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Ecological Footprints of Acetaminophen: Environmental Fate, Ecotoxicological Impacts, Detection Approaches, and Sustainable Remediation Strategies

Mamta Verma [1], Neha Agarwal [1], Joy Sarkar [2] and Sudakshina Trivedi [2,*]

[1] *Department of Chemistry, Navyug Kanya Mahavidyalaya, Lucknow.*

[2] *Department of Chemistry, University of Lucknow, Lucknow.*

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Abstract

Acetaminophen (common name-paracetamol) is one of the most widely used analgesics and antipyretics used throughout the world. It's been frequently discovered in aquatic systems as it has been continuously added to the environment, not totally eliminated in wastewater treatment, and then dumped by pharmaceutical producing organizations. Emerging pharmaceutical contaminants, such as acetaminophen and transformation products can pose ecological risks at low concentrations. In this review, the sources, occurrence, fate and transformations, toxic effects, analytical detection methods and advanced remediation technologies of acetaminophen contamination in the environment are discussed. The conventional biological treatment, advanced oxidation processes, adsorption, nanotechnology-based methods and biological degradation methods are fully explored. Future prospective for the sustainable, cost-effective and scalable treatment technology is also emphasized.

Keywords: Acetaminophen; Analgesics; Antipyretics; Wastewater; Biological Treatment; Remediation

1. Introduction

In Mediterranean countries, plants in public parks and municipal landscapes are irrigated using reclaimed (recycled) water. Reclaimed water is wastewater that has undergone treatment to eliminate particles and specific contaminants before being utilized for irrigation in landscaping. Utilizing the treated wastewater for approved municipal sustainable gardening irrigation applications is a common method of recycling and recharging. It is meant to be used exclusively for non-potable purposes in the majority of places [1]. Because pharmaceuticals and their metabolites and transformation products are widely and increasingly used in human and veterinary medicine and are constantly released into the environment, their presence in the environment is becoming a cause for concern. These compounds may have negative effects on living organisms.Numerous environmental samples from throughout the world have been found to contain a variety of medications. Surface water, ocean, groundwater, soil, sediment, fish, and sewage treatment plant effluents have all been found to contain them [2–5].

Reclaimed water is not treated in accordance with drinking water regulations by the utilities that supply it for non-potable uses. Different levels of viruses, medications, and other trace contaminants can get through the filtering and treatment process and endanger people. This issue might be partially resolved by contemporary technology like reverse osmosis. One significant class of putative endocrine disruptors (EDs) that has recently drawn a lot of interest from the global scientific community is pharmaceuticals. They are new environmental pollutants that are being employed widely and more frequently in veterinary and human medicine. Many of these substances are persistent in the body and are made to have a particular mode of action. In numerous nations, they have been found in trace amounts in a variety of environmental samples, including groundwater, surface water, ocean, and wastewater from sewage treatment plants

* Corresponding author: Sudakshina Trivedi

[2-5]. Among the most often used medications are non-steroidal anti-inflammatory drugs like aspirin (acetylsalicylic acid) and acetaminophen [6]. Significant volumes of a variety of metabolites are released into the aquatic environment as a result of the transformations that many medications experience in the human body. During sewage treatment, these metabolites may undergo further transformations. Biotic and/or abiotic processes, such as hydrolysis and photolysis, can also break down pharmaceutical materials.

Acetaminophen, is one of the most widely used pharmaceutical compounds for its analgesic and antipyretic effects. It is commonly used as an OTC medicine and thus has been continually introduced to the environment [7]. It is also used as intermediate for pharmaceutical and azo dyes , stabilizer for hydrogen peroxide, photographic chemicals and for the control of Brown Tree Population [8]. Pharmaceutical contaminants are not like conventional pollutants, which are typically inert molecules, because they are biologically active molecules that are intentionally created to have a physiological response even at low concentrations [9]. Once it is given, acetaminophen is metabolized in the liver via glucuronidation and sulfation. Some of that fraction, however, does not change and gets excreted by people and added to the wastewater systems. Acetaminophen contamination is found in many streams and is caused by pharmaceutical wastes, hospital effluents and domestic wastes **[Figure 1].**

1.1. Pharmaceutical Industry Effluents

Pharmaceutical factories produce pharmaceutical waste comprising active pharmaceutical ingredients, intermediates and degradation products. Industrial plant effluents may contain significant amounts of acetaminophen if discharged improperly [10]. As one of the most widely produced and used analgesics and antipyretics, acetaminophen is frequently found in hospital and pharmaceutical effluent streams. If left untreated, leftover acetaminophen and its transition products from medicine formulation, production, and processing operations may find their way into aquatic habitats. Research has shown that acetaminophen is present in wastewater treatment plant influents and pharmaceutical facility outputs, with concentrations differing based on wastewater parameters and industrial activity [11]. Even though acetaminophen can be largely removed by traditional biological treatment, persistent residues may still be present in treated effluents, requiring sophisticated oxidation, adsorption, or catalytic degradation techniques for full mineralization [12].

1.2. Domestic Wastewater

One of the largest diffuse sources of acetaminophen release is human consumption and excretion. Wastewater treatment plants are known to have incomplete elimination efficiencies in conventional systems [13]. acetaminophen (acetaminophen) is among the most frequently detected pharmaceutical contaminants in domestic wastewater due to its widespread over-the-counter use and subsequent excretion through human urine. After consumption, a significant fraction of acetaminophen and its metabolites is discharged into municipal sewer systems, where conventional wastewater treatment processes may not completely eliminate these compounds [14]. Consequently, acetaminophen residues have been reported in wastewater treatment plant influents, effluents, and receiving aquatic environments [15]. Its continuous input, high consumption rate, and potential formation of toxic transformation products highlight the need for effective treatment strategies, including advanced oxidation processes and catalytic degradation, to minimize its environmental impact.

1.3. Hospital Wastewater

Hospitals discharge complex pharmaceutical mixtures, which include analgesics, anti-bacterials and other active ingredients [16]. Because of its widespread use in medicine, acetaminophen is often found. Hospital wastewater is a major point of release for acetaminophen (acetaminophen), which is widely used in hospitals to treat pain and lower fever [17]. Hospital wastewater includes unmetabolized acetaminophen, its metabolites, and other pharmaceutical residues from clinical procedures, drug disposal, and patient excretion. Research has shown that traditional wastewater treatment systems may not be able to completely remove acetaminophen from hospital wastewater streams, allowing it to be released into receiving water bodies [18]. Advanced treatment techniques like adsorption, photocatalysis, ozonation, and other oxidation processes are being researched for efficient removal because of its ongoing occurrence and possible ecological impacts.

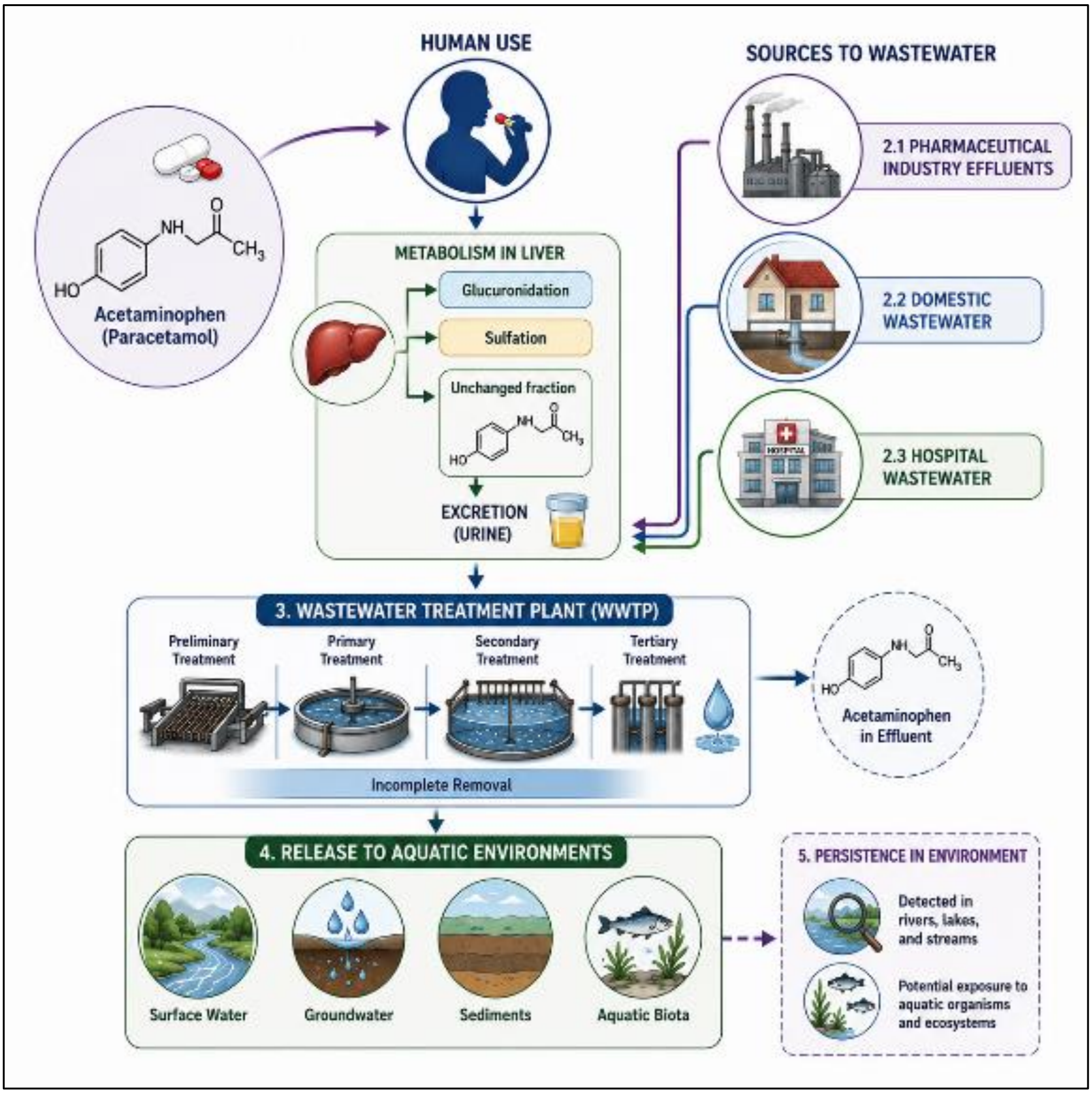

Figure 1 Schematic Representation of Acetaminophen Sources, Wastewater Pathways, and Environmental Fate

2. Environmental Occurrence and Fate

Acetaminophen has been detected in surface water, ground water, wastewater effluents and sediments. It has environmental behaviour that is affected by physicochemical parameters, microbial activity, exposure to sunlight, and interactions with natural organic matter [19]. The toxicity of transformation products (e.g., 4-aminophenol) can differ from that of the parent compound.

3. Ecotoxicological Impacts

3.1. Aquatic Toxicity

Pharmaceutical residues are present in the water at all times, and are in the water stream where they affect aquatic organisms such as algae, fish, and microorganisms. Acetaminophen exposure may result in biochemical changes, metabolic disruptions and oxidative stress [20] [Figure 2].

3.2. Oxidative Stress Mechanism

Generation of ROS may lead to lipid peroxidation, imbalance of enzymes, damage to cells and decrease in antioxidant defence mechanism [21]. By encouraging oxidative stress in exposed organisms, acetaminophen pollution in aquatic habitats can have ecotoxicological effects. Environmentally relevant amounts of acetaminophen may produce reactive oxygen species (ROS), which can cause oxidative damage, lipid peroxidation, DNA changes, and disruption of antioxidant defense mechanisms in aquatic creatures, even though it is thought to be rather safe at therapeutic dosages in humans [22]. Research has shown that fish and other aquatic species exposed to acetaminophen have elevated activity of oxidative stress indicators as catalase, superoxide dismutase, and glutathione-related enzymes [23]. In contaminated environments, these biochemical disruptions may worsen physiological processes and increase long-term ecological dangers.

3.3. Microbial Community Effects

Pharmaceutical contamination can disrupt the microbial diversity and alter ecological functions (including nutrient cycling) [24].

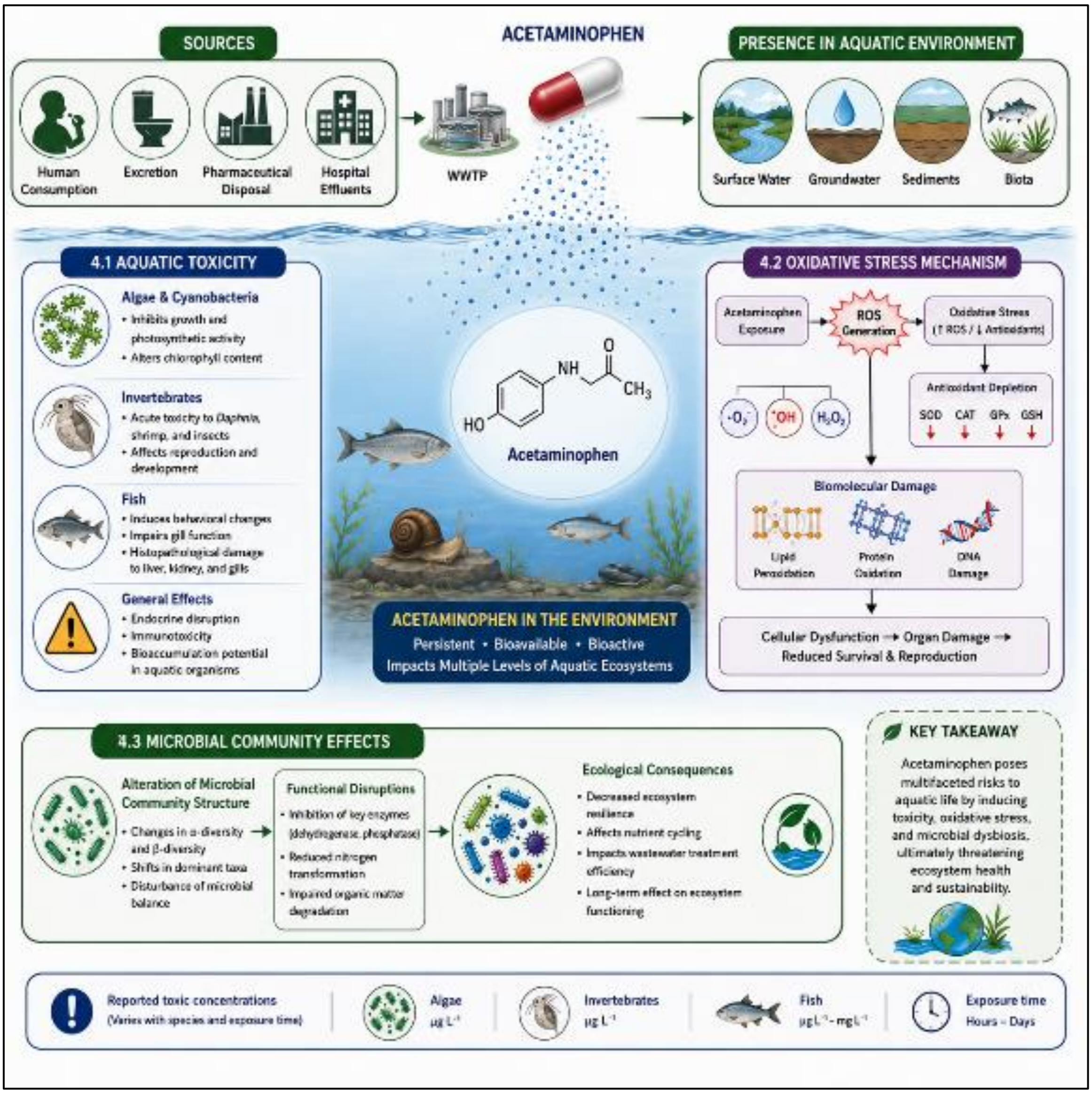

Figure 2 Ecological Footprints of Acetaminophen: Ecotoxicological Impacts

4. Detection and Analytical Approaches

The proper identification and quantification of acetaminophen is crucial for environmental monitoring. HPLC, LC-MS/MS and GC-MS are high sensitivity and high selectivity chromatographic techniques. Newer alternatives are spectroscopic and sensors such as UV-visible spectroscopy, FTIR, electrochemical sensors, and biosensors based on nanomaterials (NMs) [25].

5. Conventional Remediation Technologies

5.1. Biological Treatment

The environmentally friendly degradation by microorganisms can be useful, but the efficiency of the degradation will be dependent on the microbial communities as well as on the operating conditions. Biological treatment, which relies on microbial degradation and enzymatic transformation under aerobic or anaerobic conditions, is an environmentally friendly method of removing acetaminophen from wastewater. Through processes including hydroxylation, deacetylation, and ring-cleavage reactions, a number of bacteria found in activated sludge systems can metabolize acetaminophen, turning it into simpler intermediates and, in certain situations, complete mineralization to carbon dioxide and water [26,27]. However, variables including pollutant content, hydraulic retention time, and the makeup of the microbial population affect how effective biological processes are. Although sophisticated procedures could be necessary for total removal, acetaminophen's comparatively strong biodegradability permits partial removal in traditional wastewater treatment facilities.

5.2. Advanced Oxidation Processes

Pharmaceutical contaminants are eliminated by highly reactive radicals using advanced oxidation processes such as ozonation, photocatalysis, Fenton oxidation or photo-Fenton systems [28, 29]. The capacity of advanced oxidation processes (AOPs) to produce extremely reactive hydroxyl radicals (•OH) that may oxidatively break down the aromatic structure of the molecule makes them one of the most efficient methods for the breakdown of acetaminophen in wastewater. Effective methods for removing acetaminophen and mineralizing it into CO_2, H_2O, and inorganic ions include photocatalysis, ozonation, Fenton oxidation, electrochemical oxidation, and sulfate radical-based oxidation [30]. AOPs can break down persistent pharmaceutical residues without creating concentrated secondary waste streams, in contrast to traditional biological techniques. For large-scale applications, catalyst recovery, energy demand, and operating expenses continue to be significant obstacles.

5.3. Adsorption Processes

Acetaminophen is removed from the water by an activated carbon and biochar-based material through adsorption mechanisms such as hydrogen bonding and π–π interactions. Because of its high removal efficiency and operational flexibility, adsorption is regarded as a straightforward, effective, and cost-effective method for eliminating acetaminophen from wastewater. Through processes like hydrogen bonding, π–π interactions, pore filling, and electrostatic attraction, a variety of adsorbents, such as activated carbon, charcoal, graphene-based materials, metal oxides, and porous polymers, have been studied for acetaminophen uptake [31]. Because of its large surface area and high adsorption capacity, activated carbon is one of the most extensively researched adsorbents. However, the disposal of concentrated contaminants and the regeneration of used adsorbents continue to be significant constraints. The creation of sustainable, inexpensive adsorbents using materials produced from biomass is receiving more and more attention.

5.4. Nanotechnology-Based Approaches

The metal and metal oxide nanoparticles such as TiO2 and ZnO based photocatalysts are more active on the surface and more efficient for the degradation of pollutants [32, 33]. Because of the special physicochemical characteristics of nanoparticles, such as their large surface area, increased catalytic activity, and adjustable surface chemistry, nanotechnology-based treatment approaches have become attractive methods for removing acetaminophen. TiO_2, ZnO, FeO_4, and advanced nanocomposites are examples of metal oxide nanoparticles that have been extensively investigated for photocatalytic degradation of acetaminophen by producing reactive oxygen species [34]. Graphene oxide and carbon nanotubes are examples of carbon-based NMs that have demonstrated promise as catalytic supports and adsorbents. For sustainable wastewater treatment applications, more research is necessary due to issues with nanoparticle aggregation, recovery, toxicity, and large-scale deployment, despite their great efficiency.

5.5. Enzymatic Degradation

Biological oxidation pathways can be used to transform aromatic pharmaceutical molecules by enzymes, such as laccase and peroxidase. Using the catalytic activity of oxidoreductase enzymes such laccase, peroxidase, and tyrosinase, enzymatic degradation is an eco-friendly method of removing acetaminophen. Through electron transfer processes, these enzymes encourage the oxidation of acetaminophen, producing less hazardous intermediates that can go through additional biodegradation. When compared to chemical oxidation methods, enzymatic treatment has several advantages, such as good selectivity, gentle operating conditions, and less production of hazardous byproducts [35].

However, widespread use is constrained by enzyme instability, high production costs, and environmental sensitivity. Enzyme immobilization on polymeric and NM supports has been investigated to increase stability and reusability.

5.6. Fungal and Microbial Bioremediation

White rot fungi and certain microorganisms have the ability to breakdown acetaminophen and related compounds by secreting extracellular enzymes [36]. By utilizing microorganisms' metabolic capacities to convert pharmaceutical contaminants into less hazardous substances, fungal and microbial bioremediation offers a sustainable method for removing acetaminophen. White-rot fungi have shown promise for oxidative acetaminophen breakdown, especially those that produce ligninolytic enzymes such laccase, manganese peroxidase, and lignin peroxidase. Through enzymatic pathways including hydrolytic and aromatic-ring degradation processes, bacterial populations isolated from wastewater settings can also use acetaminophen as a source of carbon or nitrogen [37]. Degradation efficiency is influenced by variables like acclimation time, pollutant toxicity, and process management, despite the fact that microbial treatment is economical and environmentally friendly.

6. Comparative Evaluation of Treatment Technologies.

The AOP's have high degradation efficiency but can be energy intensive. Biological systems are sustainable, but may have a longer treatment time [38]. Nanotechnology-based approaches are very active catalysts, which needs to be evaluated in scaling up [39].

Table 1 Compared Performance and Limitations of Different Treatment Methods

Treatment Method	Removal Mechanism	Advantages	Limitations	Typical Performance for acetaminophen Removal	Reference
Biological Treatment	Microbial metabolism involving enzymatic transformation, deacetylation, hydroxylation, and aromatic-ring degradation	Environmentally sustainable, low operating cost, suitable for large-scale wastewater treatment, low energy requirement	Incomplete removal under certain conditions, dependence on microbial community and operating parameters, formation of transformation products	Moderate to high removal depending on acclimated microbial population and treatment conditions	[40]
Adsorption	Surface adsorption through hydrogen bonding, π–π interactions, pore filling, and electrostatic interactions using activated carbon, biochar, graphene-based materials, etc.	Simple operation, high removal efficiency, low initial investment, suitable for polishing treatment	Pollutant transfer to adsorbent phase, adsorbent regeneration/disposal issues, reduced efficiency after saturation	Often achieves high acetaminophen removal (>80–95%) depending on adsorbent properties and conditions	[41]
Advanced Oxidation Processes (AOPs)	Generation of highly reactive radicals ($\bullet OH$, $SO_4\bullet^-$) that oxidize and mineralize acetaminophen molecules	Rapid degradation, effective against persistent pollutants, potential for complete mineralization	High energy/chemical consumption, catalyst recovery issues, possible formation of intermediate products	High degradation efficiency, frequently >90% under optimized photocatalytic, ozonation, or Fenton conditions	[42]

Nanotechnology Based Treatment	Photocatalytic oxidation, adsorption, and catalytic transformation using nanoparticles/nanocomposites such as TiO_2, ZnO, Fe_3O_4, graphene-based materials	High surface area, enhanced catalytic activity, tunable properties, improved degradation efficiency	Nanoparticle aggregation, recovery, possible nanotoxicity, high-scale application challenges	Very high removal efficiency due to enhanced catalytic activity of NMs	[43]
Enzymatic Degradation	Oxidation of acetaminophen by enzymes such as laccase, peroxidase, and tyrosinase producing less toxic intermediates	High selectivity, mild reaction conditions, environmentally friendly, reduced secondary pollution	Enzyme instability, high production cost, sensitivity to pH and temperature, limited reusability	Efficient degradation possible using free or immobilized enzymes	[44]
Fungal and Microbial Bioremediation	Oxidative degradation by fungal ligninolytic enzymes (laccase, Mn-peroxidase, lignin peroxidase) and bacterial metabolic pathways	Cost-effective, sustainable, complete mineralization potential, minimal chemical requirement	Slow degradation rates, requirement of suitable microbial conditions, inhibition by high pollutant concentrations	Significant acetaminophen degradation reported using white-rot fungi and adapted bacterial strains	[45]

7. Conclusion and Future Perspectives

Acetaminophen has become one of the most frequently detected pharmaceutical contaminants in water bodies due to its extensive use and continuous discharge into municipal, hospital, and industrial wastewater. Over the years, a wide range of treatment technologies, including advanced oxidation processes, adsorption, nanotechnology-based materials, and biological methods, have shown promising results for its removal. However, important challenges still remain. In many cases, these technologies achieve only partial degradation rather than complete mineralization, resulting in the formation of intermediate products whose toxicity is often unknown. In addition, issues related to catalyst stability, treatment cost, secondary pollution, and large-scale application need to be addressed before these technologies can be widely adopted. Future research should therefore focus on developing more stable and efficient catalysts, ensuring complete mineralization, assessing the toxicity of transformation products, and exploring integrated biological and chemical treatment approaches. More studies using real wastewater and comprehensive life cycle assessments are also needed to evaluate the practical feasibility and long-term sustainability of these treatment systems. With continued research and technological advancements, integrated treatment strategies have the potential to provide efficient, environmentally friendly, and economically viable solutions for the removal of acetaminophen and other emerging pharmaceutical contaminants from wastewater.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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