photocatalytic systems show promise, though questions of scalability and by-product management remain unresolved.

In the Australian context, several research teams are advancing PFAS treatment through photocatalysis and advanced membranes, reflecting both recognition of the issue and commitment to innovation. Internationally, the integration of AI and machine learning is emerging as a tool for optimising treatment processes and supporting predictive monitoring.

Addressing PFAS contamination demands a combined strategy: advancing technological performance, integrating digital tools, and aligning regulatory frameworks. Continued investment in translational research will be critical to move these laboratory advances into scalable, real-world solutions that safeguard public health and environmental resilience. The cost of inaction is continued community-level harm and

escalating national and global health burdens, whereas decisive investment in these solutions offers the opportunity to break the cycle of persistent contamination.

Acknowledgements

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Advanced Separation and Digital Strategies for Chemical Warfare Agent Mitigation

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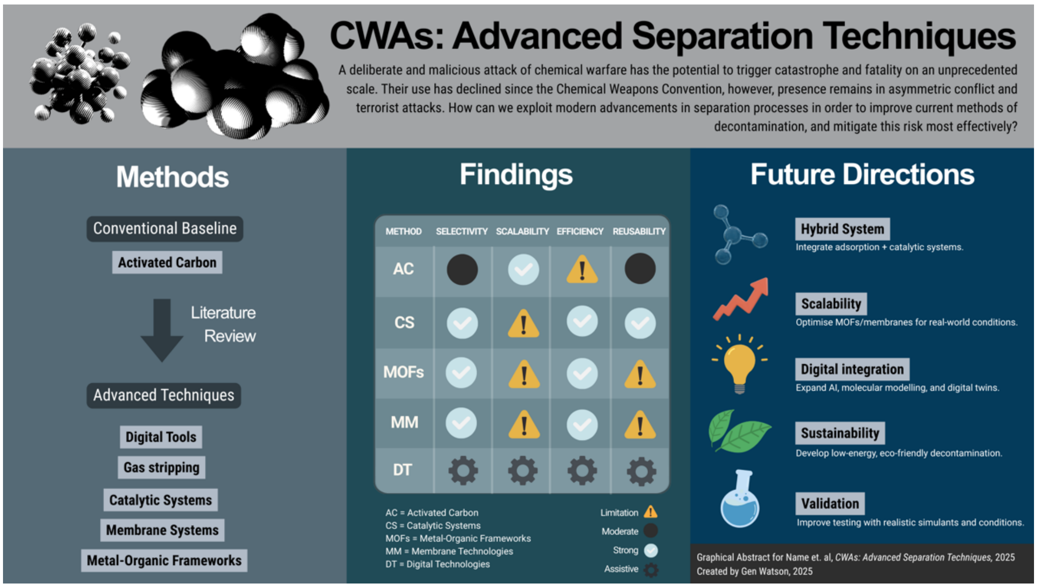
Graphical Abstract



CWAs: Advanced Separation Techniques

A deliberate and malicious attack of chemical warfare has the potential to trigger catastrophe and fatality on an unprecedented scale. Their use has declined since the Chemical Weapons Convention, however, presence remains in asymmetric conflict and terrorist attacks. How can we exploit modern advancements in separation processes in order to improve current methods of decontamination, and mitigate this risk most effectively?

Methods

Conventional Baseline
Activated Carbon
Literature Review
Advanced Techniques
Digital Tools
Gas stripping
Catalytic Systems
Membrane Systems
Metal-Organic Frameworks

Findings

METHOD	SELECTIVITY	SCALABILITY	EFFICIENCY	REUSABILITY
AC	●	✓	⚠	●
CS	✓	⚠	✓	✓
MOFs	✓	⚠	✓	⚠
MM	✓	⚠	✓	⚠
DT	⚙	⚙	⚙	⚙

AC = Activated Carbon
CS = Catalytic Systems
MOFs = Metal-Organic Frameworks
MM = Membrane Technologies
DT = Digital Technologies

Limitation ⚠
Moderate ●
Strong ✓
Assistive ⚙

Future Directions

Hybrid System
Integrate adsorption + catalytic systems.

Scalability
Optimise MOFs/membranes for real-world conditions.

Digital integration
Expand AI, molecular modelling, and digital twins.

Sustainability
Develop low-energy, eco-friendly decontamination.

Validation
Improve testing with realistic simulants and conditions.

Graphical Abstract for Name et. al, *CWAs: Advanced Separation Techniques*, 2025
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Abstract

The persistent threat posed by chemical warfare agents (CWAs) arises from their acute toxicity, rapid environmental mobility, and long-lasting physiological and ecological impacts. Effective emergency response requires rapid and reliable decontamination strategies, and separation-based processes have emerged as critical tools for isolating, capturing, and neutralising these agents across air, water, and surface environments. This review synthesises recent advances in adsorption technologies, metal organic frameworks (MOFs), membrane filtration, gas stripping, and catalytic and oxidation-based approaches, highlighting how engineered materials and tuneable interfaces have enhanced selectivity and efficiency in CWA separation. Complementing these developments, molecular modelling, Monte Carlo and molecular dynamics simulations, high-throughput screening, and machine learning driven prediction have accelerated material discovery and deepened understanding of the structural and chemical factors governing CWA capture and degradation. Despite these advancements, persistent challenges including limited real agent validation, scalability constraints, fouling and material degradation, and uncertainties in computational models continue to restrict widespread field deployment. Emerging digital tools, such as AI assisted analytics, real-time data interpretation, and early-stage digital twin frameworks offer significant potential to strengthen situational awareness and operational readiness. Overall, continued progress will depend on integrating traditional separations with advanced computational and digital methods to develop robust, adaptive, and field ready decontamination systems capable of responding to evolving chemical threats.

Keywords: chemical warfare agents, adsorption, metal organic frameworks, membrane filtration, gas stripping, digital tools

1. Introduction

Terrorism utilising chemical warfare agents (CWAs) remains one of the most pervasive and escalating threats to global health and security.[1] Originally designed for military deployment, their indiscriminate impact has disproportionately harmed civilian populations.[2] CWAs - highly toxic chemicals used in World Wars I and II, the Cold War, and the Iran-Iraq War - caused millions of deaths, most during World War I.[2] The devastating persistence was exemplified in Halabja (1988), causing thousands of deaths and long-term disease.[3] International frameworks such as the Geneva Protocol (1925) and the Chemical Weapons Convention (CWC, 1993) prohibited their use. However, CWAs have re-emerged in recent conflicts, such as Douma (2018), and Salisbury (2018).[2]

The persistence of CWAs reveals their catastrophic potential. Advances in synthesis, the accessibility of precursors, and online information further exacerbate this risk.[4] CWAs exist as gases, liquids, aerosols, or powders, with diverse toxicological harms. Nerve agents inhibit neurotransmission, blister agents harm skin and lungs, and choking agents impair respiration.[4-8] Rapid toxicity and environmental stability enhance lethality, complicating medical countermeasures; no universal decontamination method exists.[4]

Traditional decontamination: chlorine neutralisation, water hydrolysis, and oxidation, are effective but limited.[4,9] In contrast, separation-based decontamination offers selective capture and immobilisation of CWAs. Activated carbon is widely used for adsorption, but it does not fully degrade all agents.[10] These limitations emphasise the need for advanced separation techniques with greater selectivity, reusability, and deployment potential. Emerging technologies, such as MOFs, membrane filtration, gas stripping, and catalytic systems offer greater selectivity, efficiency, and scalability.[11-14]

To address this persistent challenge, this review explores modern separation-based strategies for CWA decontamination. It first outlines the historical and contemporary scale of the problem, then surveys current and emerging separation techniques - including adsorption, metal-organic frameworks (MOFs), membrane filtration, and gas stripping. Finally, it discusses the major technological and practical gaps that remain.

Although 99% of declared stockpiles were destroyed under the CWC by 2023,[15] the threat of CWAs persists in asymmetric and terrorist contexts.[16] Recent incidents include Syrian government attacks (2013),[17] Iraq Islamic State assaults (2017),[17] and nearly 7,000 chemical events in Ukraine (2023-2025), causing thousands of injuries and deaths.[18] The impacts extend beyond mortality. Survivors suffer long-term respiratory, neurological, and psychological damage, creating humanitarian crises marked by forced migration, food insecurity, and loss of livelihoods. The 1988 Halabja attack exemplifies these consequences: 5000 deaths, mostly civilians, and decades of chronic illness among survivors.[3] CWAs also cause severe environmental damage. Their persistence in soil and water enables contamination lasting weeks to months.[19] Following World War II, 50,000 tons of CWAs were dumped in the Baltic Sea, releasing toxic by-products into sediments and marine food webs.[20] Research shows arsenic-containing degradation products in fish and ecosystem stress in marine organisms.[21,22] Similarly, soil contamination reduces microbial communities, disrupts nutrient cycling, and spreads through wind erosion, posing risks to ecosystems and human health for decades.[16]

Economic estimates are limited, but bioterrorism figures provide an analogue: events could cost USD \$477.7 million - \$26.2 billion per 100,000 exposed.[23] The 2001 US anthrax attacks cost \$6 billion[24] in cleanup, healthcare, and productivity losses.[25] Comparably, CWAs would likely incur similar costs for decontamination, remediation, and loss of public trust.[26]

Recent literature has concentrated on the selective capture and degradation of CWAs using advanced separation materials and hybrid systems. MOFs stand out due to high surface area, tuneable pore structures, and catalysis: Huang et al. (2024) showed that MOF-polymer composites achieve near-complete detoxification of VX and mustard gas simulants.[13] Onodera et al. (2023) discussed a reactor that doubled removal efficiency compared to conventional stripping, suggesting potential for liquid-phase CWA decontamination.[14] Catalytic materials have 70-100% degradation efficiency but remain in early development phases, with Boddu et al. (2025) showing the need for scalable, low-energy systems.[12] Membrane filtration is highly suited for aqueous applications, and Bernardes et al. (2025) emphasises designs to improve selectivity and energy efficiency.[11] Activated carbon can be further enhanced: Verma et al. (2024) showed zirconium hydroxide integration increased adsorption and partial catalytic conversion of organophosphate simulants.[27]

Despite significant progress, several key challenges remain. Research still relies on simulants rather than live agents, scaling limits MOFs and membranes, and digital applications are constrained by data quality and computational resources. Moreover, conventional separations such as gas stripping and membrane filtration lack modern performance validation under realistic field conditions. These issues highlight the need to reassess how separation methods, catalytic reactivity, and digital tools can be integrated for safer, scalable, and sustainable CWA mitigation.

Consequently, this review addresses three overarching research questions. How can separation and catalytic strategies be engineered for high efficiency, scalability, and reusability in real-world environments? What are the comparative advantages and limitations of traditional (adsorption, gas stripping) and emerging (MOF, membrane technologies) separation platforms? How can computational and digital tools, such as machine learning, molecular models, and digital twins, be leveraged to accelerate material discovery, process optimisation, and risk reduction?

This review critically examines the advanced separation methodologies for CWA decontamination, focusing on MOFs, membrane filtration, gas stripping, and activated carbon, alongside their integration with catalytic and digital tools. While many studies demonstrate laboratory feasibility, the review emphasises the challenges of scaling to operational conditions.

This review includes 4 key objectives. Recent advancements and demonstrated performance of separation methods will be summarised. The critical challenges with scalability, selectivity, and long-term stability will be identified. It will evaluate integration opportunities with catalytic and digital technologies. Overall, this will highlight emerging directions that combine multiple separation or catalytic mechanisms to improve efficiency, sustainability, and deployability. This review does not address detection and sensor systems, real-time surveillance networks, or post-deployment forensic analysis, as these lie beyond the scope of separation-based decontamination.

2. State of the Art in Advanced Separation Strategies

2.1 Current Methodologies

The neutralisation of chemical warfare agents (CWAs) has been historically dominated by adsorption-based systems, with activated carbon forming the industrial baseline for protective technologies such as respirators, decontamination filters, and fixed-bed units.[8] The mechanism of such systems relies primarily on physical adsorption; however the use of impregnated carbons presents the added capacity of enhanced catalytic degradation, converting the captured CWAs into less toxic compounds.[28] Although highly scalable and cost-effective, conventional carbons are restricted by relatively low adsorption capacities, fragile catalytic sites, and limited structural tunability, thereby driving the need for more advanced separation and catalytic strategies to combat prevailing issues of CWA usage in conflict-prone environments.[29]

2.1.1 Activated Carbon (Conventional Baseline)

A study conducted by Yu et al. (2019) exemplifies the potential of engineered activated carbons through the synthesis of a porous carbon material from chitosan, a natural biopolymer, using potassium carbonate as the activating agent. The resulting carbon was tested against dimethyl methylphosphonate (DMMP), a commonly used nerve-agent simulant, where optimised carbons demonstrated an exceptionally high adsorption capacity of 432 mg g^{-1}, far exceeding many conventional carbons (50-150 mg g^{-1}).[30] Such a performance was attributed to controlled porosity, with higher activation ratios yielding surface areas greater than 1700 m^2 g^{-1}, large pore volumes, as well as to nitrogen-doping from the chitosan precursor, which facilitated strong polar interactions with DMMP molecules that accommodated their capture. These outcomes illustrate how biomass-derived activated carbons can be engineered to rival advanced materials such as metal–organic frameworks (MOFs) in terms of simulant capture, while offering advantages in cost, sustainability, and scalability.[31] However, this study only explored a single stimulant, where long-term stability or reusability under repeated cycling was not extensively characterised - a primary limitation. As such, further optimisation is required prior to extending the use of such materials from a laboratory environment to an industrial or field scale.[30]

2.1.2 Catalytic Materials as Alternatives to Carbon

To overcome the passivity of carbon adsorption, research has been increasingly focused on catalytic materials, including metal oxides, polyoxometalates, and metal clusters.[8] These systems possess large pores, high surface areas, and abundant active sites, enabling the direct chemical decomposition of CWAs - typically by disrupting the phosphorus-oxygen (P-O) bond in organophosphate nerve agents.[32] Unlike activated carbon, which merely sequesters toxic molecules, catalytic platforms can transform CWAs into benign products, thereby reducing risks of secondary contamination.[8]

A study by Kim et al. (2023) provides a compelling case of this approach through the development of a hybrid catalyst comprising MgO nanoparticles incorporated into mesoporous SBA-15 silica and covalently linked to graphene oxide (GO). Tested against the nerve agent simulant DMNP, the composite (MgO@SBA-15@GO) exhibited rapid degradation kinetics, achieving a half-life of 15 minutes under infrared (IR) LED irradiation, compared with ~ 45 minutes in the absence of IR exposure. This threefold improvement in reaction rate was attributed to the photothermal effect of GO, which locally elevated surface temperatures by 20-30 °C, thereby accelerating reaction kinetics without requiring external heating. Simultaneously, the SBA-15 support maintained a large pore volume (~ 0.8 cm^3 g^{-1}) and surface area exceeding 700 m^2 g^{-1}, stabilising MgO nanoparticles against aggregation and promoting efficient molecular diffusion to the active sites - factors that are essential in maintaining high reaction rates and reliable detoxification performance.[32]

Importantly, the composite retained over 90 % of its conversion efficiency after five consecutive reuse cycles, confirming its durability under repeated photothermal conditions.[32] Collectively, these results highlight how integrating oxide catalysis with ordered mesoporous frameworks and photothermal components can deliver self-sustaining detoxification systems that outperform adsorption only carbons, while simultaneously mitigating the stability and reusability challenges often encountered in MOF based catalysts.

2.1.3 Metal Organic Frameworks (MOFS)

MOFs represent another promising class of materials that combine extreme porosity with catalytic functionality.[33] Constructed from metal clusters that act as Lewis acid centres and multidentate organic ligands that provide structural flexibility, MOFs are capable of both adsorbing CWAs and catalysing their hydrolytic breakdown into non-toxic products. The chemical versatility of linkers further enables MOFs to serve as photocatalysts, converting light into chemical energy while expanding the operational window for targeted detoxification.[28]

Recent innovations in MOF development were reported by Oh et al. (2023),[34] who evaluated the zeolitic imidazolate framework-8 (ZIF-8), a subclass of MOFs, for its ability to adsorb the CWA simulants CEES and DMMP. By synthesising four different morphologies, cubic, rhombic dodecahedron, leaf-shaped and plate-shaped, the study systematically showed that adsorption efficiency is strongly dependent on morphology and surface charge. The cubic form of ZIF-8, which carried the highest positive surface charge (approximately +30 mV compared with +8 mV to +15 mV for other shapes), exhibited the greatest uptake, achieving adsorption capacities of approximately 620 mg g^{-1} for CEES and 480 mg g^{-1} for DMMP under comparable conditions. This characteristic was attributed to the favourable polar interactions between the positively charged MOF surface and the electron-rich moieties of the simulants. Notably, the cubic ZIF-8 retained over 90 % of its initial adsorption capacity after five reuse cycles, with minimal changes in BET surface area (< 3 % loss) and pore volume (< 5 % change), underscoring its cost-effectiveness and potential for waste minimisation in decontamination applications. These findings clearly highlight how precise control over ligand chemistry, surface charge and morphology can tailor MOFs for selective and highly efficient CWA-simulant detoxification.[35]

2.1.4 Gas Stripping

Gas stripping presents an alternative strategy for the capture and removal of volatile or semi-volatile CWAs from aqueous environments, operating through the transfer of contaminants from the liquid to the gas phase via a carrier gas stream. This mechanism is governed by Henry's Law, where the partial pressure difference between phases drives the volatilisation required for separation.[28]

The performance of gas stripping is strongly influenced by the choice of carrier gas: air and steam are frequently employed, with steam offering the advantage of heat-assisted volatilisation that reduces solubility and improves removal efficiency.[36] Conversely, inert gases (such as nitrogen) can be used where the prevention of oxidative side-reactions is required.[28] Stripping has been operationalised using conventional chemical engineering equipment, including packed towers, air-sparged hydrocyclones, and aeration basins, which facilitate efficient mass transfer through enhanced gas-liquid contact.

Unfortunately, there are minimal bench scale evaluations of the capacity of gas stripping in explicitly decontaminating CWAs, with MOFs and related technologies subsuming primary roles in overcoming CWA contamination instead. However, evaluations of liquid-gas phase transitions conducted by Asha et al. (2017)[37] confirm that simulants of CWAs with analogous properties such as CEES and DMMP readily partition into the vapour phase, thereby instating the suitability of stripping as a supporting separation method.[37] However, it is necessary to understand that simulants cannot fully replicate the complex physicochemical behaviour of true CWAs, particularly in terms of volatility, persistence, and interaction with real environmental matrices.[38,39] Thus, while gas stripping is validated at the conceptual level through simulant studies, further empirical research using safe but structurally analogous systems is essential to quantify its true efficiency and scalability in realistic emergency response scenarios.

Another key limitation of such a technique lies in the fact that CWAs are transferred rather than destroyed, necessitating additional downstream treatment to ensure safe neutralisation. However, the integration of this technology with advanced sorbent or catalytic systems addresses this challenge, where stripped vapours can be effectively polished using activated carbons or MOFs while catalytic reactors ensure the breakdown of volatile products into non-toxic compounds.[40,41] As such, the use of hybrid process trains combining stripping, adsorption, and catalytic degradation proves a viable procedure to effectuate decontamination, and have demonstrated high overall removal efficiencies and reduced environmental persistence of toxic agents.[28] Overall, although gas stripping is limited in its use individually, when incorporated within engineered multi-barrier treatment systems it holds significant promise as a scalable, front-line separation stage for comprehensive CWA decontamination.

2.1.5 Membrane Filtration

Membrane filtration, a well-established technology for wastewater treatment, is becoming an increasingly prevalent technology in CWA protection. Membrane filters behave as selective barriers, restricting the movement of particles and molecules through the membrane pores based on their sizes and chemical properties.[42] This mechanism is particularly valuable in the development of personal protective equipment (PPE) for CWAs where current methods of handling CWA exposure is by immediate detoxification through chemical reactions and catalysts, an approach effective only under certain conditions.[43] Studies on the blockage CWA permeation are limited but emerging and being realised in membrane filtration technologies, particularly polymer-based-membranes and nanomembranes.

2.1.5.1 Polymer Membranes

Amongst polymer-based-membranes, mixed membrane reactors (MMR), where solid phase catalysts are incorporated within the porous polymer matrix, have been particularly studied for CWA protection. The polymer matrix behaves as continuous diffusion nanochannels, enabling CWA movement through the matrix and in pathways that lead to the immobilised solid phase catalysts. Trapped by the catalysts within the membrane, CWAs are then catalytically degraded.[44]

Current research on MMR for CWA has predominately used MOFs as the solid phase catalyst, particularly Zirconium-based MOFs (Zr-MOF) for their high stability and efficient catalytic degradation of CWAs.[45] A study by Lee et al. (2020)[46] incorporating UiO-66 derivatives with a polysulfone (PSF) and testing against nerve agent simulant DMNP, highlights potential of MMR to refine PPE designs. High catalytic activities of MOF-808 enabled for 97% DMNP conversion on average into less toxic products of nitrophenol and DMPA. Followed by a washing process to regenerate the MMR, MOF-808 achieved 95% conversion. The ability for the MMR to regenerate and sustain high conversion performance emphasises the capacity for this technology to provide durable, reusable and, inevitably with multiple use, cost-effective protection - critical necessities for feasible high performing PPE against CWAs.[47]

Furthermore, MMR configuration can be tailored for different operational scales. Lee et al. (2020)[46] reported that both plate-in-frame (MMR-p) and hollow fibre (MMR-h) designs achieved near-complete DMNP degradation (97% and >97%, respectively). MMR-p offered high porosity and flux, compatible for small scale and surface-coating applications, while MMR-h's substantially larger surface to volume ratio (6000-8000 m^2/m^3, compared to 350-500 m^2/m^3 for MMR-p) is efficient for large scale, stockpiles of CWAs.[46] The structural variations demonstrate MMR capability to enable PPE to be adapted for diverse protection and decontamination situations. Polymer selection further reinforces this versatility. While Lee et al. (2020) opted for PSF for its high chemical and mechanical stability, Snider & Hill. (2023) utilised polymer PVDF, over poly(ethylene-co-vinyl acetate), with UiO-66 for its higher hydrophobicity provided 3.5 times more DMNP degradation.[44] Evidently, MMRs represent highly innovative separation technologies, where its structure and composition can be tuned for PPE optimisation against CWAs.

2.1.5.2 Nanomembranes

Nanomembranes represent the next stage in membrane technology for CWA protection, aiming to prevent CWA permeation for extended durations, rather than detoxify.[43] Within this emerging field, Graphene (GR) and Graphene Oxide (GO) nanosheet composite membranes have been the predominant focus, as the one-atom-thickness of these nanosheets enables for impermeability of small gases, when in a laminate structure, and yet high water-vapour moisture permeability (WVMP), mitigating heat stress and optimising PPE comfort.[47,48]

Kim et al. (2022)[43] constructed a GO and linear polyethylenimine (LPEI) membrane and found a 73% reduction in nerve simulant, dimethyl methylphosphonate (DMMP), penetration and whilst maintaining high water-vapour and nitrogen permeation of 67.91g/m^2 per day. Assembled by a spraying layer-by-layer method to control thickness and internal structure, the membrane's effective blockage owed to the sieving effect of GO nanosheets and the laminate structure, and the hydrogen bonding sites on LPEI that interacted with DMMP and limited its movement. Though there is incomplete blockage, the high (WVMP) and relatively simple method of construction (spraying layer-by-layer) is not to be overlooked and highlights the potential for GO based nanomembranes to balance breathability alongside protection and construction ease - essential design criteria for feasible, wearable PPE.[47]

A similar study by Song et al. (2022)[49] using also a multilayer design of GO laminate layer except on MOF-loaded membrane, obtained complete blockage for 2750, 1075, 176 min, and 7 days for CWAs ammonia, mustard, soman and dimethyl methyl phosphonate (DMMP), respectively, whilst retaining high moisture permeability, much above the required minimum of 1500-2000 g/m^2 per day. Both studies highlight that the barrier performance of nanomembranes not only depends on nanosheet arrangement, but also the multilayer design. Kim et al. (2022)[43] compared the LPEI/GO membrane with globular PEI/GO membrane and reported that the denser arrangement achieved by LPEI's linearity provided for smaller free voids (0.22nm) than the globular PEI (0.33nm), a more disorganised arrangement, ultimately leading to improved CWA blockage that was 72.65% greater. Song et al. (2022)[49] highlighted that the serial reinforcement of MOF-loaded layers is necessary for complete blockage as singular layers alone are inefficient. Collectively, these findings demonstrate that nanomembrane performance is governed by both nanosheet organisation and multi-layer reinforcement, and such integration establishes a design foundation for breathable, yet highly protective PPE against CWAs.

2.2 Integration of Emerging Technologies

2.2.1 Machine Learning

Machine learning (ML) is undeniably playing a significant role in advancing CWA separation research by accelerating material selection and performance prediction. The separation performance of MOFs depends strongly on compatibility of pore size, shape and chemical functionality with the particular

CWA.[50] As experimentally screening through thousands of possible MOFs is time consuming and hazardous to workers, Wang et al., 2023 combined a Computational-Ready Experimental MOF data base with high-throughput computational screening to train several ML models to efficiently predict the most effective MOF for CWA simulants. The best performing model, Extreme Gradient Boosting (XGB), achieved a high predictive R^2 of 0.80 ± 0.01 for simulant TSN, indicating potential for rapid and reliable identification of the best performing MOF material for CWAs. Furthermore, the ML analysis revealed key structure properties that enabled certain MOFs to outperform others, highlighting porosity, Henry's coefficient and hydrogen bonding. Ultimately, insights from Wang et al., 2023[50] underscores the integral role of ML in advancing MOF development for CWA separation, having the potential to enhance design decisions of MOFs based on feature importance reports, and expedite efficiency in accurately selecting the most suitable MOF to implement into PPE.

ML has also made a notable imprint on membrane-separation research by handling high dimensional chemical data based on membrane composition, properties and environment conditions, to accelerate the development of membranes that provide an optimised separation performance.[51] Though current ML work focuses mainly on gas separation and other non-CWA separation applications, these successes establish the foundation for the future integration of ML for CWA-specific membrane development as data resources specific to this application become more available.[51]

2.2.2 Molecular Models and Simulation Tools

Molecular modelling enables researchers to investigate how toxic compounds, such as nerve agent simulants (e.g., DMMP, CEES), interact with advanced materials like MOFs or graphene membranes before conducting hazardous experiments. This approach reduces experimental risk while saving both time and cost in the design of decontamination and separation systems.[52] Energetic modelling provides insights into CWA behaviour toward new materials. Although ab initio quantum methods are accurate, they are computationally expensive, promising the use of classical force fields such as UFF, DREIDING, and TraPPE for high throughput screening of MOFs. These methods, however, may overlook complex interactions at open metal centres. Monte Carlo simulations are often employed to predict adsorption isotherms and estimate uptake capacity, while Molecular Dynamics reveals diffusion and transport through pores, directly informing membrane design and personal protective equipment (PPE) filters. High-throughput screening further accelerates the evaluation of thousands of MOFs, enabling the discovery of structure property relationships such as pore size selectivity trends. More recently, genetic algorithms have been applied to evolve MOF structures with optimised uptake, suggesting that design principles from gas storage can be adapted to CWA capture.[52]

2.2.3 Digital Twins

Digital twins are dynamic virtual representations of physical assets, systems, or processes that mirror their real-world counterparts, enabling real time monitoring, analysis, and simulation.[53] In the chemical industry, they have become essential tools for enhancing operational efficiency, optimising processes, and supporting sustainable growth by integrating sensor data, historical information, and advanced analytics. The combination of AI, machine learning, IoT, big data analytics, and edge computing allows digital twins to provide deeper insights, predictive modelling, and faster decision making, transforming conventional approaches to chemical manufacturing. Beyond conventional operations, digital twins can also be applied to hazardous chemicals, including chemical warfare agents, to improve safety and risk management. By simulating processes, monitoring critical parameters in real time, and predicting potential failures, digital twins enable virtual testing of containment, decontamination, and mitigation strategies without exposing personnel to toxic substances. This reduces operational risk, strengthens environmental stewardship, and supports the efficient use of resources in high-hazard chemical environments.[54]

The defence sector can benefit greatly from Digital Twin technologies. By creating digital replicas of military assets, operations, and infrastructure, defence organisations can perform detailed simulations, optimise resources, and conduct predictive evaluations. This technology enables real-time monitoring of military equipment and facilities, supports proactive maintenance, and optimises logistics, offering substantial improvements in asset availability and efficiency. Digital Twins can be considered a foundational tool for protection against CWAs on which different additional technological instruments are implemented to enhance capabilities, for example by automating data flow, optimising data analytics, automating data flow, and extending functionality.[54]

Internet of Things (IoT) and Sensors: The current landscape of military Internet of Things (IoT) and sensor technologies is characterised by rapid advancement and broad integration into defence applications including CWAs. These technologies are central to enhancing operational capabilities, improving situational awareness, and providing critical operational and environmental data ensuring timely detection of a hazard whilst improving safety and risk management. In addition, Military IoT encompasses a network of interconnected devices that collect, exchange, and process data to facilitate real-time decision-making and strategic planning. Modern Sensor technologies in recent years are also capable of detecting a wide range of physical, chemical, and biological stimuli with high precision. Integrating sensors with AI and ML algorithms further amplifies their utility. Large datasets generated by these sensors can be processed in real time to identify patterns, predict equipment failures, and detect anomalies.[54]

Artificial Intelligence and Machine Learning Technologies: The combination of AI and ML driven technologies allows digital twins to analyse extensive data streams, facilitate pattern recognition, and improve situational awareness. ML methods such as deep learning, neutral networks and key algorithmic approaches including supervised and unsupervised learning, reinforcement and incremental learning, and anomaly detection, all of which enable systems to learn from historical data of the effects of CWAs (toxic chemicals, reactions, material behaviour) and adapt to evolving conditions, thus enabling faster decision making.[54]

Extended Reality (XR): Extended Reality (XR) comprises a spectrum of technologies. These include Augmented Reality (AR), which overlays digital content onto the real world, and Virtual Reality (VR), which immerses users in synthetic environments. XR solutions involve the replacement of traditional displays by laser-based projections or headsets which can integrate digital information into human perception. XR-based training has proven to be impactful in defence and can also be extended to their role in CWAs. In fact, XR has been implemented into use by the Netherlands Ministry of Defence. Operationally, XR can facilitate mission planning, remote assistance, and augmented operator field-of-view with labels or annotations, simplifying CWA detection and enhancing situational awareness. Given XR's ability to deliver intuitive, real-time interactions, it is exceptionally well suited for integration with digital twins.[54]

2.3 Comparative Analysis of Separation Methodologies

2.3.1 Adsorption

Adsorption remains one of the most widely used separation technologies due to cost effectiveness, and environmental friendliness. [50] However, traditional adsorbents such as activated carbon and metal oxides show weak interactions with CWAs, especially at low concentrations. Their amorphous nature, irregular pore sizes, and limited chemical tunability restrict selective adsorption performance.[50] Zeolites and activated carbon also suffer from limited capacity, low productivity, and high energy demands.[55]

To enhance performance, researchers have modified these materials with additives such as triethylene-diamine or metallic salts (Zn, Cu). However, because their pore structures remain amorphous and unpredictable, systematic performance improvements remain challenging. Recent studies suggest that MOFs offer solutions to these limitations.[56]

2.3.2 Metal Organic Frameworks

Compared to conventional porous materials, MOFs exhibit larger surface areas, higher porosities, and tuneable structures.[56] Despite these advantages, MOFs in powdered form are difficult to process, prone to agglomeration, and less efficient in real world applications. A promising alternative is the development of MOF gels, which feature gel networks with enhanced mass transfer, reduced diffusion barriers, and superior catalytic and adsorption activity. Beyond CWAs, MOF gels have also shown potential in addressing broader environmental challenges, including the remediation of heavy metals, toxic gases, organic pollutants, and fine particulate matter (PM2.5/PM10).[33]

2.3.3 Gas Stripping

Gas stripping operates on a simple principle of transferring contaminants from liquid to gas using carrier gases such as air, steam or inert gases. It is especially effective in the removal of volatile and semi-volatile CWAs like CEES and DMMP. However, the process requires solvents with specific properties (low volatility, high solubility), limiting its applicability.[57] Additionally, it is energy intensive, expensive, and often inefficient for large scale decontamination scenarios, as long processing times are required to handle high contaminant loads.[57]

2.3.4 Membrane Filtration

Membrane filtration has gained increasing attention as a selective barrier against CWAs. Advanced nanomaterial-based membranes, particularly those incorporating GO or hybrid composites, can block highly toxic vapours such as DMMP.[53] These membranes are lightweight, can be fabricated into ultrathin films, and have potential applications in protective apparel and filtration systems. Despite their promise, membrane technologies face challenges such as costly and energy intensive fabrication, reliance on hazardous synthesis routes, and degradation due to fouling, hardness, and prolonged exposure to harsh chemicals.[58]

While recent advances in metal-organic frameworks, AI driven predictive simulations, and digital twin technologies are rapidly changing the face of separation science, traditional separation techniques like gas stripping and adsorption continue to form integral parts of chemical decontamination systems. Modern computational methods such as molecular simulations and digital twins have further advanced understanding of adsorption mechanisms in MOFs, enabling predictive insights into pore structure, active site chemistry, and agent–material interactions.[28,33,50] Additionally, traditional methods such as gas stripping remain attractive due to their operational simplicity and scalability, despite well-documented limitations including solvent dependency and high energy consumption.[57,59] Similarly, membrane-based protection systems continue to offer strong selectivity and tunability for toxic vapour filtration, yet still face challenges related to fouling, long-term stability, and permeability–selectivity trade-offs.[11,43]

By integrating classical separations with advanced modelling and AI tools, researchers can now identify key structure property relationships that were previously inaccessible through experimentation alone. This combination bridges the gap between empirical design and predictive optimisation, improving process efficiency and safety in emergency decontamination scenarios. Nonetheless, practical implementation still faces barriers related to cost, energy requirements, and recyclability, highlighting the need for balanced hybrid solutions that leverage the robustness of traditional processes alongside the precision of modern technologies.

3. Challenges and Future Perspectives

3.1 Identified Challenges in Advanced Separation

Research into chemical warfare agent separations is shaped by several pressing challenges. One major issue is the limited availability of reliable data, since the extreme toxicity of CWAs necessitates the use of safer simulants such as DMMP for sarin or 2-CEES for mustard gas. While these analogues capture some of the relevant chemical properties, they do not fully replicate the reactivity of the real agents, creating gaps in accuracy and reliability.

Computational simulations and high throughput screening of materials such as metal organic frameworks (MOFs) have been used to address this limitation, yet these methods often yield invalid or inconsistent results.[56] Scalability is another hurdle, as MOFs are typically synthesised in powder form, which leads to handling difficulties, low volumetric efficiency, and pressure drop.[56] Although MOF based aerogels, which integrate the high porosity of aerogels with the adsorption and catalytic activity of MOFs, have been developed to address this, large scale synthesis, drying methods, and structural stability continue to limit practical applications.[60] A further challenge is the lack of up-to-date validation for conventional separations such as membrane filtration and gas stripping. Much of the available literature is based on earlier experimental studies, leaving uncertainty about their efficiency and relevance for modern emergency response contexts, as research focus has shifted toward advanced materials and digital strategies. Finally, the application of artificial intelligence (AI) in this domain faces difficulties due to the complexity of quantum systems, the need for high quality datasets, and the limitations of generalising across diverse chemical systems.[61] Since direct experimentation with CWAs is hazardous, data remain scarce, and simulations often require extensive computational resources.

Figure 1 presents a comparative overview of separation methodologies, highlighting their progression, and key limitations.

3.2 Critical role of Separation Strategies

Despite these obstacles, advanced separation techniques remain critical for developing effective responses to chemical threats. MOFs, with their ultra-high porosity, large surface area, structural stability, and tuneable pore size, have proven particularly effective for adsorption and degradation of CWAs. Compared with traditional materials such as activated carbon, enzymes, zeolites, and metal oxides, MOFs offer broader structural diversity, stronger adsorption capacity, more active sites, and faster reaction kinetics.[56] Complementing these materials, digital twins enable real time monitoring and virtual simulation of decontamination systems, allowing responders to test strategies before

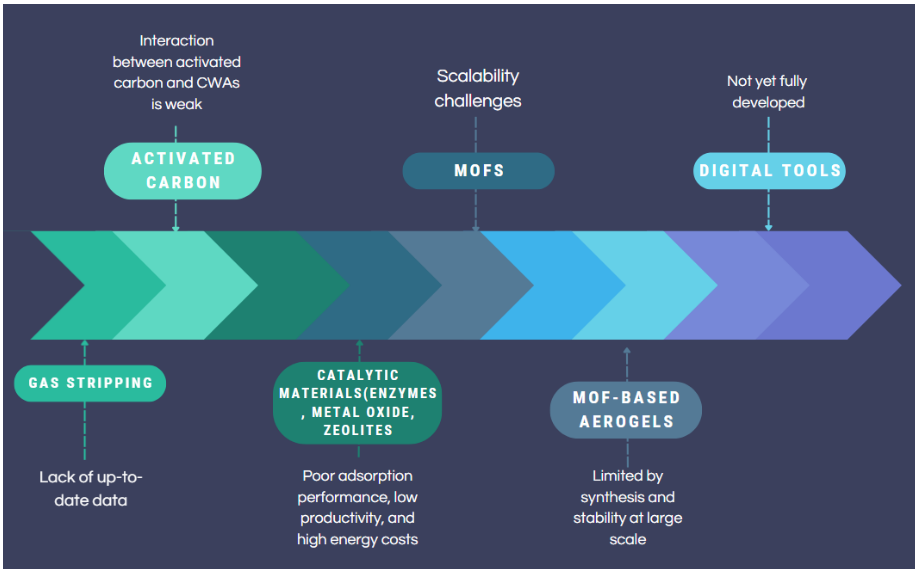

Figure 1: Evolution of separation and decontamination strategies for CWAs, with associated challenges.

deployment in the field, thereby improving decision making, reducing risk, and ensuring more efficient responses.[61] Similarly, AI and machine learning provide powerful predictive tools for identifying optimal separation materials and processes. Unlike traditional high throughput simulations, which are slow and often unreliable, machine learning can accelerate these processes by up to three orders of magnitude, while improving accuracy and guiding the identification of MOFs most suitable for decontamination.[56] Together, MOFs, AI, and digital twins represent promising directions that complement conventional approaches. While they do not fully overcome challenges, they provide safer, faster, and more adaptable tools that improve current research practices and pave the way for future advances in CWA mitigation.

3.3 Future Directions and Research Outlook

Looking forward, future research should aim to improve the balance between effectiveness and sustainability in separation methods, ensuring that new solutions do not introduce additional environmental hazards. The development of universal and eco-friendly approaches capable of neutralising CWAs across multiple forms, while minimising effluent production and energy consumption, will be critical. Greater emphasis should be placed on optimising existing techniques, combining complementary methods such as reactive membrane with gas stripping, and exploring novel materials and digital technologies. Ultimately, prioritising efficiency, safety, and environmental compatibility will be essential to ensure that separation strategies both protect human health and minimise ecological impact in the event of chemical emergencies.

4. Conclusion

Chemical warfare agents (CWAs) continue to pose a critical global threat due to their extreme toxicity, environmental persistence, and potential use in modern conflicts. Although international conventions prohibit their use, recent incidents underscore the ongoing need for rapid, efficient, and sustainable decontamination strategies. This review demonstrated that while conventional adsorption materials such as activated carbon are still relevant, newer separation-based technologies, including metal organic frameworks (MOFs), catalytic materials, membrane filtration, and gas stripping, offer superior selectivity, reusability, and structural tunability. MOFs and MMR show considerable potential for integrating adsorption and catalytic degradation within a single system, advancing the development of self-regenerating and environmentally responsible protective materials.

The integration of digital technologies further enhances these advancements. Machine learning accelerates the discovery and optimisation of novel materials, while molecular simulations and digital twins enable predictive performance assessment under controlled virtual conditions. However, significant challenges remain in scalability, cost effectiveness, data accessibility, and experimental validation with live agents. Future research should prioritise hybrid systems that combine multiple separation and catalytic processes, guided by artificial intelligence and life cycle sustainability principles.

Ultimately, the future of separation-based decontamination relies on translating laboratory scale innovations into robust, scalable, and sustainable technologies capable of mitigating the environmental and societal risks associated with chemical warfare agents.

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Separation Technologies and Policy Challenges in Addressing Microplastic Pollution

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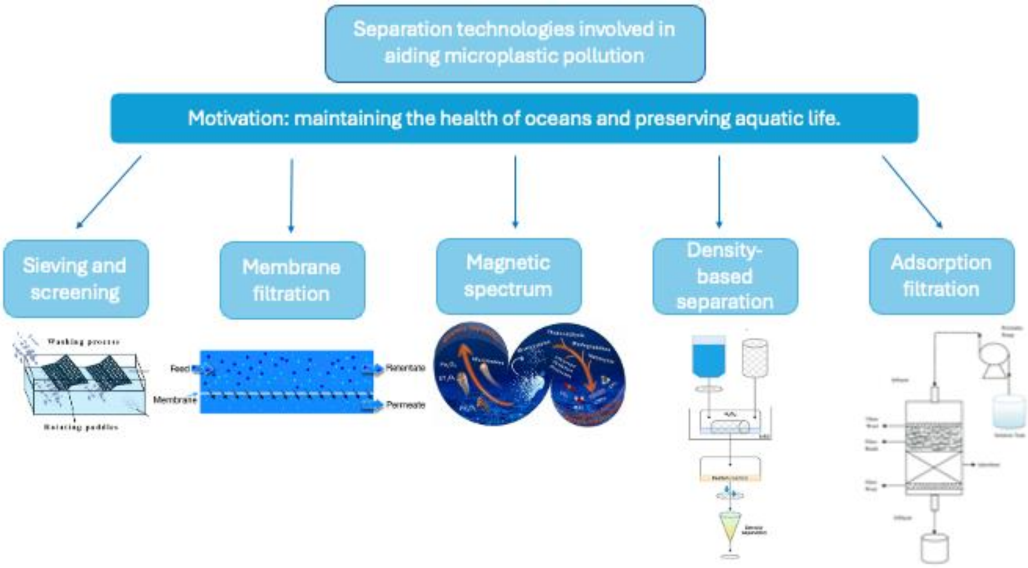
Graphical Abstract



Abstract

Microplastic accumulation in aquatic systems has emerged as a critical environmental and public health issue, with particles detected in human organs and across diverse ecosystems[1]. Despite growing awareness, current treatment technologies remain insufficient to address the pervasive contamination. Existing separation methods—physical, chemical, and biological—show variable efficiencies ranging from 65% to 100%, yet challenges persist due to microplastics' small size, heterogeneous composition, and continuous release into the environment[2]. Recent advancements include adsorption, membrane filtration, photocatalysis, electrochemical processes, and biological or enzymatic degradation, complemented by artificial intelligence-driven detection and hybrid systems integrating multiple mechanisms such as sieving, density, and magnetic separation[3]. However, literature highlights key challenges: limited scalability, energy intensity, secondary pollution, and inconsistent removal across particle sizes. To overcome these limitations, computational modelling and machine learning offer promising pathways for optimising process parameters, predicting separation efficiency, and designing adaptive treatment systems. Future research should focus on integrating advanced separation technologies into existing water treatment infrastructure, developing sustainable materials for microplastic capture, and establishing standardised assessment frameworks. Addressing these gaps is crucial to mitigate ecological disruption, protect biodiversity, and ensure safe water resources.

1. Introduction

1.1 Context and Relevance

Microplastics are small pieces of plastic less than 5 mm in size that can come from either primary sources - intentionally designed for use in industrial, commercial, or personal care products- or secondary sources - generated through the chemical, physical, and biological breakdown of larger plastic products[4]. These microplastics can enter the environment through spills or other releases during manufacturing or shipping, industrial process waste-stream management, and product use.

The growing global concern of the presence of microplastics is due to their persistent, low biodegradability and bio-accumulative behaviour. The pollution of microplastics has emerged as a critical environmental issue, with evidence of their presence across marine systems, terrestrial soils, and even atmospheric deposition. Studies have also reported the presence of microplastics in bottled water, tap water, table salt, seafood and even human blood and tissue, underscoring the pervasive nature of the problem and raising significant concerns over potential human health impact[5].

The worldwide production of plastic has increased dramatically, doubling from 2000 to 2019 and projected to increase further unless strong interventions are adopted. The OECD reports that plastic waste produced globally is on track to possibly triple by 2060 under these conditions[6]. The growth in plastic waste production has led to an increase in leakage of microplastics into the environment, with ramifications to ecosystems, human health, and economies.

In Australia, the Great Barrier Reef, an icon valued ecologically, economically and culturally, is under threat due to deteriorating water quality, with microplastic contamination being a growing component[7]. Microplastics threaten biodiversity, disrupt food webs, and may pose health risks, therefore, creating high environmental stakes. Therefore, it is imperative that the development separation processes are implemented as soon as possible.

From an economic and governance perspective, the required upgrades in infrastructure with advanced technologies, alongside regulatory and policy changes, represent very large investments. While the precise cost for these microplastic-specific treatments are still being established, preliminary studies reveal that some advanced wastewater treatments and separation processes are technically feasible and cost-effective, though trade-offs in energy, capital and operational expenses are non-trivial [7,8,9].

In summary, the global rise in plastic production and its leakage into natural systems highlight the urgent need for efficient microplastic separation strategies. This context establishes the environmental, economic, and policy rationale for evaluating treatment technologies in subsequent sections.

1.2 Background and literature review

Over the past decade, various separation methods including filtration, biological, and chemical, have been explored for removing microplastics from waste and wastewater. Membrane bioreactors, rapid sand filtration, coagulation/flocculation, adsorption, density separation, magnetic separation, and enzymatic or microbial degradation are among those studied. An example of one of these are membrane bioreactors combined with sludge treatment which have been identified as cost-effective options in certain contexts[7]. Reviews indicate that existing wastewater treatment plants can achieve high microplastic retention rates under specific conditions, yet many microplastics may still bypass treatment[8, 9, 10]. This highlights the inherent challenge of removing microplastics from the environment, due to their microscopic nature.

The bypassing of treatment shows how significant gaps in this technology still remain. Key challenges include energy, cost, and secondary pollution, as a higher removal efficiency often require a greater energy input, chemical usage, or generation of waste. Additionally, scalability is an ongoing obstacle to overcome, since full-scale implementation is still rare, even though it may perform well in lab or pilot settings. This is due to the heterogeneity nature of microplastics, which can complicate their separation and detection. Furthermore, policy and regulatory gaps due to the lack of standardized measurements, inconsistent regulation, and insufficient integration of separation technology into regulatory frameworks are a barrier to the elimination of microplastics.

In summary, while diverse physical, chemical, and biological separation methods have been tested, none yet deliver consistent large-scale removal across all microplastic types. These limitations underscore the importance of identifying performance gaps and innovation priorities, which are mapped in the next section.

1.3 Scope and Objectives

This review critically examines advanced separation technologies for microplastic removal, focusing on their performance, scalability, sustainability, and policy integration. It also assesses the legal, financial, and ethical challenges that influence deployment and global equity in access to clean water.

1.3.1: Objectives

- Synthesise findings from recent literature on the efficiency, mechanisms, and feasibility of physical, chemical, and biological microplastic-removal processes;

- Identify knowledge and performance gaps—including cost, energy use, and standardisation limitations—that hinder full-scale adoption;

- Evaluate the intersection between technological progress, policy frameworks, and economic realities to determine integration pathways; and

- Propose actionable directions for future research and investment, aligning engineering innovations with sustainability goals and regulatory development.

1.3.2: Scope and Roadmap

The included topics are: engineering separation technologies, process optimisation, scalability analysis, and policy implications. The excluded topics are: detailed toxicological mechanisms, nanoplastic (<1 μm) health effects, and polymer degradation chemistry beyond separation relevance. Collectively, this section establishes the conceptual framework for analysing microplastic sources and impacts, engineering separation processes, and the interconnected legal, financial, and ethical dimensions.

By outlining scope and objectives, this section provides a roadmap for how technological, policy, and economic lenses are integrated throughout the review to inform holistic solutions to microplastic pollution.

2. Origin and Accumulation of Microplastics

2.1 Sources

Microplastics are found everywhere in our everyday lives, infiltrating our water systems, ecosystems and even our blood systems. They can originate both from primary and secondary sources. Primary sources include those of intentionally manufactured microplastics, such as microbeads used in facial washes, nurdles, plastic-based glitters and more. Secondary sources include larger plastics which have deteriorated through means of mechanical abrasion, chemical hydrolysis, radiation and microbial digestion [11]. Common types of microplastics in the environment include polyethylene (PE), polypropylene (PP), polystyrene (PS), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polyamide (PA), and polyurethane (PU) [12].

Table 1: Common types and sources of microplastics [13].

Classification of microplastic	Type of microplastic	Source of microplastic
Primary microplastics	Microbead	Personal care and cosmetic items, such as exfoliating scrubs and toothpaste.
	Microfibre	Textiles like synthetic clothing, carpets, and home furnishings. Personal care products, including cigarette filters, wet wipes, and face masks.
	Resin particle	Plastic products
Secondary microplastics	Fragments	The breakdown of larger plastics.
	Fibre	Textiles, including garments, ropes, and fishing nets.

2.2: Accumulation and Harm of Microplastics

The accumulation of microplastics causes harm to all the ecosystems and environments they enter. Toxic pollutants such as polychlorinated biphenyls and dichlorodiphenyltrichloroethane (DDT) are absorbed by microplastics, thus can be transported more easily with plastic as their vector, while also persisting in the environment for much longer. Along with toxic pollutants, microplastics are also carriers for heavy metals, interacting with metals such as cadmium (Cd), lead (Pb), and arsenic (As)[14]. Heavy metals are detrimental to ecosystems as they are toxic to living organisms, posing major environmental and public health concerns, and in some cases are lethal to humans. Thus, the transport of such through microplastics is an additional complexity to the heavy metal pollution concern[15].

2.2.1: Human Body

Microplastics enter the human body through means of air, water and food, penetrating deep into the body and accumulating in tissue[16]. Microplastics have been detected in the blood, saliva, liver, kidneys, faeces, lung tissue, placenta and more[17]. Inhalation is a common route for microplastics into the human body; due of their size they evade the mucociliary clearance system and thus enter the upper respiratory tract, where they then circulate throughout the body via the upper digestive system and accumulate in various organs. Oral ingestion serves as another pathway into the human body. The intake of seafood is a major route for microplastics as they are commonly found within the tissues of marine organisms, thus facilitating their entry into humans. In Indonesia, it was discovered that 55% of fish samples were contaminated with microplastics. Bottled water similarly serves as a concern for microplastics ingestion, as consuming tap water leads to an estimated intake of 4000 microplastics annually, whereas bottled water can result in an additional intake of about 90,000 microplastics per year. Lastly, skin contact and dermal absorption similarly facilitate microplastics into the human body, for example, exposure to some cosmetics like body washes, topical medications or exposure to surgical or prosthetic devices[18].

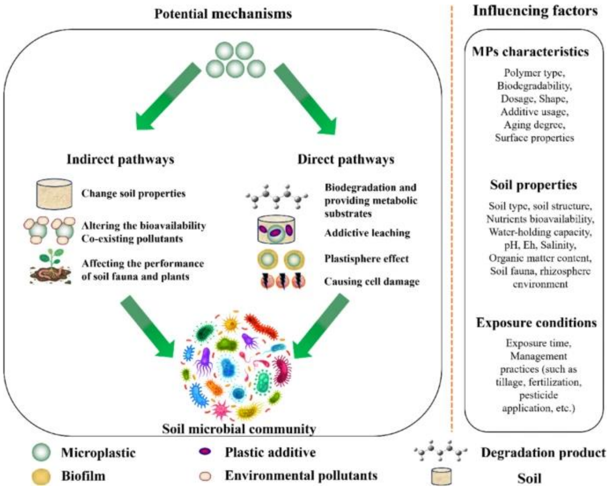
Due to microplastics' tendency to be a vector for toxic pollutants, these pollutants are released into an organism upon ingestion, resulting in toxicological effects like endocrine disruption, oxidative stress, abnormal growth patterns and many more. Cytotoxicity is an example of microplastics harm; they enter the cells and are enclosed by lysosomes for degradation, then are released into the cytoplasm. This can then result in mitochondrial dysfunction, which in turn increases the production of reactive oxygen species, an increase in such can undermine the cell's antioxidant defence systems, resulting in protein oxidation, lipid peroxidation and DNA damage. Neurotoxicity is another example, as smaller microplastics can cross the blood brain barrier and accumulate in the brain tissue, inflicting serious neuronal damage. Another implication on the brain are the reducing levels of synaptic proteins, which disrupt the neurotransmitter functions and induce neuroinflammation, which leads to deficits in learning and memory, as studied in mice. Other implications of microplastics' harm to the human body include oxidative stress, inflammatory reactions, apoptosis, gene damage, hepatoxicity, and respiratory toxicity[19, 20].

2.2.2: Soil Microbiomes

As other environmental systems, microplastics pose severe detriments to soil and the natural environment. For instance, in 2015, 79% of plastic waste ended up in landfills or the natural environment, ultimately invading soil and land. Plastics from landfills fragment and disperse into the environment through methods of leachate leakage, surface runoff, and wind dispersal, exacerbating environmental accumulation. Processes including flooding, atmospheric deposition, tire wear, and industrial/consumer waste disposal may also contribute to soil microplastic contamination. Microplastics accumulate rapidly and persist, remaining in the environment for at least 25 years, serving as a significant depository for microplastics with an annual input of plastic waste into terrestrial ecosystems exceeding that of oceans by 4 - 23 times. During their long life time they disrupt soil ecosystems by substantially altering soil structure, porosity, bulk density, water-holding capacity, pH value, and nutrient availability, therefore notably reducing soil health[21].

As previously discussed, microplastics have a tendency to carry heavy metals, and this leads to synergistic effects on plants, increasing the likelihood of plants becoming toxic, as both disrupt various biological and physiological processes. The presence of microplastics in soil will affect root development, soil aeration, diminishing soil fertility and altering the nutrient cycle[14].

Figure 2: Potential mechanisms of Microplastics on soil microbial communities



2.2.3: Marine Environments

Plastic and furthermore microplastics are a large contributor to marine pollution, they cover almost all aquatic environments and thus have reduced the sources for safe pollutant safe water, causing severe issues as the demand for water nearly doubles every 20 years, due to industrial expansion and population growth. It is estimated that 8 million tonnes of plastics enter the oceans and seas every year. Microplastics are among the most damaging and harmful marine pollutants. Plastics enter the ocean through urban, industrial, boating, shipping, fishing, and aquaculture activities, as well as accidents like container spills, shipwrecks, or collisions that release raw materials, which later degrade into microplastics[14].

Similar to humans, microplastics inflict harm on marine organisms, including genotoxicity, neurotoxicity, reduced feeding activity, growth delays, and decreased reproductive fitness[14]. As mentioned previously, microplastics have a tendency to attach to other harmful pollutants and in marine environments they attach to hydrophobic pollutants, which are not degradable and harmful to organisms[22]. Below in table 2 are examples of the harm microplastics cause to marine animals.

Table 2: Deleterious effects of microplastics on diverse types of marine animals[14].

Effects	Mechanisms	Marine animals affected

Physical ingestion: Blockage and damage of digestive systems, leading to starvation and reduced growth	MPs accumulate in the digestive tract, creating blockages or damaging internal tissues	- Zooplankton: Copepod (Neocalanus cristatus) - Crustacean: Norway lobster (Nephrops norvegicus) - Fish: salmon-bass (Argyrosomus regius) - Sea turtle: Loggerhead turtles (Caretta caretta)
Energy depletion: Reduced energy stores due to false satiation	Organisms sense "fullness" after ingesting indigestible MPs, leading to a lack of appetite	- Coral: Stony cup coral (Astroides calycularis) - Crustacean: Crab (Carcinus maenas) - Fish: Zebrafish (Danio rerio) - Sea turtle: Green turtles (Chelonia mydas)
Habitat disruption: Smothering of benthic habitats and coral reefs	MPs settle on seabed and reefs, physically blocking light and oxygen flow	- Coral: Branching coral (Pocillopora acuta), - Benthic invertebrates: Tubeworm (Spirobranchus triqueter)
Reproductive effects: Impaired reproduction, reduced fertility, and abnormal development	MPs interfere with gamete quality, embryo development, and larval growth	- Crustacean: Marine copepod (Tigriopus japonicus) - Mollusk: Pacific oyster (Crassostrea gigas) - Fish: Zebrafish (Danio rerio)
Immune suppression: Oxidative stress leading to reduced immune responses	Microplastic-induced stress lowers the ability to fight infections, increasing susceptibility to disease	- Crustacean: Pacific White Shrimp (Litopenaeus vannamei) - Mollusk: Blood clam (Tegillarca granosa)

3. Engineering Separation Processes for Microplastic Removal

3.1: Overview of Separation Methods

The separation of microplastics from water and wastewater has become a paramount focus of environmental engineering, and consequently, there are various processes for separation that are current, with more advanced processes emerging as the issue persists. These methods are grouped into four broad categories; mechanical size based separation, filtration technologies, density-driven processes and emerging advanced hybrid approaches[23]. Traditional physical methods like sieving, sand filtration and sedimentation are productive for larger particles, but are often unable to capture nano and micro-sized plastics, particularly in more complex environmental matrices. Conversely, more advanced methods, like membrane filtration, electrocoagulation and magnetic separation are effective in capturing smaller fractions, however, come at significantly higher costs combined with operational complexity, therefore are often unable to be used in less developed communities[23].

3.2: Sieving and Screening

Used as a pre-extraction technique, sieving and separation are moderately effective for the removal of larger microplastics (1.18–5 mm), still visible to the human eye[24]. This method separates microplastics from the soil, sand and sediment with the use of granulometric fractions, dividing it into different-sized components, allowing smaller particles to pass through, while retaining larger ones. It is a simple, low-cost separation method, with minimal energy demands[25]. For PET particles in the 1.18-5mm range, removal efficiencies reached up to 99.2%, while in a border range (0.15-5mm) the average was 76.1% [24]. This indicates that sieving is a highly effective technique when separating larger microplastics, however, as the particle size shrinks, it loses efficacy. As it is unable to remove a large amount of microplastics, sieving cannot be used as a separation method in isolation. This makes it useful as a pretreatment, removing larger coarse fragments before the use of one of the following separation methods.

3.3: Filtration Technologies

Similarly to sieving, filtration uses filters of specific pore size to separate a solid phase from a liquid phase, however on a more minute scale. It is often used in conjunction with other microplastic separation methods like density separation (5.4) and chemical digestion[26], either during stages, or at its beginning.

3.3.1: Membrane Filtration

Membrane filtration is a pressure-driven separation process, where water passes through a semi-permeable membrane while microplastics are retained. Membranes are specified by their pore size[27], with reduced sizes becoming increasingly more effective in retaining most microplastics; microfiltration (MF): 0.1-10 µm pores, ultrafiltration (UF): 0.01–0.1 µm pores, nanofiltration (NF): 0.001–0.01 µm pores and reverse Osmosis (RO) <0.001 µm pores, capable of retaining nearly all microplastics, and salts[28]. NF and RO membranes can remove over 95% of micro and nanoplastics in controlled conditions, however, as real-world applications introduce challenges, like fouling, membrane filtration becomes less effective. As separation in increasingly smaller pore sizes requires greater pressure[29],with RO requiring pressures between 30 and 80 bar[30], a trade-off between cost and efficiency emerges, requiring expansive amounts of energy to properly separate[31]. To combat this, a combination of membranes are used, where MFs and UFs are used first to filter out larger microplastics and reduce fouling, followed by NF and RO for finer microplastics and dissolved pollutants.

3.3.2: Adsorption Filtration

Adsorption filtration separates microplastics from water by binding them to porous mediums with large surface areas. Water passes through a column packed with adsorbent materials[32], with which the microplastics interact with and are subsequently retained. The treated water exits the stream with a reduced microplastic concentration. These adsorbents can be regenerated by washing, heating, or magnetic separation for reuse. Common adsorbents include activated carbon, clays, biochar, graphene-based materials and magnetically modified sorbents[33]. Depending on the absorbent utilised, this filtration is driven by different forces including Van der Waals forces, electrostatic interactions and hydrophobic interactions[34]. Activated carbon is the most industrially used adsorbent, capturing microplastics through hydrophobic interactions and capable of reaching removal rates of 90%. However, more typically ranging from 60-80%[35]. Despite not being used in full-scale treatment plants due to high variable dependence on the chemistry of the water (due to its low cost and versatile technique), it becomes a promising technique when combined with membrane filtration, to reduce fouling, operational costs, and energy consumption.

3.3.3: Magnetic Separation

An emerging separation method, used only at the lab scale at this stage, is magnetic separation. Essentially an extension of adsorption, it uses magnetically responsive materials like iron oxides to absorb and bind microplastics to their surface and then remove them using an external magnetic field. The magnetic particles can be either free nanoparticles which absorb microplastics through electrostatic interactions, hydrophobic interactions or functionalised composites, where the magnetic core is coated with sorbents like biochar or graphene oxide that aid microplastic adhesion. In recent lab tests, this strategy has at >95% removal consistently, with the use of Fe_3O_4-biochar composites[36].

3.4: Density-Based Separation

Density-based separation uses the density differences between plastics and the extraction solution to extract microplastics. These plastics will either float, if they are less dense than the medium (flotation), or sink, if they are denser (sedimentation). Using gravitational settling, sedimentation removes up to 50–70% of microplastics >300 µm, which are mostly fibres and fragments[37]. Moreover, air flotation units can recover 50-80% of lighter microplastics in lab scale studies. The separation process can be sped up, with the application of centrifugal forces accelerating the rate of sedimentation/flotation. By creating a hydrocyclone, sedimentation and flotation can occur at significantly faster rates, in a process that typically takes days to statically complete. Density-based separation works passively for large volumes of water, and requires low energy. However, it becomes ineffective when plastics have densities that are close to water, such as PET, PVC and PS, making separation unfeasible via sedimentation or flotation. In some large-scale separation plants, density-based separation is combined with NF and RO membrane filtration[38], creating a hybrid separation method that balances energy output and efficacy of microplastic removal

Table 3: Comparison Table of Microplastic Separation Technologies

Technology	Efficiency	Scale	Key Advantage	Limitations
Sieving and Screening	Up to 99.2% for large PETs (1.18–5 mm). Avg. 76% (0.15–5 mm)	Full-scale	Simple, low-cost, low-energy	Ineffective for particles <1 mm: only suitable as pretreatment
Membrane Filtration	>95% for NF/RO, MF & UF effective for larger MPs	Pilot to Full-Scale	Very high efficiency; capable of removing microplastics, nanoparticless, and salts	Fouling, high energy demand (up to 80 bar) and expensive operation
Adsorption Filtration	Typically 60–90%, depending on adsorbent and variables of medium	Lab to Pilot-Scale	Low-cost, regenerable, reduces membrane fouling	Variable efficiency, sensitive to water chemistry; not used standalone
Magnetic Separation	>95%, lab-scale using Fe_3O_4-biochar	Lab-scale (emerging)	Rapid, selective, reusable, low-energy	Nanoparticle leaching risk; currently unscalable

	composites			
Density-Based Separation	50–70% (sedimentation) 50–80% (flotation)	Lab to industrial-scale	Low-energy, scalable for large volumes, simple operation	Ineffective for plastics with densities similar to water (e.g. PET, PVC, PS)

4. Legal, Financial, and Ethical Considerations

4.1: Legal Considerations

To address general health hazards and different issues globally, the United Nations put in place their 16 Sustainable Development Goals. SDG 3,6,12,13 and 14 (Life Below Water) all indirectly address microplastic pollution, but only SDG 14 specifically targets plastics but excludes microplastics, and current monitoring still relies mainly on citizen science for larger debris, with no standardised international protocol yet in place[39]. Additional measures taken by the EU such as the Marine Strategy Framework Directive and the Water Framework Directive establish obligations for member states to monitor and reduce pollutants, but issues regarding microplastics and their regulations remain underrepresented[40]. Similarly, the U.S. Environmental Protection Agency has no specific regulations targeting microplastics, though the Microbead Free Waters Act of 2015 prohibited microbeads in cosmetics[41]. The OECD (Organisation for Economic Co-operation and Development) and non-OECD countries are adopting new measures to address plastic and microplastic pollution. They want to improve waste management policies, implement bans on frequently littered single use plastic items, and restrict the manufacturing and sale of personal care and cosmetic products containing microplastics. In addition, the OECD highlights that addressing microplastics from textiles and tyres requires policy mixes that combine innovation incentives, industry standards, and extended producer responsibility schemes to ensure long term reductions[42]. Despite these steps, the absence of harmonised global standards creates legal uncertainty for industries and utilities. If separation systems fail, liability may shift to municipal operators or technology providers, showing the urgent need for enforceable discharge limits in wastewater and drinking water systems.

4.2: Financial Considerations

In 2024, the global market for microplastic filtration systems was valued at USD 12.82 billion and is forecasted to reach USD 35.48 billion by 2034. Advanced separation processes such as membrane filtration, electrocoagulation, and hybrid technologies dominate the industry with their higher efficiencies but carry a high capital and have high operational costs, particularly due to membrane fouling, energy consumption, and maintenance requirements[43]. For developed economies, the costs can usually be managed by slowly upgrading their water systems. However, in developing countries, the high costs could make it harder for people to get equal access to clean water, creating inequalities in water access. Cost benefit analyses show that although microplastic removal technologies are expensive at the start, they can save money in the long run. A long-term economic benefit can be deduced through the reduction of health problems, lowering the costs of cleaning up damaged ecosystems, and protecting industries like fisheries, therefore the benefits outweigh the upfront investments. Regarding the adoption of a suitable solution will depend on the different socioeconomic context. No single solution works everywhere; the right choice depends on local conditions such as money, infrastructure, and community capacity[44].

4.3: Ethical Dimensions

The ethical considerations surrounding microplastic pollution are tied to various issues such as environmental and social justice, intergenerational equity, and corporate responsibility. Firstly, equitable access to clean water must be prioritised, imposing the cost of advanced treatment solely on communities with limited resources deepens global injustice. In addition, the long term and largely unknown health risks of microplastic exposure raises ethical and equity questions because vulnerable communities are likely to suffer the most from microplastic pollution, and waiting for complete proof before taking action can cause larger problems down the line. Therefore, there is abstraction of intergenerational justice,; future generations will have to deal with pollution and health issues they did not create and the long term persistence of microplastics shows that the damage accumulates over time. Furthermore, because microplastics are so small, people often overlook them and may not feel responsible for their impact, even though companies and individuals continue to pollute shared resources like oceans and air that everyone depends on, a problem known as the tragedy of the commons. From a global perspective, international justice is also impacted, since pollution crosses borders and all nations share responsibility for addressing it. Real solutions may require systemic change, with societies rethinking how plastics are produced, used, and valued. Ethical accountability lies not only with governments but also with plastic producing industries, which play a key role in both prevention and remediation of the issue[45]. Therefore, ignoring the health and ecological consequences of microplastics risks creating long lasting harm, raising serious questions about the responsibility of producers versus consumers in tackling plastic pollution.

5. Challenges and Future Perspectives

5.1: Identified Challenges

Although there are notable advancements within the field of separation processes for the removal of microplastics within our ecosystem, several persistent challenges limit real-world deployment. A major challenge is scalability: despite many processes performing well at lab-scale methods, it is unclear whether they would be feasible on a larger scale. This is because there are more factors that need to be taken into account, such as the economics of scaling up (for example the cost of equipment, staff, permits, etc). This is particularly applicable for developing nations, in which they would face energy and cost barriers, which would limit their applicability.

Maintenance is an important challenge to consider, due to material durability and reusability. In separation processes like membrane filtration and adsorption filtration, materials are a key component of the separation, therefore, the decision in selecting the material that is the most efficient, whilst also ensuring it is sustainable, durable, and if it can be reused. If it cannot be reused, then it must be considered as to how will it be disposed of in a sustainable manner.

Another identified challenge is the lack of standardised testing for removal efficiency. In 2023, the International Standardisation Organisation (ISO) published one of the first internationally recognised microplastic testing standards, ISO 24187 – Principles for the analysis of microplastics present in the environment. This document describes the principals to be followed in the analysis of microplastics in various environmental matrices[46] and provides guidelines for sampling, sample preparation, and data processing[47]. Although this is a step in the right direction, broad uptake and further method comparisons are required to enable reliable cross-study comparisons and regulatory acceptance.

5.2: Future Directions

As the worldwide consumption of plastic increase, it is imperative that we as a society implement the changes necessary to produce a difference, and to sustain the habitability of the earth for future generations. Looking forward, there are some key factors to apply, such as the need for standardised monitoring and reporting. The expansion of international standards is needed to harmonise reporting matrices, and regulation and monitorisation is essential in ensuring that the technologies developed are ethical and safe to use. This can be supported through policy-driven research funding and global cooperation. By investing into these emerging methods, it allows for the rapid development and scalability of the technologies, meaning it can be applied sooner outside of the laboratory.

Furthermore, despite the technologies being advanced, it is vital to ensure it is sustainable, low cost, and high efficiency, especially if they are to be used in less built-up areas. Additionally, its maintenance must be considered, as this can provide unnecessary barriers. This ensures that there is a bridge between lab-scale operations and worldwide implementation.

By combining clear regulations and technological innovation, this will improve that the feasibility of microplastic separation solutions, and help translate promising lab results into quantitative reductions of microplastics in our environment.

6. Conclusion

This review has reaffirmed the significance of the removing microplastics from our oceans and ecosystems. They are at the centre of various environmental concerns, such as the release of toxic additives[48] and its bioaccumulation in marine life. Therefore, its remediation is critical.

The main method of achieving so is through separation processes – this is central to the solution; however, it is not sufficient to remove the copious amounts from our oceans. A combined engineering and policy approach is needed to ensure that the application of the separation processes discussed is implanted in an efficient manner.

Sophisticated separation techniques must be complimented by robust policy, increased international standards, and investments into scale-ups to produce notable change, to create a greater environment for all and preserving the natural beauty of our planet.

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Removal of Melamine from Adulterated Milk Formula: Advances in Separation Technologies and Challenges

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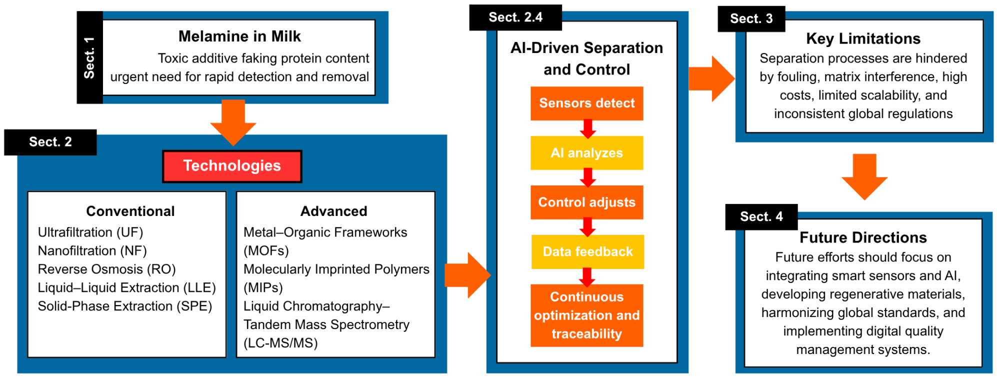
Graphical Abstract



Abstract

This article reviews recent advances in the detection and removal of melamine from adulterated dairy matrices, focusing on industrial-scale separation and real-time monitoring. Traditional unit operations—ultrafiltration/nanofiltration/reverse osmosis, liquid-liquid extraction, and solid-phase extraction—offer continuous processing and tunable selectivity, but suffer from issues such as scaling, matrix effects, and cost/volume tradeoffs. Confirmatory chromatography-tandem mass spectrometry (LC–MS/MS) can achieve sub-ppb sensitivity but still requires significant funding and expertise. Emerging materials (metal-organic frameworks [MOFs], molecularly imprinted polymers [MIPs]) can improve molecular recognition capabilities, while optical spectroscopy and smart sensors enable rapid, non-destructive screening to identify batches requiring LC–MS analysis. Beyond technical challenges, inconsistencies in regulatory allowances and the lack of a unified incident database also hinder coordinated risk assessments and cross-border enforcement. Finally, we developed a roadmap linking methodological harmonization, field validation, and digital quality systems to provide auditable, scalable, and cost-effective assurance for liquid foods.

Keywords: Melamine; Dairy matrices; Membrane filtration; MIPs; MOFs; Food safety; Real-time detection

1. Introduction

1.1 Melamine Contamination: Background and Impact

Food safety is becoming crucial, in dairy industry, the safety of milk products, the removal of contaminants or excess substances like melamine is critical. Melamine is a nitrogen-rich compound, which can be illegally added to dairy products, such as milk formula, to artificially increase detected protein content level, exploiting the limitations of traditional detection methods. The Kjeldahl method, widely used to measure protein content, based on total nitrogen without molecular selectivity, causing it incapable of distinguishing non-protein-based nitrogen compounds like melamine from actual proteins [5]. This vulnerability enables such fraudulent activities that compromise food safety and public health for business interest.

A widely related case is the 2008 China "Sanlu" melamine milk scandal, where melamine-contaminated milk formula affected over 300,000 infants, leading to severe health issues, like kidney damage, and eventually prompted global product recalls [3]. The melamine levels detected in raw milk source for infant formula ranged from 118 to 4,700 mg/kg, which exceeds the later on announced safety limits of 1 mg/kg for infant formula and 2.5 mg/kg for other dairy products [3, 6]. This incident exposed both legal policy integrity and critical weaknesses in traditional separation and detection techniques. This scandal highlights the urgent need for wider variety of detection methods and advanced separation technologies capable of removing melamine at trace levels to ensure the safety of dairy products.

This scandal directly undermines SDG 2 (Zero Hunger) by compromising access to safe and nutritious food, particularly infant formula essential for child growth and development, thereby posing malnutrition risks in vulnerable populations. It also violates SDG 3 (Good Health and Well-Being) through widespread health crises, including kidney stones and failures in over 300,000 children, highlighting the need for robust safeguards to prevent such events. Furthermore, it impacts SDG 6 (Clean Water and Sanitation) as contaminated dairy processing generates hazardous wastewater with melamine residues, posing risks to water quality and ecosystems. Finally, it violates SDG 12 (Responsible Consumption and Production) by exposing fraudulent practices in supply chains that prioritize profit over ethical production, necessitating greater transparency and sustainable sourcing to restore consumer trust.

1.2 Challenges in Current Detection and Removal Methods

Significant challenges persist in the detection and removal of contaminants from dairy products. Conventional methods, such as spectroscopy and chromatography, often lack the sensitivity and selectivity required to reliably detect melamine at low concentrations [4]. Techniques like membrane separation, liquid-liquid extraction, and chromatography-mass spectrometry are typically applied independently, with minimal integration or optimization across technologies [2]. This fragmented approach limits efficiency and scalability in industrial applications. Furthermore, the integration of artificial intelligence and machine learning (AI/ML) for real-time, high-throughput online monitoring of detection and separation remains underexplored [1]. The absence of intelligent, automated systems limits the development of robust online monitoring solutions for ensuring food safety in large-scale dairy production.

This review focuses exclusively on industrial-scale liquid food processing (e.g., dairy, plant-based milks, juices, and process water), excluding solid foods, clinical diagnostics, or environmental remediation. Readers will gain actionable decision frameworks from Section 2 onward, including comparative performance metrics (Table 1a–c), AI/ML integration strategies (Section 2.4), and KPI-driven control loops to guide technology selection, process design, and regulatory compliance. The AI and digitalization components are positioned not as standalone tools but as enablers of closed-loop optimization—transforming sensor data into real-time parameter adjustments (e.g., TMP, pH, flux) for robust, multi-contaminant removal across variable feed conditions.

2. State-of-the-Art in Separation Strategies for Melamine Removal

2.1 Conventional Approaches and Limitations

Traditional separation techniques remain the foundation for melamine removal in dairy products. Among them, membrane-based methods are valued for their efficiency, but often face fouling and performance issues, while solvent and solid-phase extraction approaches provide high selectivity yet struggle with practical constraints such as solvent use, sample preparation, and scalability. The following subsections discuss these two main categories in detail.

2.1.1 Membrane-based Separation: Efficiency and Fouling Challenges.

Membrane filtration techniques, including ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO), have been applied to remove melamine from adulterated milk formula [7]. Two key parameters are used to characterize membrane processes: the transmembrane pressure (TMP) and the molecular weight cut-off (MWCO, usually expressed in Da). TMP acts as the driving force for membrane transport, while MWCO determines the filtration capability of the membrane separation process [8]. A major advantage of these pressure-driven techniques is that they operate continuously without requiring additional solvents or reagents, thereby avoiding chemical residues in the product. Among them, NF and RO are the most widely used in melamine removal from milk, since they can simultaneously remove melamine and enrich the active nutritional components of dairy products, providing high efficiency and energy savings [9]. Under typical operating conditions, NF/RO membranes achieve permeating fluxes on the order of tens of liters per square meter per hour (LMH) at their design TMP [8], which means they can process substantial volumes continuously.

With respect to specific separation mechanisms, melamine (molecular weight ≈126 Da) is much smaller than the MWCO of UF membranes (1,000–100,000 Da), which allows it to pass through easily [7, 8]. This also explains why UF cannot effectively remove melamine and is generally applied as a pretreatment step, such as for removing fats and bacteria, rather than as an effective barrier for melamine. In comparison, NF membranes (100–1,000 Da) have tighter pores and often carry surface charges, which enables partial removal of melamine through a combination of size exclusion and electrostatic interactions. In practice, NF typically provides moderate melamine rejection, achieving around 55% removal [7, 8]. In theory, RO membranes (1–100 Da) have the smallest pores, allowing them to reject small molecules with much higher efficiency [7]. However, some melamine molecules may still permeate due to their very small molecular size and neutral character (polarizability ≈1.32E-23 cm^3) [10]. Reported removal efficiencies of RO membranes are generally high, often exceeding 90% depending on operating conditions [7]. Feed solution pH also influences melamine rejection: melamine is mostly unchanged at milk's natural pH (~6.7), but it becomes protonated (positively charged) in acidic conditions ($pH < 5$) [8]. A charged melamine molecule experiences stronger electrostatic repulsion by NF/RO membranes, so lowering the pH can enhance its rejection. (In practice, extreme pH adjustments are limited in milk processing to avoid damaging the product. [8]

Nevertheless, significant challenges remain in achieving consistently high rejection of melamine. It's very small size and strong polarity make it difficult to retain, while its high solubility in water and lack of strong charge at neutral pH reduce electrostatic interactions with membrane surfaces, further lowering retention probability [11]. As a result, melamine can more easily permeate with the solvent stream. Supporting this, studies have shown that polar and hydrophilic compounds tend to be less rejected by NF membranes, indicating that melamine is difficult to distinguish from water and other small solutes in milk during separation [12]. Moreover, even under the stronger separation conditions of low-pressure RO operations (such as ESPA2 membranes), neutral and hydrophilic small molecules can still exhibit permeation levels of up to 25% [12]. Taken together, these findings highlight the inherent limitations of conventional NF and low-pressure RO membranes when dealing with contaminants like melamine, which are small, neutral, and highly hydrophilic. Another operational challenge is the energy demand of high-pressure RO. Operating at 30–100 bar translates to significant energy use – for example, RO systems for seawater desalination typically require on the order of 2–4 kWh of electricity per cubic meter of water treated [8]. While removing melamine from milk involves a less saline feed (lower osmotic pressure than seawater), RO still consumes more energy than NF due to its higher pressure, impacting overall efficiency and cost.

2.1.2 Solid/Liquid Phase Extraction: Selectivity vs Practical Constraints.

Solvent extraction (SE) is a separation and purification method based on the relative solubility of a substance in two immiscible liquids, characterized by high selectivity [13]. Melamine is a small molecule polar compound that can be hydrolyzed under both acidic and alkaline conditions. Therefore, polar solvent systems such as methanol/water and diethylamino/water are often used in the SE process of melamine [14, 15]. It is worth mentioning that the trichloroacetic acid (TCA) protein precipitation method is a specific evaluation method for infant formula and can be used in SE analysis [29].

Solid-phase extraction (SPE) is another commonly used method for online and offline separation of trace analytes in food. Because melamine is positively charged under acidic conditions, cation-exchange SPE (such as strong cation-exchange sorbents) is often used to extract melamine, particularly in milk-related samples [13]. This technique offers fast reaction times, high efficiency, excellent reproducibility, and low or zero organic solvent consumption [16]. The technique offers high capacity (0.8 meq/g) and high recovery (82%) for infant formula. The development and use of appropriate molecularly imprinted polymers as solid phase extraction adsorbents can significantly improve the selectivity of SPE [17]. When using SE or SPE to separate melamine and its analogues from milk-related samples, it is usually necessary to treat the sample with trichloroacetic acid solution to reduce the influence of protein on the separation effect [14].

Enriches target molecules using solvent or solid sorbents, commonly combined with chromatographic techniques (e.g., SPE–HPLC, SPE–LC–MS/MS) to improve sensitivity [18]. Nevertheless, these methods are time-consuming, require large solvent volumes, and are unsuitable for high-throughput analysis.

2.2 Recent Advances in Innovative Separation Strategies

Building on the limitations of conventional methods, recent research has focused on developing innovative separation strategies with higher sensitivity, selectivity, and adaptability for real-time monitoring. These emerging approaches include advanced chromatographic techniques, novel adsorptive materials, and integrated optical–sensor platforms, which together aim to overcome the shortcomings of traditional methods and enable more efficient melamine detection.

2.2.1 Chromatography – MS: Sensitivity vs Practicality.

High-performance liquid chromatography (HPLC), ultra-performance liquid chromatography (UPLC), and gas chromatography (GC) are widely used separation techniques in food testing. However, when used only with conventional detectors such as UV or fluorescence, their sensitivity and selectivity are limited [13].

In recent years, coupling chromatography with tandem mass spectrometry (MS/MS) has enabled detection at the ppb level, becoming an internationally recognized standard for food safety testing [13]. Both FAO and WHO recommend this method for monitoring melamine and related compounds in food [19].

Building on this recognition, UPLC–MS/MS and GC–MS/MS achieve sub-ppb sensitivity and superior accuracy in melamine detection in dairy and pet food, significantly outperforming HPLC–UV [13]. Nevertheless, their widespread application is restricted by high equipment costs, technical expertise requirements, and complex sample preparation, thus confining their use mainly to laboratories [20].

In the future, integration with emerging sensor technologies and advanced materials could maintain high sensitivity while improving efficiency and expanding applications.

2.2.2 MOFs & MIPs: Selectivity through Design.

In the research on melamine detection and removal, high-selectivity adsorptive materials have demonstrated significant application potential, among which metal–organic frameworks (MOFs) and molecularly imprinted polymers (MIPs) represent two typical categories.

MOFs are assembled from metal ions or clusters and organic ligands, featuring exceptionally large surface areas and tunable pore structures. Their unique porous architecture provides abundant sites for the entry and binding of melamine molecules [21]. Moreover, by introducing different functional groups onto the pore surfaces, MOFs can enhance hydrogen bonding and π–π stacking interactions with melamine, thereby achieving efficient and specific adsorption [22]. However, in food-contact uses, MOF stability and metal ion leaching must be assessed to meet safety standards, while viscous dairy matrices may cause higher pressure drops requiring optimized pore design [30].

In contrast, MIPs rely on a “lock-and-key” mechanism to achieve recognition and capture of target molecules [23]. During their preparation, melamine molecules are introduced as templates into the polymer matrix. Once polymerization is complete and the template is removed, recognition cavities that are highly complementary to melamine in shape, size, and functional groups remain within the polymer. These cavities enable selective recognition and enrichment of melamine in subsequent detection processes [23]. To further improve sensitivity, MIPs are often combined with solid-phase extraction (SPE) and chromatographic techniques, thereby offering both specificity and high analytical accuracy [24]. Practical implementation also requires consideration of polymer regeneration, fouling resistance, and cost-effectiveness, especially under high-protein and high-fat conditions common in milk-based samples [31].

In summary, MOFs and MIPs, by virtue of their distinct structural features and recognition mechanisms, provide a reliable material basis for the highly selective detection of melamine. Nevertheless, large-scale use in dairy processing must balance adsorption efficiency with regulatory compliance, cleaning feasibility, and economic availability.

2.2.3 Optical Spectroscopy & Smart Sensors: Toward Real-Time Detection.

Optical spectroscopy combined with smart - sensor technologies is an effective route to rapid, non-destructive and on-line screening of melamine in dairy matrices. Near-infrared (NIR), mid-infrared (MIR), Raman and fluorescence methods probe characteristic vibrational/electronic signatures of melamine, while selective adsorptive materials (e.g., SERS substrates, MIPs/aptamers) pre-concentrate targets and suppress interferents—together enabling high-throughput, in-line monitoring and triage to confirmatory LC–MS when necessary [25, 26].

Progress over the past decade has improved sensitivity, selectivity and robustness: better optics and detectors, rigorous preprocessing (baseline correction, SNV/derivatives) and chemometric modelling (PLS/one-dimensional CNNs) have expanded real-time applications beyond the laboratory [25, 26]. Even so, the complex milk matrix—proteins, fats and lactose—can distort bands or add background, so calibration transfer, matrix-matched standards and targeted substrates (e.g., SERS with affinity ligands) remain important to stabilize predictions [26].

“Smart” sensors complement optics where portability and immediacy are critical. Electrochemical platforms (enzyme/aptamer/MIP-based, often nano-enabled) offer low cost, miniaturization and second-to-minute response; integrated in production lines they shift quality control from delayed confirmation to proactive monitoring and hold-release decisions [27]. In parallel, electronic-nose (E-nose) arrays with pattern-recognition classifiers provide binary/ordinal “adulterated vs clean” judgements suitable for front-end screening and triaging [28].

A literature-derived performance envelope summarizes what is practical today: NIR/FTIR screens commonly report LOD around ~1 ppm for melamine in milk; Raman/SERS spans ~0.01–5 ppm depending on substrate and pretreatment; electrochemical sensors reach sub-μg L^{-1} to tens of μg L^{-1} in real matrices; E-nose studies typically achieve ~90–97% overall accuracy on held-out sets (hence only a few-percent false decisions), with performance governed by dataset balance and thresholding [25–28]. These ranges guide operating windows and alarm settings in Section 2.4’s KPI design, while site validation should finalize thresholds for specific products and instruments.

Finally, coupling these measurement streams to machine-learning pipelines (feature extraction, outlier detection, calibration transfer) turns heterogeneous signals into auditable decisions, ensuring fast screening without sacrificing traceability across batches and seasons [25–28].

2.3 Comparative Insight

To compare the overall performance of each separation method, **Table 1a** summarizes their selectivity, sensitivity, scalability, and energy demand, together with the main advantages and limitations [32, 33].

Separation Technique	Selectivity	Sensitivity	Scalability	Energy/Throughput	Key Advantages	Major Limitation
UF/NF/RO	Moderate	-	High	High throughput/Moderate energy	Continuous operation, modular design	Poor matrix compatibility, fouling risk
LLE	Moderate-Good	Moderate	Medium-High	High energy/Medium throughput	Adjustable selectivity, mature chemistry	Emulsification in milk, complex operation
SPE	High	High	Medium	Low-moderate energy/Moderate throughput	High enrichment efficiency	Requires defatting/deproteinization
Chromatography–MS/MS	Very High	Very High	Medium	High energy/Low throughput	Benchmark accuracy, regulatory approval	Expensive/expert operation
MIPs/MOFs	Very High	High	Medium	Moderate	Tunable selectivity by design	Limited industrial maturity
Optical Spectroscopy & Smart Sensors	Moderate-High	Moderate	Very High	Very low energy/High throughput	Rapid, non-destructive screening	Matrix interference affects accuracy

Table 1a Comparison of Technical Performance (Selectivity, Sensitivity, Scalability, and Energy Demand)

Table 1b presents the adaptability of each technique to dairy matrices, along with the associated operational complexity and regulatory maturity [34, 35, 36].

Separation Technique	Matrix Compatibility	Operational Complexity	Regulatory Maturity
UF/NF/RO	Poor (high fouling in fat/protein media)	Moderate (cleaning, pressure control)	Low
LLE	Poor (emulsion risk)	High (solvent handing and safety)	Medium
SPE	Good (with pretreatment)	Moderate	High
Chromatography–MS/MS	Excellent (handles complex matrices)	High (calibration, expert setup)	Very High
MIPs/MOFs	Good	High (material synthesis/optimization)	Low-Medium
Optical Spectroscopy & Smart Sensors	Fair-moderate (matrix background strong)	Moderate (calibration/AI processing)	Medium

Table 1b Process Adaptability and Operational Complexity

Table 1c highlights how experimental factors—including pH, ionic strength, and fat-protein content—affect the performance and stability of different separation methods [37, 38, 39].

Separation Technique	pH Effect	Ionic Strength Effect	Fat–Protein Load Effect
Membrane Separation	pH deviation damages membrane or alters surface charge	High salinity reduces flux and electrostatic repulsion	Fats and proteins cause pore fouling and frequent cleaning needs
LLE	pH affects partition coefficient and solubility	High ionic strength induces emulsions and phase instability	Fats and proteins promote emulsification and slow phase separation
SPE	pH controls adsorption–elution balance	High salinity disturbs ion-exchange equilibrium	Proteins and fats block sorbent and compete for binding sites
Chromatography–MS/MS	pH and salt affect ionization efficiency	High salt suppresses signals and increases matrix effect	Protein/fat residues cause column contamination
MIPs/MOFs	pH strongly alters binding site ionization	High ionic strength screens electrostatic binding	Fats and proteins block pores and reduce capacity
Optical Spectroscopy & Smart Sensors	pH shift changes spectral intensity	High salt alters optical background and refraction	Fats/proteins induce scattering and fluorescence quenching

Table 1c Experimental Conditions and Their Effects

Overall, variations in pH and ionic strength strongly influence separation efficiency, while high fat or protein loads tend to cause fouling or signal interference, emphasizing the need for tailored pretreatment in dairy applications.

2.4 ML/AI Integration

Across the separation train, machine learning (ML) turns routine plant and QA signals into actionable guidance that reduces trial-and-error and raises assurance. For membranes, physics-informed ML (PIML) couples first-principles constraints (mass balance, pressure-driven transport, fouling kinetics) with data on pH, ionic strength, temperature, MWCO, trans-membrane pressure (TMP) and recovery to predict melamine rejection and energy per m^3. Compared with purely black-box regressors, PIML improves extrapolation, enforces physical bounds and yields engineer-readable sensitivities to define a robust operating zone while maintaining compliance [40]. For spectroscopy, automated pipelines—SNV/baseline correction and first/second derivatives feeding PLS or lightweight 1D–CNNs—convert NIR/MIR/Raman signals into concentration or pass/fail outputs; physics-aware and domain-adapted models help stabilize vibrational-spectral inference under instrument drift and limited labels, so only suspicious lots are escalated to LC–MS [41]. For chromatographic method development, Bayesian optimization supports data-efficient, closed-loop, multi-objective search over column/gradient/temperature/flow to reach target LOQ/resolution with minimal runtime and solvent, accelerating method transfer in dairy matrices and reducing analytical bottlenecks [42]. To operationalize these models in an auditable way, this review sets out a KPI-driven digital loop with tiered alarms and confirmatory testing, and a concise dashboard of batch compliance, re-test rate, energy per m^3, throughput/flux, CIP pass rate, spectral false-positive/negative rates, wastewater (TOC/melamine) compliance, and time-to-disposition. Thresholds are literature/spec-based and capability-guided (SPC bands ±2σ/±3σ); soft-sensor cut-offs are ROC-derived. Models are cross-validated (AUC/RMSEP) with an independent hold-out; LCMS follows best-practice QC (system suitability, blanks/QC injections, drift control) [43]. Process/spectral drift is monitored by distribution tests and multivariate statistical process control, with retraining and re-qualification defined in SOPs. Together, a PIML membrane soft-sensor, transfer-robust spectral analytics and BO-assisted LC methods provide a coherent, auditable path to faster screening, fewer false holds and lower energy at constant compliance.

Digital loop: Sensors (TMP, flux, ΔP, temperature, conductivity, TOC) → data hub/LIMS → PIML soft-sensor (rejection & risk) → tiered alarms (Warning → Action → Isolation) → LC–MS confirmation → DCS/MES/LIMS reporting & disposition.

Unit	Variable	Target / Range	W/A/I thresholds	Fallback	KPI
NF/RO	TMP (bar)	Operate mid-range within vendor window	W: > upper; A: upper+1 bar; I: spec breach	Lower recovery; evaluate CIP	Energy ($kWh·m^{-3}$)
NF/RO	Flux (LMH)	≥ 0.8× design flux or ≥ 0.9× J_0	W: NFD≤−10% (≥5 min); A: ≤−15%; I: persistent drop + ΔP spike	Raise T / switch train	Throughput, downtime
NF/RO	Rejection (%)	≥ compliance spec (e.g., 99.5%)	A: soft τ(ROC); I: LC–MS fail	Isolate lot → LC–MS; hold release	Compliance, re-test
Spectroscopy	RMSEP / score	RMSEP ≤ 0.2–0.3× legal limit	A: Outlier / Hotelling T^2 > τ; I: repeated QC fail	Route to LC–MS; lock lot	FP/FN rate
LC method	LOQ / runtime	LOQ ≤ 0.5× legal limit; t ≤ policy	A: LOQ>spec; I: repeated system-suitability fail	Revert to long gradient	Cost / sample
CIP/SIP	Cond./Temp/time	Per SOP	A: any under-spec; I: repeat under-spec	Extend CIP / re-run	CIP pass rate
Wastewater	TOC / melamine	≤ regulatory/SOP limit	I: > limit	Stop discharge; divert	Release compliance

Table 2 KPI matrix (Targets and thresholds follow the rules described in Section 2.4 (see refs. [40–43]). Values are illustrative for a review and will be set site-specifically during validation.)

Warning: enter pre-alert band (e.g., NFD ≤ −10% or soft-sensor rejection within +0.2% of target for ≥5 min); adjust recovery/temperature; increase sampling.

Action: soft-sensor < target or Risk > τ(ROC), or LOQ failure; isolate lot and send LC–MS; rollback to robust zone.

Isolation: confirmed non-compliance or repeated alarms; stop line/CIP; resume after re-qualification.

Method notes.: Targets derive from literature/specs (vendor TMP window, design-flux×0.8, LOQ ≤ 0.5× legal limit). Alarms follow SPC bands (±2σ/±3σ) and ROC-based soft-sensor cut-offs; values are illustrative for a review and will be site-specific at validation.

3. Challenges and Future Perspective

3.1 Technical Challenges

Due to its small molecular size, chemical stability, and intense interaction with milk proteins, removing melamine from milk powder presents significant technical challenges. Although separation technologies have made progress, as mentioned earlier, achieving efficient, selective, and safe removal remains a complex problem.

In terms of detection and separation, the nitrogen-rich structure of melamine can interfere with protein assays, making it difficult to distinguish using conventional analytical methods. An ideal melamine detection and analysis technology should possess the following characteristics: high sensitivity, high specificity, short detection time, low cost, and minimal or no sample pretreatment steps [44]. However, most current detection methods do not meet all these criteria [45]. For example, techniques such as HPLC or LC–MS require complex sample preparation and may not be suitable for large-scale modular monitoring.

Concurrently, significant hurdles are encountered in the realm of removal technology. Traditional SPE adsorbents typically lack selectivity for specific mixtures, resulting in low extraction efficiency. Adding molecularly imprinted polymers (MIPs) during the separation process can address this issue to some extent; however, polymers prepared by this method are usually micrometer-sized (40–200 µm), resulting in low melamine adsorption capacity and hindering the adsorption and elution of target molecules [46].

Generally, highly sensitive classification methods have higher material and labor costs. Many efficient and highly selective laboratory methods cannot eliminate these costs at the factory scale. Strict regulatory limits force companies to adopt expensive, high-throughput quality assurance methods, leading to a significant increase in product costs and a burden on consumers [47]. Therefore, before promoting a particular separation application in the dairy industry, efficiency, safety, and cost must be weighed.

3.2 Regulatory and Industrial Challenges

The vary limits set by different countries for melamine content have created discrepancies in safety standard, which is a main challenge for diary industry. After the 2008 food adulteration scandal, the Codex Alimentarius Commission established guidance limits (1 mg/kg in powdered infant formula and 2.5 mg/kg for other foods) to help harmonize regulations and protect trade [48]. Many national authorities have adopted these recommendations—for example, China's Ministry of Health adopted provisional limits of 1 mg/kg for melamine in infant formula and 2.5 mg/kg for dairy products and similar limits have been established by agencies in the EU, Australia, and New Zealand [49]. However, there are still some important differences remaining. Health Canada sets a maximum level of 0.5 mg/kg for melamine in powdered infant formula, which is stricter than most countries. While the U.S. Food and Drug Administration (FDA) states that melamine levels in infant formula below 1 mg/kg (and below 2.5 mg/kg in other foods) do not cause a health risk [49]. This consistency complicates international food trade and enforcement. Because products may follow the complaint in one jurisdiction, which may exceed limits elsewhere. Due to lack of uniform regulations, some countries may face issues such as import bans and recalls, when some foreign products cannot meet domestic standards [50]. This not only disrupts global supply chains but also hinders unified risk assessments—regulatory agencies must independently determine safe exposure levels, leading to fragmented consumer protection measures.

Another challenge is the lack of a centralized global food safety database and standardized testing procedures for containments such as melamine. Currently, melamine contamination information is shared through systems such as the INFOSAN alert system, rather than through any comprehensive, unified database [50]. This fragments monitoring means that all stakeholders may not have access to critical data on adulteration incidents at the same time. Furthermore, laboratory methods for detecting melamine vary across industries and countries. The detection methods include chromatographs, mass spectrometry, and rapid immunoassays. There is no universally applicable standardized procedure. The lack of standardized analytical methods and reference databases leads to inconsistent sensitivity, making it difficult to compare test results between countries [51]. This problem is highlighted by the 2008 infant formula scandal. The melamine-contaminated formula circulating globally until coordinated action forced many countries to implement piecemeal recalls and bans [50]. In conclusion, without a unified monitoring database and standardized testing procedures, identifying and eliminating adulterated products remains a slow and difficult global process. This event also highlights the necessity for strengthened international cooperation in food safety data sharing and methodological harmonization.

3.3 Future Directions

Future directions in contaminants removal emphasize AI-driven intelligent separation platforms that integrate membrane filtration (e.g., NF/RO), high-selectivity adsorbents (e.g., MOFs/MIPs), and smart sensors (e.g., NIR/Raman, electrochemical arrays) with real-time monitoring to address diverse contaminants including melamine, antibiotics, pesticides, mycotoxins, heavy metals, and microplastics across liquid foods including dairy, juices, plant-based beverages, and water. Rather than optimizing individual units in isolation, future intelligent separation systems will form a complete optimized control loop, enabling continuous monitoring and automatic adjustment of separation parameters such as pH, TMP, flux, temperature, and ionic strength to enhance multi-contaminant selectivity, process robustness, and energy efficiency [40, 42]. Digitalized process design will leverage machine learning to predict performance, optimize materials and operations, and adapt to variable feed matrices via physics-informed and transfer-learning models [41]. Globally, food safety oversight will advance through digitalized platforms integrating AI and blockchain for end-to-end supply chain transparency, real-time risk assessment, harmonized standards, and rapid cross-border response to emerging threats. These innovations enable scalable, proactive, and sustainable contaminant management across the food industry.

4. Conclusion

Melamine contamination in milk and dairy-based products continues to pose a major food safety challenge due to its colorless, odorless, and highly stable nature. Numerous analytical and separation techniques have been developed to detect and remove melamine, including membrane filtration, solid-phase extraction, liquid–liquid extraction, and chromatographic methods. Among these, membrane-based processes offer operational simplicity and scalability but still suffer from fouling, low selectivity, and energy-intensive operation. Meanwhile, advanced materials such as molecularly imprinted polymers (MIPs) and metal–organic frameworks (MOFs) demonstrate promising specificity and adsorption capacity, although their large-scale application in food systems remains limited.

Recent progress in data analytics and machine learning provides new opportunities to integrate smart monitoring and predictive control into separation technologies. The coupling of artificial intelligence with sensor networks and membrane systems may enable real-time, automated detection and removal of contaminants like melamine, contributing to a safer and more sustainable dairy industry.

Future research should focus on optimizing material stability under real food-processing conditions, improving regeneration and reusability, and standardizing global regulations for melamine limits in dairy products. Achieving these goals will require collaborative efforts between academia, industry, and policymakers to ensure effective, scalable, and environmentally responsible food safety solutions.

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