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Review article: Biodegradation of Pharmaceutical Pollutants: Challenges, Mechanisms, and Environmental Implications

Wafaa A. Alobaidi[1], Ayat Abd-Aljaleel Nsaif [2,*], Nooralhuda Aljawhar[3]

[1] Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq.
[2] Department of Pharmacology and Toxicology, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq.
[3] Microbiology Department, College of Veterinary Medicine, University of Diyala, Diyala, Iraq.

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ABSTRACT

The emergence of such widespread pharmaceuticals as a pollutant has become one of the world's critical environmental problems that may lead to both the public's health and biodiversity deterioration. This article provides an exhaustive account of the current understanding of the environmental persistence of pharmaceutical contaminants following in-depth analysis of the additive effects of existing natural biodegradation pathways on the human health impact of these drugs. Paying special attention to biodegradation decomposing agents such as bacteria, fungi, and algae the paper estimates their ability to convert drug ingredients to compound that is eventually less toxic. Although these biologic systems contain an enormous potential for killing the unwanted pollutants, the variability in the complexity and endurance of the pharmaceutical substances overburden the degradation capabilities of these organisms thus necessitating improved biodegradation methods. Addressing the above-mentioned environmental factors, which include temperature, pH, and the occurrence of other contaminants, play a crucial role and have a direct impact that on the process of biodegradation, enhancing pollutants removal rate. To sum up, this paper enables the environmental science, microbiology and bioengineering enables creating progressively more functional and sustainable techniques of neutralizing these long-standing toxins; thus, protecting ecosystems, as well as human health.

1. Introduction

Industrial revolution brought about toxic materials being dumped across the globe, therefore which turned into a global environmental problem of many diverse chemicals that it is related to [1]. Among all industrial discharges, pharmaceutical waste is considered to be one of the most hazardous pollutants. The other environmental factors like pH, temperature and other factors play significant

*Corresponding author email : ayat.abd@uomustansiriyah.edu.iq

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role to biodegradation of drugs that is being discharged [2]. Destiny and effectiveness of removing pollutants affect by a range of physical as well as chemical characteristics i.e. solubility, volatility, and biodegradability [3].

The settings under consideration, like soil type and pH, temperature as well as the light have the ability to influence the survival of the pharmaceutical materials in the environment [4]. Moreover, co-existence of other drugs in the same environment increases the drug type and the microbial response of these drugs responsible for their degradation also affects their biodegradation [5].

The faster biodegradation rates at elevated nutrient (nitrogen) loading rates as well as differences in pharmaceutical compounds are based on their chemical structures has been found. Some of the components (sugar moieties) and the presence of other compounds (halogens) in the pharmaceutical components can impact on the degradation rates [6]. The microorganisms such as fungi and bacteria make use of these genetic and metabolic structural functions in the treatment of the recalcitrant contaminants [1].

The real purpose of biodegradation is producing metabolites either that are less toxic or totally not harmful to diminish the negative effect on environment [7]. Via a combination of pharmaceutical pollutants, co pollutants and microbial communication in various ecological environments researcher can elaborate information for bioremediation [8]. Therefore, the study aimed to exploration of degradation mechanisms for these pollutants has emerged as international level to advance environmental sustainability.

2.Environmental Impact of Pharmaceutical Pollutants

Recently, everyone knows that the pharmaceutical residues, which usually enter water bodies, cause environmental destruction and raise a number of human health concerns [4]. The challenge, in this case, is that the pollutants are not only widespread, they are also numerous, eventually harming the ecosystems' functions. Along with consumers and companies in the pharmaceutical sector, directly or indirectly, contaminating the environment by discharging active compounds of medicines back to the atmosphere during their life cycle is partly the problem [9]. These pharmaceutical pollutants intrude into oceans, inland territories, and even the atmosphere due to human activities, leading to ecosystem disturbance [1]. Once in the air, these pollutants can be deposited back into aquatic and terrestrial ecosystems through processes such as precipitation, contributing further to the pollution load [2]. Additionally, pharmaceutical residues can also contaminate interstitial spaces in soils, affecting the soil microbiome and altering soil chemistry [5]. This contamination can hinder plant growth and disrupt the natural soil filtration processes, further exacerbating environmental degradation [6].

The pollutants affect habitats of invertebrates and vertebrates [10]. As organisms accumulate these substances at different steps through the food chain, the affected organisms suffer, and the complexity of formulating policies to deal with the drug menace includes establishing rehabilitation aims that accommodate the harmful effects of drugs [3]. The ecological parameters such as pH of the water, soil compositions, temperature, persisting chemicals, and co-occurring pharmaceuticals are key factors accountable for expanding the compounds' persistence in the environment [11]. The microbial consortia are one of the main microbes that would aid bioremediation processes if they enter the attenuation mechanisms via natural attenuation pathways [12].

Human and animal health problems due to the logic activity of pharmaceutical pollutants are the long-term consequences that occur in the bodies of the animals [13]. Mucosal microbes' participation in inducing, degrading, and transforming these compounds is essential for microbial degradation [14]. A key impact of concomitant pollutants in the environment is that they promote the biodegradation of other pharmaceutical contaminants [15]. Scientists have found that the combination of other pollutants, like metals, nanoparticles, pesticides, and multiple pharmacological compounds, can make naturally occurring bacteria less active or accelerate the population of microorganisms, which can produce other unexpected effects on the microbial world (Figure 1) [16]. This interference avails the undesirable effects associated, for example, with the reductive abilities of the system, minimizing its efficiency in the removal of pharmaceutical compounds and affecting the ability of bioremediation technologies [14].

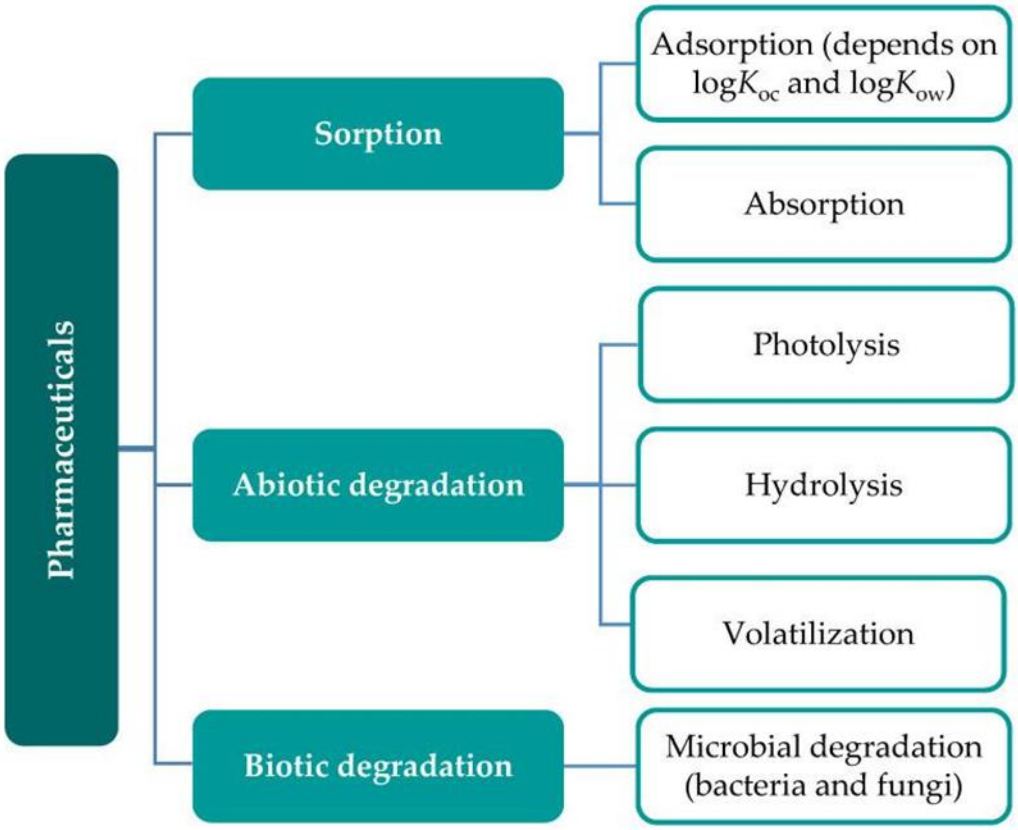

Fig. 1. Different removal mechanisms of pharmaceuticals that can occur in the environment [1].

3. Challenges in Biodegradation

3.1. Persistence and recalcitrance of pollutants

The threat by pharmaceutical pollutants to environment is substantial due to their nature and resistance [17]. These contaminants in a variety of ecosystems, including water sources, food chains, and human tissues, resulting in harmful biological consequences [18]. A major obstacle in breaking down these pollutants through biodegradation is their chemical flexibility, making natural degradation a challenging task [1]. One potential solution lies in the use of Rhodococcus spp., which have displayed as effective tools for combating pharmaceutical pollutants [19]. These microorganisms exhibit a broad array of degrading abilities and contribute to natural processes in polluted surroundings. Rhodococcus spp. are recognized for capability to produce specific enzymes and natural substances that breaking down pharmaceutical compounds [20]. Their involvement in biocatalysis and biotechnology presents for pharmaceutical product advancement [21].

Nevertheless, obstacles in comprehending the metabolic pathways and breakdown products of pharmaceutical pollutants during biodegradation processes [19]. Identifying metabolites formed during degradation for evaluating biodegradation and ensuring that toxic substances are not generated. Additionally, factors like variations in environmental conditions and limited knowledge on metabolites add complexity to the biodegradation process, figure (2) [22].

The resistance of pharmaceutical pollutants needs more than strategy to know harnesses microbial enzymes, genetic pathways, and metabolic capabilities. Future research should concentrate on deepening our understanding of Rhodococcus spp.'s potential as degraders and exploring novel biotechnological solutions for advancing environmental sustainability [3].

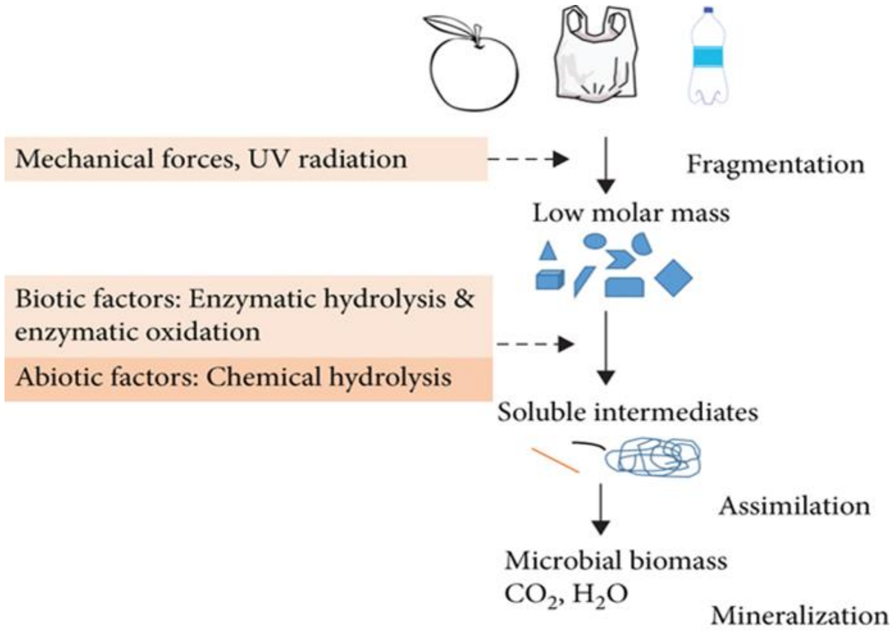

Fig. 2. Biodegradation process [23].

3.2. Variability in environmental conditions

Environmental variation is a major reason for failure of pharmaceutical pollutants to decompose as their decomposition is heavily dependent on several factors such as temp and the pH level [24]. Temperature also has an impact on how quickly foreign compounds degrade, and usually, the most optimal temperature for the process to occur will be between 30-40°C. Temperature can help to pin down bacterial membranes, and this in return can hinder the enzymes activity and on the other hand, temperature can lead the proteins that are associated to the membrane to coagulate [25]. In addition to it, the pH level of water often serves as a clue that tells us about certain microbial activities or membrane features which then inevitably bring about changes in ionization of the drugs or their bioavailability, whatever terms that might be used [26].

During the case of a common drug like acetaminophen in case of changes in pH drug's structure can be deprotonated - whether it is protonated or phenolate - which in turn influences the rate drug quickly breaks down [27]. It is being commented that an environmental factor that paracetamol degrades most quickly is the pH of 7. Likewise, another strain of microorganisms Pseudomonas moorei KB4 seems to achieve the highest activity of around 7.0 pH for metabolizing paracetamul. The revelation not only draws attention to environmental conditions that happens to possess the ability to substantially alter the biodegradation process of drug pollutants but also hints to the concerning prospect of ecological alterations brought about by drugs [28].

Furthermore, as the two different compound react or microorganisms can positively or negatively affect breakdown [29]. Unlike pharmaceuticals, disintegration of such organic contaminants may not exert the life of microorganisms or may cause antagonistic actions which hamper the process efficiency [30]. The variation of incubation time period by different components speeds up the removal of the substances meanwhile, different substances may degrade at different speeds over different incubation periods [29].

3.3. Limited knowledge on metabolites

Lack of knowledge about the metabolic byproducts create the greatest problem for the biodegradation of the pharmaceutical pollutants [31]. It was found that microbiotas or different bacteria strains play a key role in degradation of only certain medicine groups. However, there are still many gaps in the knowledge about the products of those pathways [32]. The biodegradation metabolites play a significant role in evaluating whether the biodegradable process is likely to improve the environmental effects or it is more likely to continue in the same way as the original compounds [33].

The absence of information on metabolites produced while biodegrading may cause our understanding of the metabolic pathways and the end-degradation substances not to complete. This deficiency reveals the need for another research undertaking with the purposes of determine and delineating these metabolites. For example, in cases like that concerning halogenated pollutants, microbial species can play a vital role in inhibiting their environmental persistency. Informing these metabolic changes is important for both The preparation of more targeted and efficient bioremediation strategies and The evasion of big environmental damage [34] showed in figure (3).

The degradation of pharmaceutical pollutants might concurrently occur with others like heavy metals, nanoparticles and pesticides; thereby, their interplay in biodegradation should be investigated [35]. The pollutant can either interfere or result in unintended consequences, which may stall the bacteria performance in verses degradation efficiency [36].

In brief, it is necessary to fill in the gap in the gatherings of metabolites created in the bio-degradation of pharmaceutical pollutants for the purpose of improving the bioremediation technologies and preserve the ecological sustainability [4]. Advanced investigation of performing the identification and the description of those metabolites will burden the capabilities needed to effectively address the environmental effects of pharmaceutical toxicity [3] and [37].

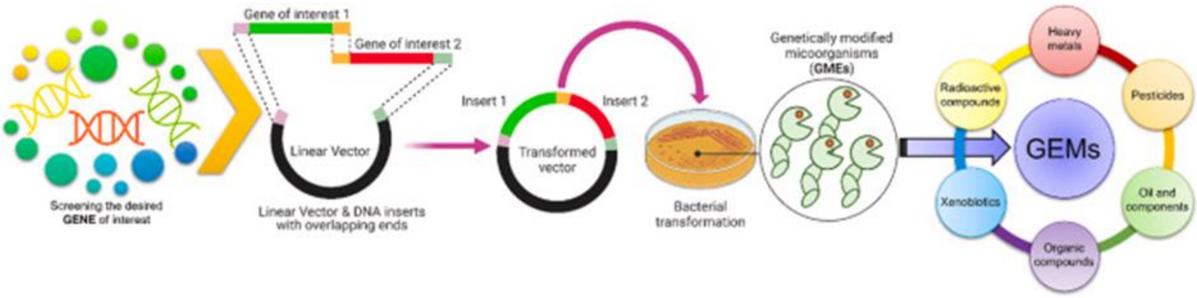

Fig. 3. Genetically engineered microorganisms (GMEs) for environmental remediation [38].

4. Mechanisms of Biodegradation

4.1. Microbial enzymes involved

The microbial enzymes provide the required solution to degrade pollutants of pharmaceutical sources emotionally the diverse sources of microorganisms like bacteria, fungi and some [39]. The main responsibilities are to employ these biocatalysts to speed up the chemical reactions that break down water bodies filled with persistent pollutants. Through the use of enzymatic pathways, microbiota are able to establish steps to have either a permanent or great impact on various chemical pollutants such as pharmaceutical and micro-pollutant substances. These enzymes can act as catalysts to bring about the conversion of existing particulate matter into exceptionally smaller molecules consisting of just carbon dioxide and water [40].

One of the key benefits of relying on enzymes of microbial origin targets degradation is their high rate and specificity. Microbes have an arsenal containing mostly catalytically active enzymes in a great number, thus, they are very competent and flexible in decomposing pharmaceutical contaminants [19]. These enzymes can act as microscopic catalysts degrading organic and inorganic pollutants in water. The reaction products are same as CO2, water, biomass, and biodegradable by-products that do not upset ecosystem balance [31]. Identifying a set of microbial strains with the specific capabilities to metabolize the toxins broadly found in the aquatic systems into the harmless products could be the milestone in the long way of environmental recovery achievements. Again, genetic engineering has not only made this possible but also made creation of GM organisms with modified genetic makeup for pollutant degradation achievable [19].

4.2. Role of fungi, bacteria, and other microorganisms

The microbial communities that function in the process of biodegradation involve important actors for the elimination of these pollutants that contaminate the environment [41]. These bioremediation communities are the backbone for sustaining ecosystems and their processes of natural pollution removal, which occurs through metabolic activities and enzyme release by bacteria [42]. The choice and isolation of nature’s native microorganisms that can degrade all types of pollutants selectively is a prerequisite for developing microbial inocula as bioremediation agents. These agents need to do their job without altering the microbiota of the contaminated sites over long periods [43].

Common blending of microorganisms shows more potency than single bacterial cells in the destruction of pollutants due to the combined metabolic activities and synergistic reactions between bacteria [44]. Bioremediation technology is based on the fact that micro-organisms can degrade contaminants using their own metabolic capabilities and oxidize pollutants as a food and oxygen source [45]. This approach has provided a wide range of organic pollutants with results indicating effective remediation for hydrocarbons, pesticides, polychlorinated biphenyls, and pharmaceuticals [40].

The breakdown of pharmaceutical substances occurs based on natural processes where microbial enzymes serve as catalysts and could be sourced from various organism types such as fungi and bacteria [46]. Among these bacteria, there are Pseudomonas species that can degrade pharmaceutical micropollutants precisely, and Cupriavidus species, which are well known for phthalate degradation due to their ability to break down these compounds. A good example is the links between Penicillium oxalicum and diclofenac compounds as shown in Table 1 [47].

Smoke from industries, car emissions, and agriculture affects microbial communities due to pollutions affecting the quality of air. PM, NOx, SOx, and VOCs can also re-suspend at the water surface and are causes of secondary water pollution. Furthermore, these pollutants can influence the health and performance of microbial population which is useful in bioremediation systems. For example, high concentration of NOx and SOx results in the occurrence of acidic rain; this decreases the pH level of water, thus affecting the metabolic activities of microorganisms and enzymes [49].

Another problem with bioremediation is interstitial pollution which is contamination of the pore spaces of soils and sediments. Solids like heavy metals, microplastics, and POPs can build up in these interstices, which foreshadows the complications of microbial life. These pollutants are known to negatively affect the activities and survival of the useful microbial populations; thus, their effect should be considered when it comes to bioremediation [50]. Techniques like bioaugmentation whereby particular microorganisms are added in to the system in order to increase the rate of pollutant degradation can be very effective in interstitial pollution [51].

Hence, the capability of microorganism-driven biodegradation to patrol pollutants from the aqueous environment may end up as a sustainable green strategy [1]. The application of microbial communities that possess a diverse metabolic profile enhances these communities’ capacity to mitigate the impact of these pollutants for environment negativity while at the same time enhancing efforts aimed at environmental sustainability [48] and [5].

Table 1: Microbial remediation studies on the removal efficiency of pharmaceutical pollutants.

Study Reference	Year	Microorganism Used	Pharmaceutical Pollutant	Removal Efficiency (%)	Methodology
[49]	2018	Serratia marcescens	Ibuprofen	93.47%	cultivation with yeast powder at 30°C and pH 7
[50]	2016	S. maltophilia	Tetracycline	93%	pH 9 and 30 °C, HPLC
[46]	2020	Penicillium oxalicum	Diclofenac	100%	28 °C, 120 rpm, HPLC, UPLC
[51]	2020	Trichoderma spp.	Ciproflaxacin	81%	25 °C, 135 rpm, LCMS
[52]	2023	Bacillus subtilis, Pseudomonas putida, Escherichia coli	Amoxicillin	97.9%	pH of 7, temperature of 29 °C, 0.8 V, and an inoculum dose of 1% w/v
[53]	2019	Bacillus clausii	Cefuroxime	100%	37 °C, 220 rpm, Uv-spec, RT-PCR
[54]	2021	Brevibacterium	Paracetamol	97%	cultured in liquid mineral salt medium (MSM)
[55]	2021	Penicillium oxalicum	Erythromycin	84%	35 °C, pH 6.0, 96 h, HPLC-MS
[56]	2023	Aminobacter sp	Metformin	79%	16s sRNA

4.3. Genetic and metabolic pathways

The pharmaceutical pollution degradation occurs in a system of genetically controlled and metabolically downgraded pathways [57]. These lines of microorganisms perform the conversion of complex molecules into their less harmful test samples [58]. Various microorganisms such as fungi and bacteria play a significant role in this process, each employing specific enzymes to facilitate degradation reactions [8]. For instance, some infections by ascomycetes fungi have been shown to degrade diclofenac congeners by producing hydroxylated metabolites, which occur as a result of the detoxification process [14].

Bacteria can also significantly aid in the removal of medico-chemical pollutants. Among many, Pseudomonas strains have been observed to decompose ibuprofen and paracetamol, while Cupriavidus species are known for breaking down aromatic compounds [59]. The structure and function of microorganism groups in the community are altered with the increasing load of pharmaceuticals, which impacts the community microorganisms change [60].

Enhanced metabolic evolution and recent developments in increasing the degradation of these contaminants provide new opportunities in pharmaceutical biodegradation [61]. By engineering synthetic metabolic pathways and designing enzymes for specialist degradation functions, researchers aim to create microbes that can overcome existing deficiencies, leading to better waste management [38]. Researches in genetics have also located genes associated with metabolism of pharmaceuticals where genetic engineering can modify such genes to enhance the biodegradation results [62], [23].

Furthermore, pharmaceuticals are not only pollutants of the aquatic systems, but of the gaseous and intersitial ones as well. Ambient pharmaceuticals can come about by the evaporation of polluted water bodies, unadmirable disposal of chemical substances, and industrial emissions. Some of these pollutants can change in the atmosphere and create other pollutants referred to as secondary pollutants that are damaging to human health and the environment. For example, the issues with interstitial pollution, understood as contamination of the pore-water in soil and sediments as well, arise from landfill leaching, agriculture effluence, and wastewater irrigation. This can disturb the balance of microbial in these ecosystems, thus reducing the rate at which pollutants break down [6].

In other words, application of effective environment cleanup techniques requires more information on genetic and metabolic processes. Therefore, through manipulating microbes and applying genetic engineering procedures, it is possible to improve efficiency and independency of the biodegradation processes concerning pharmaceutical pollutants [5], [63]

5. Conclusion

Biodegradation of drug contaminants will be able to be the solution that supports environmental sustainability with utilizing enzymes and other microbial processes and knowing how the disruption of molecular and metabolic pathways can safely degrade the pollution. The existence of scope of co-pollutants and the availability of pollutants in the environment also play an important role in biodegradation processes.

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التحلل البيولوجي للملوثات الصيدلانية: التحديات والآليات والبيئة

وفاء عبدالرحمن العبيدي[1]، ايات عبدالجليل التكريتي[2,*]، نورالهدى الجوهر[3]

[1]قسم علوم الحياة ،كلية العلوم ، جامعة بغداد ، بغداد ، العراق.

[2]فرع الادوية والسموم ، كلية الصيدلة ، الجامعة المستنصرية، بغداد ، العراق.

[3]فرع الاحياء المجهرية ، كلية الطب البيطري ، جامعة ديالى، ديالى ، العراق.

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الكلمات المفتاحية

الملوثات الصيدلانية 1، التحلل البيولوجي2، التأثير البيئي3، المعالجة الحيوية4، الآثار البيئية5.

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الملخص

أصبح ظهور المستحضرات الصيدلانية المنتشرة على نطاق واسع كملوث إحدى المشاكل البيئية الحرجة في العالم والتي قد تؤدي إلى تدهور الصحة العامة والتنوع البيولوجي. تقدم هذه المقالة سردًا شاملاً للفهم الحالي للاستمرار البيئي للملوثات الصيدلانية بعد تحليل متعمق للآثار المضافة لمسارات التحلل البيولوجي الطبيعي الحالية على تأثير صحة الإنسان على هذه الأدوية. بالاضافة الى إيلاء اهتمام خاص لعوامل التحلل الحيوي مثل البكتيريا والفطريات والطحالب وتقدير قدرتها على تحويل مكونات الدواء إلى مركب أقل سمية في النهاية. على الرغم من أن هذه النظم البيولوجية تحتوي على إمكانات هائلة لقتل الملوثات غير المرغوب فيها، فإن التباين في تعقيد وتحمل المواد الصيدلانية يثقل كاهل قدرات التحلل لهذه الكائنات الحية مما يستلزم تحسين طرق التحلل البيولوجي. وتؤدي معالجة العوامل البيئية المذكورة أعلاه، والتي تشمل درجة الحرارة ودرجة الحموضة وحدوث ملوثات أخرى، دوراً حاسماً ولها تأثير مباشر على عملية التحلل البيولوجي، مما يعزز معدل إزالة الملوثات. تبحث هذه المقالة في تأثيرات العوامل ذات الصلة التي تنطوي عليها عملية تحلل المواد الصيدلانية، وتوفر حلولاً للظروف التي تسرع من معدل التحلل.

باختصار، تمكن هذه المقالة التخصصات المشتركة في العلوم البيئية وعلم الأحياء المجهرية والهندسة البيولوجية من إيجاد تقنيات أكثر فعالية واستدامة بصورة تدريجية لتحييد هذه السموم الطويلة الأمد ؛ وبالتالي حماية النظم الإيكولوجية وصحة الإنسان.

*Corresponding author email : ayat.abd@uomustansiriyah.edu.iq

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